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Reports of the workshops:

Theranostics for personalized medicine – Bologna 2014
Theranostics for P4 Medicine – Florence 2016

WG HEALTH

Science and Technology Foresight: from society to research
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from society to research

Report

"Theranostics for Personalised Medicine"

19-20 May, 2014 - Bologna

WG HEALTH

National Research Council of Italy

Science, Technology and Business Foresight Project

Report on the Exploratory Workshop

"Theranostics for Personalised Medicine"

National Research Council of Italy (CNR) – Bologna Research Area

Via Piero Gobetti 101, 40129 Bologna, Italy

19th - 20th May 2014

Science, Technology and Business Foresight Project
National Research Council of Italy
P.le Aldo Moro, 7
00100 ROMA (Italy)
http://www.foresight.cnr.it

Edited by *Francesco BALDINI, Caterina CINTI, Alek DEDIU, Sabato D'AURIA, Gabriella LEO, Luisa TONDELLI and Maria Giovanna TRIVELLA (Health Foresigth Group - National Research Council of Italy – CNR - August 2014)*

***Contact**: Caterina Cinti (ccinti@ifc.cnr.it) and Luisa Tondelli (luisa.tondelli@isof.cnr.it)*

1. Introduction

The workshop was held in Bologna on Monday, May 19th and Tuesday, May 20th 2014. It gathered 7 distinguished scientists from European and US academies and clinics plus 7 high level experts from the National Research Council of Italy and Area Science Park.
Starting from the analysis of the state-of-the-art, the exploratory workshop "Theranostics for personalized medicine" proceeded with the identification of medium-long term potential applications and socio-economic impacts of priority topic areas, pointing out obstacles, gaps in knowledge, education and technology transfer, market needs and potential, societal challenges and social acceptability: the final aim was to select the specific topics with the highest priority for the future study and analysis and for potential inclusion in future Face to Face (F2F) workshops.

2. Methodology

The workshop gathered experts from a variety of fields, including nanotechnology, biochemistry and biophysics, computational sciences, molecular biology, pharmaceutics, regenerative medicine and medical sciences, including surgery. With the participation of experts in theranostic sciences from basic research to clinical applications, the workshop was also expected to provide a learning opportunity and a fruitful exchange of ideas among a highly-qualified interdisciplinary group of people. The agenda and attendance list are attached (Annexes I and III).
In the preparatory phase, written contributions were requested from experts in the form of a contribution sheet (Annex II), with both the analysis of the state-of-the-art (SWOT analysis) and suggestions for short and long-term solutions to main challenges (deadline: 23rd April 2014).
On May 8th the final agenda was shared with all experts, together with the request of preparing a 10 minute presentation (max 3 slides, deadline May 15th), i.e.:
Slide 1- analysis of the state-of-the-art (SWOT analysis)
Slide 2- the most significant developments (short term vision: 5-10 years)
Slide 3- the expected socio-economic impacts (long term vision > 10 years).
The experts were also invited to send any additional and relevant material considered useful for the workshop and its follow-up.
The workshop started on May 19th at 10.30 am: after the introductory talk by Ezio Andreta, coordinator of the ST&B Foresight Group, the main trends of each technical area were presented by all experts. A first discussion session followed, moderated by Stephen Taylor, focused on a long-term vision (> 20 years), in order to firstly identify a tentative roadmap towards theranostics for personalised medicine. Preliminary comments, suggestions and contributions were collected among all the workshop participants.
The following morning, all participants joined a fruitful brainstorming activity with open discussion and debates, once again moderated by Stephen Taylor: the general aim was to identify the most important bottlenecks and solutions that could favour theranostics market applications and widespread adoption in the short (5-10 years) and longer term (> 10 years).

The workshop ended on May 20th at 1pm with the final remarks of the organizers, who highlighted the importance of this exercise and the value of the outcome of the workshop, fundamental for the future planning of the face-to-face workshop.
This report presents the exchange of ideas among the participants and the suggestions agreed by the audience. Participants agreed to appoint the organisers as the official *rapporteur* of the workshop: the draft report of the workshop was circulated among all participants and the final report will be signed by all experts. To make it available to all interested parties, its publication on the Foresight Group webpage was agreed.

3. Discussion

The entire workshop was moderated by Stephen Taylor, who stimulated the discussion asking participants to:

- Keep a long term vision, i.e. > 20 years from now;
- Try to identify a roadmap towards theranostics;
- Identify the main obstacles and the milestones to be considered.

All participants actively contributed in an open and wide-ranging discussion tackling research and development in theranostics from their different points of view.

The following priorities were identified:

PRIORITY	**0-5 YEARS**	**5-10 YEARS**
VERY HIGH	1) OMICS profiles for physiopathology of cancer and neurodegenerative diseases.	1) PERSONALISED NANOTOOLS (New Tools Predicting Individual Responses to Drug/Treatments before Treating Patients by PoC and Omics).
HIGH	1) PUBLIC / PATIENT INVESTMENT (group sensitive science). 2) **N**ext-**G**eneration **S**equencing (NGS), **N**ext **G**eneration **I**nterference (e-health, computerization / standardization), trans-omics imaging & quantitative multi-scale power. 3) DEVELOPMENT OF *IN-VITRO/IN-VIVO* MODELS (clinical reflective models).	1) WIRELESS COMMUNICATION with theranostic nanostructures.
MEDIUM	1) TRAINING OF MEDICAL DOCTORS. 2) INFORM POPULATION on nanomedicine.	1) Expansion of SMART PHONES-BASED PoC testing (Glucose, blood pressure etc).
MEDIUM - LOW	1) Development of TOOL BOX OF NANOELEMENTS 2) BIOMARKERS of organ rejection, blood circulating cancer markers.	1) CONVINCE SOCIETY to change technologies (e.g. test glucose, blood/body physiopathological variables). 2) A flexible, industrially feasible platform/technology enabling MINIMALLY INVASIVE THERANOSTICS (e.g. nanosized materials). 3) Mini-RNA for theranostics (e.g. diabetes). 4) MONITORING DRUG AND MULTIPLE DRUGS IN SINGLE TESTS to avoid toxicity and optimize efficacy.
LOW		1) New 1 billion dollar GENOME PROJECT to correlate genome with pathology prediction and related diseases.

PRIORITY	10 – 20 YEARS	> 20 YEARS
VERY HIGH	1) IN VITRO NANOTECHNOLOGY BASED-THERAPY: 3D cellular architectures as precursors for personalised organ repair (e.g. 3D imaging for cardiac electrical distribution).	1) PREVENTION (i.e. smart vaccines, smart biosensors for pathological markers). 2) EMBRACING 4P MEDICINE: Predictive, Preventive, Personalised, Participatory.
HIGH	1) PREDICTIVE BLOOD TEST for Alzheimer. 2) TRANSPLANTATION immunosuppressant dosage. 3) PERSONALISED CANCER VACCINES (personalised microbiomas). 4) INTEGRATION OF THINGS FOR HEALTH (personalised medicine integrating environment, social, medical information and remote treatment).	1) TISSUE SPECIFIC SYNTHETIC EXTRA-CELLULAR matrix and growth factors analogues. 2) SMART PATIENTS (the more affluent + educated) throughout more transparency of data and knowledge on the interdependencies of life style impact and health. (more responsibility). 3) PERSONALISED SMART SYSTEMS, able to internally regulate health conditions.
MEDIUM	1) SMART T-SHIRTs TO DETECT MARKERS (i.e. cardiac stress) for early-detection prevention. 2) NEW CARE PATHWAY (need to create new skills and jobs with high specialisation in healthcare – monitor/interpret data etc).	1) THERANOSTICS FOR SEPSIS PoC + devices. 2) TRANSLATIONAL RESEARCH physiology and pathophysiology, education for MULTI-DISCIPLINARY / INTERDISCIPLINARY TEAMS.
MEDIUM - LOW	1) 30% LESS HOSPITALISATION due to PoC technology. 2) MEDICAL CALL CENTRES to replace many hospital doctors via GPS (de-skilling by technology). 3) PERSONALISED THERAPY for cardiac diseases (non invasive cardiac cell therapy in cat-lab).	1) PERSONALISED THERAPY FOR HEART FUNCTIONS (ultra-mini, versatile, non-invasive, LVAD) as a bridge to recovery or DT/CT. 2) MULTIPLE DETECTION of state of health in real-time of individuals and data transmitted to doctors (health chambers/multi device, sweat/breath, whole person fingerprints/eye analysis, microcirculation etc) to detect homeostasis, person health and wireless database auto - filling (multiple detection).
LOW		1) Extension of test menu for NON INVASIVE TESTING (internalization of hospital in the body). 2) Effect on health of USE OF NANOPARTICLES in cosmetics (like asbestosis).

All participants were then asked to highlight the expected BENEFITS, the missing FUNCTIONS and the necessary ENABLING TECHNOLOGIES for the exploitation of successful theranostics approaches in the medium-long term [The **X** indicate votes cast by the participants to show the most important topics].

Product	< 5 YEARS	5-20 Years	> 20 YEARS
BENEFIT	1. **X** PUBLIC / PATIENT INVESTMENT (group sensitive science). 2. **X** INFORM POPULATION on nanomedicine.	1. **XXXXXXX** PERSONALISED NANOTOOLS (new tools predicting individual responses to drug/treatments before treating patients by PoC and omics). 2. **XX** IN VITRO NANOTECHNOLOGY BASED-THERAPY: 3d cellular architectures as precursors for personalised organ repair (e.g. 3d imaging for cardiac electrical distribution). **3.** **X** TRAINING of medical doctors. 4. **X** NEW CARE PATHWAY (need to create NEW SKILLS AND JOBS with high specialization in healthcare – monitor/interpret data etc). 5. INTEGRATION of things for health (personalised, integrating environment social medical etc information, remote treatment). 6. 30% LESS HOSPITALISATION due to PoC technology.	1. **XXXX** PREVENTION (i.e. smart vaccines) 2. **XX** EMBRACING 4P MEDICINE: Predictive, Preventive, Personalised, Participatory. 3. **XX** TRANSLATIONAL RESEARCH physiology and pathophysiology, EDUCATION FOR MULTIDISCIPLINARY /INTERDISCIPLINARY TEAMS. 4. **X** EXTENSION OF TEST MENU FOR NON INVASIVE TESTING (internalisation of hospital in the body). 5. **X** SMART PATIENTS (the more affluent + educated) throughout more transparency of data and knowledge on the interdependencies of life style impact and health. more responsibility. 6. INTERNALISATION OF HOSPITAL in human body (>30 years). 7. SMART VACCINES prevention. 8. NEURODEGENERATIVE DISEASE prevention. 9. PERSONALISED SMART SYSTEMS, able to internally regulate health conditions.
FUNCTION			1. **XXXX** THERANOSTICS FOR SEPSIS PoC + devices. 2. PERSONALISED THERAPY for heart functions (ultra-mini, versatile, non-invasive, LVAD) as bridge to recovery or DT/CT. 3. MULTIPLE DETECTION of state of health in real-time of individuals and data transmitted to doctors (health chambers/multi device, sweat/breath, whole person fingerprints/eye analysis, microcirculation etc) to detect homeostasis, person health and wireless database auto-filling (multiple detection).

ENABLING TECHNOLOGIES	1. **XX** OMICs PROFILE of physiopathology cancer and neurodegenerative diseases: A) **X** next-generation Sequencing (NGS) TRANS-OMICS imaging + quantitative multiscale power. B) **X** next-generation Interference (e-health, computerization /standardization of protocols for data and validation). 2. **X** CLINICALLY REFLECTIVE IN VITRO /IN VIVO MODELS for nanotoxicology. 3. DEVELOPMENT OF NANO-ELEMENTS tool box. 4. BIOMARKERS OF ORGAN REJECTION.	1. **XXXXX** EXPANSION OF SMART PHONES-BASED PoC TESTING (glucose etc). 2. **XX** SMART T-SHIRT TO DETECT MARKERS (i.e. cardiac stress condition and heart reaction) EARLY DETECTION PREVENTION. 3. **X** FLEXIBLE, INDUSTRIALLY, FEASIBLE PLATFORM/ TECHNOLOGY enabling MINIMALLY INVASIVE THERANOSTICS (e.g. nanosized materials). 4. **X** CONVINCE SOCIETY TO CHANGE TECHNOLOGIES (e.g. glucose). 5. BLOOD TESTS for Alzheimer. 6. TRANSPLANTATION IMMUNOSUPPRESSANT DOSAGE. 7. SMART DECISION SUPPORT SYSTEMS for therapy. 8. WIRELESS COMMUNICATION with theranostic nanostructure. 9. Mini-RNA FOR THERANOSTICS (e.g. diabetes). 10. MONITORING DRUG AND MULTIPLE DRUGS IN SINGLE TESTS TO AVOID TOXICIY AND OPTIMIZE EFFICACY. 11. PERSONALISED THERAPY FOR CARDIAC DISEASE (non invasive cardiac cell therapy in cat-lab).	1. **X** TISSUE SPECIFIC SYNTHETIC extra-cellular matrix and growth factors analogues. 2. BIORECOGNITION PROGRAM for enabling technologies (contrast agents ecc). 3. Effect on health of use of NANOPARTICLES IN COSMETICS (like asbestosis).

PoC	Point-of Care
LVAD	Left Ventricular Assistance Device
DT	Development Tension (ventricular pressure)
CT	Computed Tomography scan

4. Targets, needs and bottlenecks

The following *target pathologies* were considered to be the main challenge for the future, with the greatest societal impact:

- Neurodegenerative Diseases
- Cancer
- Cardiovascular Diseases
- Diabetes
- Infectious diseases

The following *unmet needs* were identified:

- Development of a TOOLBOX OF NANOELEMENTS that can be combined to assemble personalized nanotools to treat specific diseases
- TRANSLATIONAL MEDICINE: there is a lot of knowledge that has to be transferred
- PREVENTIVE MEDICINE on the population at large by means of "vaccine-like" nano-elements that can treat specific diseases before symptoms appear: cancer, infectious diseases, neurodegenerative disorders, heart disease …
- Target the definition of proteomic-genomic-level details for pathological/physiological conditions to guide toolbox development (acquisition and handling of data, availability of the large data sets that will derive from these studies)
- TRAIN BIOLOGISTS/MDs towards these new opportunities
- Inform the population at large of the principles of this new technology (learn from reaction/aversion to GMOs)

The following *main technological bottlenecks* were identified:

- TISSUE REGENERATION
- TOXICOLOGY as an obstacle to the spreading of nanotechnologies
- COMPUTING TECHNIQUES: more transparency of data, more specialization, gathering and interpretation of data
- SYNERGISTIC TECHNIQUES: More collaboration needed between the stakeholders. Actually, everything developed in a lab, no contact with medical environment, poor interdisciplinary knowledge and lack of a global vision of both medical and social needs

The following *main non-technological bottlenecks* were identified:

- DEMAND FACTORS : Medical and Biological priorities to be defined in terms of social health.
- REGULATORY FACTORS: Surveillance, Standardize protocols, nanotechnologies regulation
- RESOURCES: Few financial investments.
    1. In Europe we do not have specialized venture capital.

2. In EU Capitalists see more risks than VC in USA. To build up now we need a change in this perspective.
3. Funding is a challenge in neurodegenerative disease
4. Cost for personalized medicine

❖ CONSTRAINTS (i.e. public acceptance):

1. Need for acceptance of nanotechnologies by the public, education of general public and medical doctor community
2. Convince society to invest in new research outcomes
3. Embracing preventive medicine, insurance company are interested, need for changing attitude (insurance push on patient to take more care of their health)
4. Ethical issues and data protections

5. Conclusions

The participants foresee that, in the long-term period (> 20 years), the big challenge will be a preventive personalized medicine able to prevent and fight diseases with high social impact such as cancer, neurodegenerative, cardiovascular and infectious diseases (i.e smart vaccines, theranostic tools).

The following features have been identified during the workshops and agreed by all participants:

ROADMAP:

- Through a multidisciplinary approach, a "CREATIVE ASSEMBLING" of available tools and technologies should be performed to develop personalized smart systems able to internally regulate health conditions.
- Solve the mismatches between the potential of technologies and needs.
- Stakeholder cooperation and innovation governance
- Embracing 4P MEDICINE: Predictive, Preventive, Personalised, Participatory

OBSTACLES

- New highly specialized stakeholders in healthcare
- Education for multidisciplinary/interdisciplinary teams
- Regulatory Factors

MILESTONES

- Theranostics tool as nanosensors/nanodetectors of disease.
- Expansion of smart phones-based PoC testing
- Wireless communication with theranostic nanostructures
- Clinically reflective in vitro /in vivo models for nanotoxicology
- OMICS profiles of physiopathology of diseases
- Computing techniques as next generation interference for e-health

DEMAND FACTORS

- Enhance health outcome, improve quality of care and experience of patients, and contribute to more efficient use of resources in these services
- Improvements of quality and outcomes of health and social care
- Avoid any social inequality and exclusion

CONSTRAINTS

- Inform population and patients on new nanomedicine (public acceptance)
- Smart patients (the more affluent + educated) throughout more transparency of data and knowledge on the interdependencies of life style impact and health (more responsibility)
- Training new class of medical doctor (work in multidisciplinary team)

6. Final agreement on the outcome of the exploratory workshop

The discussion during the workshop was rich and open: all participants expressed their appreciation for the fruitful exercise. The debate among partners resulted in agreed suggestions to the organizers that can help them in the organization of the following face-to-face workshop. The participants agreed to contribute to this final report and to make it publicly available in the S&T Foresight webpage (http://www.foresight.cnr.it).

ANNEX I – Agenda of the Workshop

Exploratory Workshop: "Theranostics for Personalised Medicine"

Bologna, May 19th – 20th 2014 - National Research Council of Italy - Via Piero Gobetti, 101 – 40129 Bologna, Italia

Monday, May 19th 2014

10:30	***Get together***	
11:00	***Opening address***	**Ezio Andreta** *(Coordinator ST&B Foresight Project, CNR, Italy)*
11:15	***Introduction***	**Caterina Cinti** *(Topic Coordinator ST&B Foresight Project, CNR, Italy) and* **Stephen Taylor** *(Director of Technology Transfer, AREA Science Park, Trieste, Italy)*
11:45	***Nanotechnology***	**Fabio Beltram** *(Scuola Normale Superiore, Pisa, Italy)*
12:00	***Nanomagnetics***	**Mike Coey** *(Trinity College, Dublin, Ireland)*
12:15	***Point-of-care***	**Larry Kricka** *(University of Pennsylvania, USA)*
12:30	***Q&A***	**Discussion session**
13:00		***Lunch break***
14:00	***Tissue regeneration***	**Matteo Santin** *(University of Brighton, Brighton, UK)*
14:15	***Artificial organs & surgery***	**Antonio Amodeo** *(Ospedale Pediatrico Bambin Gesù, Roma, Italy)*
14:30	***Q&A***	**Discussion session**
15:00	***System biology & medicine***	**Enrico Capobianco** *(Centre of Computational Science, Miami, USA)*
15:15	***EU health foresight***	**Susanne Giesecke** *(Austrian Institute of Technology, Wien, AT)*
15:30	***Q&A***	**Discussion session**
16:00		***Coffee break***
16:30	**Discussion**	
17:30	***Conclusion***	
19:00		***Working dinner***

Tuesday, May 20th 2014

8:30	***Get together***
9:00	***Brief summary of priorities emerged from each topic*** *(Moderator: Stephen Taylor)*
9:30	Brainstorming session
11:00	***Coffee break***
11:30	Summary and wrap-up
12:30 – 13:00	Conclusion

ANNEX II – Contribution sheet

TO STRUCTURE OUR DISCUSSION …

Please complete the first section indicating the most important solutions that you think will make it into the market and widespread adoption in the short (5-10 years) and longer term (> 10 years). In the second section the Strengths, Weaknesses, Opportunities and Threats should refer to the current state of the art with reference to our capacity to develop these future solutions.

1. SUGGESTED SOLUTIONS	
SHORT TERM VISION (5-10 years) *a)Which are necessary steps in the evolution of the longer term solutions?* …… *b) Which can be more easily developed and commercialized as stand-alone solutions but will have a shorter life and ultimately be substituted by the longer term solutions?* ……	**LONG TERM VISION (> 10 years)** …… ……

2. STATE OF THE ART	
STRENGHTS …… ……	WEAKNESSES …… ……
OPPORTUNITIES …… ……	THREATS …… ……

NAME ……
AREA OF EXPERTISE ……
RESEARCH FIELD ……

ANNEX III - List of participants to the Workshop:

Theranostics for personalised medicine – Bologna, 19-20 May 2014

Surname	First name	E-Mail
AMODEO	**Antonio**	antonioamodeo@yahoo.it
ANDRETA	**Ezio**	ezioandreta@gmail.com
BALDINI	**Francesco**	f.baldini@ifac.cnr.it
BELTRAM	**Fabio**	beltram@sns.it
CAPOBIANCO	**Enrico**	ECapobianco@med.miami.edu
CINTI	**Caterina**	ccinti@ifc.cnr.it
COEY	**Mark**	jcoey@tcd.ie
D'AURIA	**Sabato**	s.dauria@ibp.cnr.it
DEDIU	**Alek**	V.Dediu@bo.ismn.cnr.it
EINAUDI	**Giorgio**	einaudi5250@gmail.com
GIESECKE	**Susane**	Susanne.Giesecke@ait.ac.at
LEO	**Gabriella**	gabriella.leo@ismn.cnr.it
KRYCKA	**Larry**	kricka@mail.med.upenn.edu
SANTIN	**Matteo**	M.Santin@brighton.ac.uk
TAYLOR	**Stephen**	stephen.taylor@area.trieste.it
TONDELLI	**Luisa**	luisa.tondelli@cnr.it
TRIVELLA	**Maria Giovanna**	trivella@ifc.cnr.it
VOLPI	**Angelo**	angelo.volpi@ieni.cnr.it

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21-23 March, 2016 - Florence

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National Research Council of Italy

Science and Technology Foresight Project

National Research Council of Italy (CNR)

www.foresight.cnr.it

Working Group HEALTH
Coordinator: Caterina CINTI

Scientific Committee
Francesco BALDINI
Daniela BANTI
Alek DEDIU
Giorgio EINAUDI
Gabriella LEO
Luisa TONDELLI
Maria Giovanna TRIVELLA

Organising committee:

Caterina CINTI *caterina.cinti@cnr.it*
Ilaria SANTONI *ilaria.santoni@ic.cnr.it*
Luisa TONDELLI *luisa.tondelli@cnr.it*

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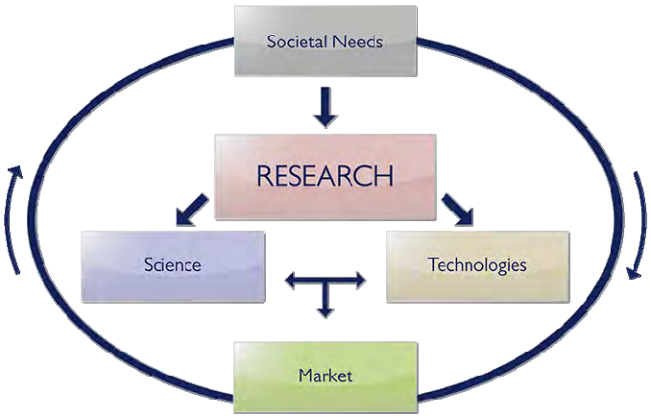
SUMMARY

1. THE BACKGROUND

1.1 THE S&T FORESIGHT PROJECT AT CNR

The Science and Technology Foresight Project (www.foresight.cnr.it) is a multidisciplinary project, which involves all CNR thematic departments. Its main aim is to define a medium to long-term vision (5-30 years) in order to elaborate coherent research strategies and to address serious socially relevant problems. While driven by societal needs and interested in identifying innovative technologies, the Project puts the scientific research at the core of its scope and looks forward to future visionary solutions able to reach the market with long-term disruptive impacts on the society.



With reference to the big challenge of innovative health systems, the main aim of Working Group Health (WG HEALTH) is to identify the priorities and technological strategies to face the challenges of future medicine and to define a roadmap to achieve this goal, with the support of a scientific committee and international experts (http://www.foresight.cnr.it/working-groups/wg-health).

Project Coordinator: Ezio ANDRETA
Scientific Director: Giorgio EINAUDI

Members of Executive Board:
Antonino ARICÒ
Cecilia BARTOLUCCI
Ruggero CASACCHIA
Caterina CINTI
Sabato D'AURIA
Gabriella LEO
Pier Francesco MORETTI
Augusta Maria PACI
Antonello PROVENZALE
Elisabetta PUNTA
Luisa TONDELLI

1.2 THE EXPLORATORY WORKSHOP " Theranostics for personalized medicine"

(Bologna, Italy, May 2014)

In May 2014 an Exploratory Workshop was held in Bologna (Italy), focused on "Theranostics for personalised medicine" and gathering 7 distinguished scientists from European and US academies and clinics, in addition to 7 high level experts from the National Research Council of Italy and Area Science Park.

Starting from the analysis of the state-of-the-art, the exploratory workshop "Theranostics for personalized medicine" proceeded with the identification of medium-long term potential technological applications and socio-economic impacts of priority topic areas, pointing out obstacles, gaps in knowledge, education and technology transfer, market needs and potential, societal challenges social acceptability.

The final aim was to select the specific topics with the highest priority for the future study and analysis as well as potential inclusion in future Face to Face (F2F) workshops.

The following priorities were identified:

- In the short-medium term period (5-10 years), the participants have identified PERSONALIZED NANO-TOOLS as the main challenge in order to predict the individual response to therapeutic compounds before starting the therapy, to early detect markers of disease, to monitor the illness and to personalize the therapy. Point of Care testing (of blood and other biological fluids), smart wearable sensors and omics profiling have been identified as technological solutions for a PREDICTIVE AND PERSONALIZED MEDICINE.
- In the long-term period (> 20 years), the participants believe that the big challenge is PREVENTIVE MEDICINE. The main group of diseases with high social impact for which unmet needs were identified are cancer, neurodegenerative, cardiovascular, metabolic and infectious diseases. Theranostic applications could allow a preventive medicine in these diseases even if they are at present still far from real application. However, THERANOSTIC NANOSTRUCTURES with the features of multiple detectors (sensors of illness, communicators of information on state of health in real-time and actuators of "therapy" internally regulating health conditions) could represent the matching of emerging technologies able to deliver new and radically innovative medical solutions (such as smart vaccines or smart biosensors) for a preventive medicine (Figure 1).

The following ROAD MAP FOR A MEDICINE OF THE FUTURE, providing higher quality of life and more efficient use of healthcare resources, has been identified and included:

- "creative assembling" of available tools and technologies to develop "personalized smart systems" providing (currently lacking) diagnostic and therapeutic options and whole person fingerprint, through a multidisciplinary approach;
- matching the potential of technologies with social needs, also in terms of communication and creation of new highly specialized stakeholders in healthcare;
- education of the medical doctors of the future able to work in multidisciplinary/interdisciplinary teams;
- embracing the concept of P4 Medicine (Predictive, Preventive, Personalized and Participatory Medicine).

Figure 1. A view of P4 medicine in relation to strategic technological solution.

2. THE FACE-TO-FACE WORKSHOP on "Theranostics for P4-medicine" (Florence – Italy, 21-23 March 2016)

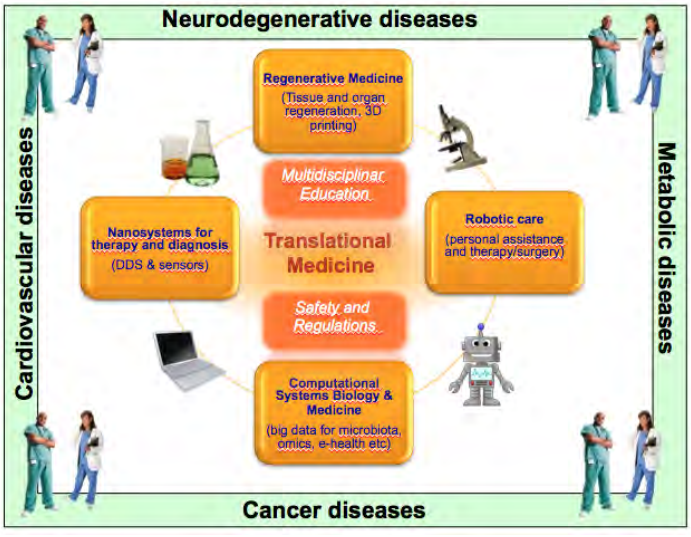
2.1 THE AIM

The transition from today population-based "reactive" medicine to the individual patient-centred data-driven medicine of tomorrow is the big challenge that the health system will face in the next years worldwide. Therefore, in addition to the clinical-pathological parameters, many other factors such as inherited genetics, ethnicity, age and gender, lifestyle including nutrition and, more generally, the socio-economic environment will have to be taken into consideration.

Within this frame, the main aim of this F2F meeting was to collect opinions from international experts in order **to identify long term future needs and bottlenecks in the exploitation of Theranostics for a Predictive, Preventive, Personalized and Participatory Medicine** (**P4-Medicine)**.

Due to the constructive and not just informative nature of the workshop, the workshop was an invitation-only meeting with approximately 50 participants attending the full 3-days-programme. Clinicians with outstanding competences on pathologies with high social impact (neurodegenerative, cardiovascular, metabolic and cancer diseases) were asked to present the main challenges in the medium-long term and to share their vision with all participants. Several experts of different technological areas (such as nanotechnologies, material science, tissue regeneration, robotics, bioinformatics etc.) as well as representatives from industries, public administrations and civil society together with relevant policymakers were also invited.

The highly interdisciplinary character of the meeting encouraged everybody to play an active role *with a visionary and open-minded approach*, taking advantage of the ample time allowed for questions and answers, as well as of plenary and small group discussion. Each expert's contribution was crucial for the elaboration of scenarios addressing urgent societal challenges and the validation of a final strategic document finalised **to design the roadmap for an innovative medicine** based on the individual needs of each patient.



Expected Outputs

✓ To identify medical needs, bottlenecks, knowledge gaps and new/emerging strategic technological solutions that should be adopted to overcome the obstacles, able to lead to a P4 Medicine.

✓ To elaborate scenarios addressing the urgent societal challenges of wellness and healthcare.

✓ To validate a final strategic document encompassing the conclusion of two full days of discussions, perspectives and recommendations.

Final Objective

To design a time-dimensioned Science & Technology roadmap for an innovative medicine based on the individual needs.

2.2 THE PROGRAMME

Face-to-Face Workshop "***Theranostics for P4 Medicine"***

March 21-23, 2016, Hotel 500, Florence, Italy

MONDAY, March 21st 2016

14:00 – 14:30	Get together and opening	Luigi AMBROSIO
14:30 – 15:30	***S&T Foresight: from society to research*** *(Key Lecture)*	Luigi NICOLAIS
15:30 – 16:00	Objectives of F2F Workshop	Stephen TAYLOR
16:00	*Coffee Break*	
16:30 – 18:00	Focus on Cardiovascular diseases	Moderator: *Maria Giovanna TRIVELLA*
19:30	*Dinner*	

TUESDAY, March 22nd 2016

08:30 – 10:00	Focus on Metabolic diseases	Moderator*: Cecilia BARTOLUCCI*
10:00	*Coffee Break*	
10:30 – 12:00	Focus on Cancer diseases	Moderator: *Paolo PAOLETTI*
12:30	*Lunch Break*	
14:30 – 16:00	Focus on Neurological and Neurodegenerative diseases	Moderator: *Luca PANI*
16:00	*Coffee break*	
16:30 – 18:30	Interdisciplinary Brainstorming	Moderator: *Stephen TAYLOR*
19:30	*Gala Dinner*	

WEDNESDAY, March 23rd 2016

08:30 - 11.00	Discussion session & Preliminary Reports *Parallel sessions with all participants, followed by plenary session*	
11:00	*Coffee Break*	
11:30 - 12.30	Conclusion	Moderator: *Stephen TAYLOR*
13:00	End of meeting	

This is an invitation-only working meeting whose participants are requested to attend all sessions.

2.3. THE INTER-DISCIPLINARY BRAINSTORMING: where are we now and how far is it realistic to go?

Following the introductory presentations, all the invited Medical Doctors (MDs) were asked to present their vision on pathologies with highest societal impact, such as cardiovascular, metabolic, cancer and neurodegenerative diseases, with the aim to identify the existing medical needs, bottlenecks and knowledge gaps. The specific content of these presentations is attached to the present report (see Annex 1). The major medical issues were then the starting point of a constructive discussion with all participants, with the aim to elaborate future scenarios and actions able to answer the urgent societal challenges of wellness and healthcare.
We here summarise the main discussion points, perspectives and recommendations as the result of all participants' contribution, according to the Chatham's rule. An effort was made to highlight the most intriguing elements, the most interesting specific needs that can be met, and the most promising emerging and/or future technological approaches useful for scientific research and innovation within the frame of a preventive, predictive, participatory and personalised medicine approach (P4-medicine).

This report presents the exchange of ideas among all participants and the consensus reached by the audience. Participants agreed to appoint the organisers as the official rapporteurs of the workshop: the draft report was circulated among all participants and the final report was approved by all experts. To make it available to all interested parties, its publication on the S&T Foresight Group webpage http://www.foresight.cnr.it/working-groups/wg-health was also agreed.

a. FROM REACTIVE TO PERSONALISED/PRECISION MEDICINE

The participants agreed that today medicine is largely reactive rather than proactive. The reactive medicine cures the symptoms and treats all diseases independently, with an extremely fragmented approach. The major issue is the lack of a global view of patient conditions as a whole and the insufficient knowledge of physiopathological mechanisms of diseases, including the similarities, the cross-talking and the overlapping features within different pathologies. Highly specialized MDs in different medical fields very rarely use a holistic approach for their patients and usually lack knowledge on the potential of emerging technologies. In a short-medium term, personalized therapeutic solutions for most diseases could be available. However, in order to lead to personalized treatments and to deliver specialized care, a better understanding of all pathologies and how the genetics, the environmental and behavioural factors play together, is required.
To go beyond the present, **a holistic approach of medicine is needed where human body is seen as a complex system and the disease is the result of phase transitions from a state of equilibrium (health) to disequilibrium (disease).** Indeed, P4 Medicine (predictive, preventive, personalized and participatory) could help changing the practices of healthcare approaching each individual with a holistic view.

A COMMON BASIC MECHANISM FOR ALL DISEASES

Even if all diseases are highly different from the clinical point of view, they could share the same ground from the mechanistic point of view. More and more frequently, it appears that complex diseases could share the same risk factors and, probably, common mechanisms. This means that apparently different diseases could be targeted as a whole and not one by one. In this case, it would be necessary to find the **common elements that can group different diseases rather than treating them separately**. This goal is highly far reaching because it also requires a full re-organisation of the related research approaches. Different research groups should work much more together and the pathophysiological mechanisms of diseases and their common basic ground need to be better understood.

THE GUT MICROBIOTA

Gut microbiota is a complex ecosystem, constantly working to maintain an equilibrium state, as guaranteed by the biodiversity and lifestyle of each individual: microbiota biodiversity changes can interfere with the trajectory of ageing altering the equilibrium state and accelerating those processes that eventually lead to age-related pathologies. In this view, it becomes mandatory to characterize those elements that lead to the lost of microbiota biodiversity. Microbiota can influence our metabolism, immunity, and even behaviour: therefore, the new field of microbioma research could lead to better understanding the role of microbiota on our health and well-being. In addition, it will be fundamental in the future to consider the incorrect or inappropriate nutrition as a risk factor that can dramatically influence microbiota biodiversity and contribute to disease development.

NUTRITION AND HEALTH

Nutrition is a key point worldwide: the impact of nutrition on health is not only a matter of education but also a matter of providing the right nutrition to people to prevent several diseases. Personalized nutrition need to be focused on individual prevention as a key for reducing the incidence of future diseases.
However, currently knowledge gaps exist on the real impact of nutrition on health. Investigating the impact of nutrition on selected healthy groups, for example children during the first 1000 days of life as well as population of centenaries, could help to **identify protective factors** preventing the occurrence of diseases. It is therefore emerging that prevention can be even approached as a matter of behavioural science that could be used to reduce risk factors and that will evolve into preventive strategies in the longer term.

AGEING: A COMMON RISK FACTOR

The altered physiological ageing has also been identified as one of the risk factors for all pathologies. Actually, ageing is a process that starts at the beginning of our life and the first part of life is extremely important for establishing the basic biochemical setting points of our body. Therefore, in order to prevent any disease, we should have a whole lifespan perspective. Seven highly intertwined pillars of ageing are metabolism, stem cells, regeneration, pathological homeostasis, adaptation to stress, macro-molecular damage and inflammation: they are all highly interrelated and are also the basic mechanisms that explain most of the pathogenesis of the diseases related to ageing. Thus, an integrated perspective targeting ageing could also favour the prevention of chronic diseases. Slowing down ageing could also postpone diseases that are not only dependent on genetic predisposition but also on lifestyle (such as nutrition influencing microbiota biodiversity and physical activity) and environmental factors.

b. TOWARDS PREDICTIVE AND PREVENTIVE MEDICINE

We need more knowledge about the diseases to correctly apply the technologies supporting the P4 medicine. A more interdisciplinary and multidisciplinary approach is required to better integrate and adapt all existing technologies to different fields and issues. However, in order to start P4 Medicine, we need to do additional research and have additional information in the areas of prevention and prediction.

INDIVIDUAL PREVENTION

To achieve the goal of preventive and predictive medicine, in the long-term period, we need to develop a model of personalized **risk stratification profile** to early detect predisposition to diseases, to timely adopt a target prevention of illnesses or, at least, to reduce the negative effects/impact of therapies.
Preventive medicine, tailored on single individuals, can modify the current (un)efficacy of early prediction of illness onset, but a better understanding of the disease mechanisms is needed in order to be able to select the proper markers within any available database and to get, at the end, the right **individual predictive models**. To this purpose, we need to define the individual *risk factors and protective factors*, but also to identify new *biomarkers of diseases and precursors of diseases* (possibly common to all diseases).

These individual models are also the basis for personalized medicine approaches that should include the monitoring and management of individual patients and not only their treatment.

OPEN DATA MANAGEMENT

The use of data is essential to give insights of where to go, even if there is currently a lack of knowledge of both the basis of all illness and factors, which are responsible for the transition from health to disease. It is emerging more and more that diseases are driven by biological changes and physiological symptoms but that also psychological, environmental and social factors can strongly influence the individual response to specific therapies or stimuli.
Therefore, the medicine of the future should not remain highly sector-based and fragmented, but should adopt an holistic approach and combine information from multiple sources of data on behaviour and lifestyle, as well as genomics and physiological data, to shift the focus from treating disease to managing health.
A large quantity of open data, generated by both individuals and private sectors (social network as Google, Twitter, Healthy App monitoring daily activities, eating habits and sleeping patterns, etc.) could be useful as background information on lifestyle and social behaviour of groups of people.
In addition, public sector's healthcare sources - such as medical records from both hospital and family doctors containing personal health history - and electronic patient portals - designed to manage individual healthcare and to address physical and mental health promotion - need to become more accessible to the scientific community. In this way, it could become easier to optimize preventive health and wellness and to develop some context around which more targeted studies can be performed.
Already existing data sources need to be made fully public and to operate according to global standards, while important issues about governance, data quality, standardization and trust need to be solved. The **Regulatory bodies** should therefore intervene in structuring the way to use these data and in regulating certain businesses that are taken forward by some companies. Data flows, cybersecurity and data exchanges should be regulated. **Ethical issues** in management of personal data without affecting patient confidentiality and in communicating diagnosis of diseases, for which we don't have any treatment, should be addressed.

BIG DATA

Computer science will drive the revolution in the management of big data as it will explore new spaces, produce simulations, make statistics and theories, and verify models. Big data will be the basis of future research as P4 Medicine will need tools able to store relevant data such as omics and clinical information and those related on lifestyle. Research on data collection, storage, harmonisation and security is needed, as well as strategies to manage these data. However data by themselves, if not correctly interpreted within a model or a theory, cannot be of much help to MDs or to make a solid predictive individual model. Therefore the priority is on scientific method and validation.

DIGITAL BIO-MARKERS

Each individual should be seen as a complex system with its own equilibrium that can move towards some "warning" critical points. The ability to early identify this warning is at the basis of prevention: bio-markers are examples of how it could be possible to reach this target, even if it remains to be defined which markers to consider and how they interact and relate to each other. A good prediction power can be obtained only with the identification of **bio-markers working as a network**, as part of a system, so that it is feasible to study the transition from equilibrium to dis-equilibrium and eventually the way back to equilibrium. Detecting the network of biomarkers, and their changing during lifetime, can allow the early identification that something wrong is happening in our body, give an indication on decisions to adopt but also monitor the success of an intervention.
This network of biomarkers will pave the way to the idea, in the future, of a "**personal digital biomarker**", based on the combination of genetic data, diagnostic digital information (i.e 3D image), vital /physiological parameters**,** personal data including familiar data and lifestyle, as well as behavioral and environmental aspects: all these data will be collected and aligned together to generate a specific "signature" for each individual. However, frequent low cost and non-invasive

tests will have to be performed to monitor changes/adaptation/modification of values just over the physiological range, in order to anticipate the transition between health and pathological conditions.

TOWARDS THERANOSTICS

Bio(digital)markers can be considered as one of the ways to move towards theranostics. Theranostic tools able to detect changes of multi-markers (physiological and pathological biomarkers) can help to early identify the transition towards a disequilibrium state. Material Science has a big potential in developing smart sensors/nanosensors able to detect any physiological change of specific markers predictor of disease. The concept of theranostics is trying to design systems that are able to recognise what the pathological sites are, as well as to deliver, for example, stem cells or appropriate proteins with appropriate morphologies able to reset the physiological conditions. This is in line with the concept of personalized medicine. New theranostic tools can also transport active components to the pathological sites, acting as sensors and actuators (therapeutics and diagnostics tools). Regenerative medicine, tissue engineering and materials science could provide high contribution in designing theranostic tools to prevent and predict pathological conditions with an inter/multi-disciplinary approach. An example is given by recently developed bio-materials able to produce what we call now "extra matrix analogues" in order to control self phenotype. This matrix can be implemented with the cells coming from the same patient, not only for therapeutic purposes but also for early diagnostic purposes. In order to adopt these strategic technological solutions, the regulatory framework has to be redefined.

c. TOWARDS A PARTICIPATORY MEDICINE

SHARING AWARENESS

The driving force of P4 Medicine is the partnership and the inter-disciplinary/multidisciplinary approach between scientists with different backgrounds and technological expertise and MDs, but also among MDs themselves with different specialisations, MDs and patients as well as the scientific community and people. Participatory medicine is the key point to create a system and acceptance of people that become part of the system. As one of the important aspects is the **psychological impact** of the disease on each individual, it is important **to increase the motivation** as a part of the participatory aspect of P4 medicine. This could be done by increasing trust between patients and MDs and by a larger involvement of informed subjects in the medical treatments. Participatory medicine needs to be viewed as an instrument to improve the patient's recovery route so that not only the patient, but also the family and other people involved, can be acknowledged about the medical status, be aware of the medical and non-medical needs and be **actively involved** in the entire recovery process. Of course, also MDs should be trained to dedicate time to the patient and to convey the right information about the correct behaviour and nutrition attitude as well as about the risk factors that can determine the disease. Within this frame, a public health systemic approach should also be implemented with guidelines to actively involve and help the single individuals and their families (participatory element) while modifying their behaviour and lifestyle: the current practice of giving general recommendations for everyone should be replaced by a personalised approach to motivate people to "participate" to their own healthcare in a way that is suitable for them.

COMMUNICATION GAPS

Unfortunately, the communication gap between the scientific community and the public is widening, thus representing a huge challenge and a bottleneck for the achievement of medical outcome: a large part of the population lives unhealthy and is not health conscious at all. We need to take a holistic approach to favour people perception of their own health and wellness and to make sure that messages are communicated to a wider community more effectively than in the past.
Social media and digital technologies can play a big role in **behavioural modification**. An example is persuasive technology (a field between computer science and behavioural science) that can engage people and keep them engaged, and induce individual behavioural changes.

As some technologies are changing and/or influencing people behaviour, we will need to adapt our approach in delivering personalized care in the future.

PEOPLE EDUCATION

Education, at different levels, is also a tool able to **motivate people to a healthy lifestyle** (preventive medicine) and to dynamic participation of individuals on own wellbeing (participatory medicine). A real systemic approach through public organizations or medical organizations and healthy people or patient communities is needed to communicate scientific results with clear and honest messages about the uncertainties. The scientific community should be able to honestly explain what is known and unknown and give recommendation to improve the own wellbeing. Patient and Public Involvement (PPI) groups can be organized to better inform on risk factors and possible new methodologies to face diseases with high social impact, but also to stimulate a dynamic participation and interaction with the community.
The level of public schools science education is actually decreasing, which makes it difficult to favour the awareness of the importance of prevention and of the potential of P4 medicine. For instance, people should understand better the concept of probability, which is in fact missing in the public opinion. Basic scientific instruction at scholar level is also essential to follow scientific advice and to promote a healthy lifestyle. If we act now with young people, we will probably see the effect in terms of preventive medicine in the next 25 years.
At present, people tend also to self-educate themselves more than in the past and this may be a problem if the incorrect information is put on the web. Therefore, we should think how to re-orient this attitude, or how to interface with this (=interventional approach). **Persuasive technology**, the new field of computer science, and social oriented digital medicine can be the instrument.

COGNITIVE HEALTH

The emerging era of "cognitive health" could transform the future of global health because it introduces a new partnership between humanity and technology[1]. Cognitive systems that understand and learn are helping people to expand their knowledge base, improve their productivity and deepen their expertise. With **cognitive computing**, we can be able to see health data that were previously hidden, and do more than ever thought. We could imagine that in 20-30 years from now computer science will make so much progress that it will empower the patients, the people and the MDs, whose role will completely change. We won't need any more doctors reading the result of analysis because the computer will do it. In 15 years it will be done in a very reliable way and the doctors will have a top layer to make the link between computer data and the patients.

DOCTORS' EDUCATION

Education of medical doctors - either in terms of technologies potentialities and advantages and in terms of the communication with people, which actually is missing - is an urgent challenge: more specifically, a new medical doctor generation able to work in an **interdisciplinary and multidisciplinary context** and able to approach the patient from a holistic point of view is urgently needed. There is currently a sort of detachment in MDs' perception about the utility of technologies and the fact that universities are strongly investing worldwide in the development and use of these new tools. Therefore, we need to encourage a better communication attitude between MDs and researchers/technologists (they have to speak the same language).
We have already technologies that can both monitor the patient and acquire information about the patient: these technologies should be added to the everyday medical practice through a correct education of MDs and people. Technologies are not at all the limitation to get to P4 medicine, as many of them are already available, but simply not yet integrated in patient care.

[1] http://www.ibm.com/smarterplanet/us/en/ibmwatson/health/

Figure 2. Participants at the Foresight Interdisciplinary Brainstorming (March 22nd 2016)

2.4. THE ROADMAP FOR THE FUTURE

To achieve the goal of Theranostics for P4 medicine, we need to:

1. **Acquire deeper basic knowledge of diseases and health, with a novel and more holistic approach**.

This means that we need to:

a. *DEFINE WHAT HEALTH IS.*
b. *MONITOR THE CHANGE BETWEEN HEALTH AND DISEASE.*
c. *TRANSFER FULL KNOWLEDGE ABOUT PATHOLOGIES INTO TECHNOLOGICAL END POINTS.*

Therefore, the following actions should be pursued:

- **Create an interdisciplinary/multidisciplinary network** of medical doctors with different specializations, informatics, bio-engineers, biologists and researchers from different fields. This requires also a network to exchange of information from the hospital to family doctors and general population with an increased number of controlled and useful information.

- **Assess data related to** the **homeostasis for a specific person** (therefore different from one to another) to acquire better knowledge about individual health status. The homeostasis is a *dynamic process characterized by phase transitions*: even if the homeostasis of the immune system probably represents the basic level, which dominates all other systems, each alteration of this equilibrium generates effects in other organs.

- **Set up longitudinal study of healthy population for a correct stratification of people** (statistic predictive model). We need to assess the evolution of each individual in the transition from health to disease. Targeting and acquiring data from younger population and very old one could be a starting model, even if individual ageing is a dynamic, multidimensional process not only in space and in time. *In order to get a full picture of personal health, the development of devices with sensors able to monitor phase transitions, to detect biomarker precursors of diseases and to integrate these data with environmental and behavioral information is necessary.*

- **Improve/support basic research on pathophysiology of disease** in order to know how to monitor the patient and when it's time for intervention. For many diseases *we don't have a full understanding of the early pathophysiology that leads to the disease* and therefore it is difficult to figure out what we should develop at technological level.

- **Look for common features in the majority of complex diseases** starting from existing cross-talking and overlapping between different pathologies. *A possible common signaling indicator could be inflammation, representing a first alarm in the* transition between wellbeing and pathology: therefore, we need to develop something that captures this signal in the body. Even if inflammation is for sure a common denominator either of most diseases (such as obesity, cancer, and several degenerative diseases), it is not the only one: to find out more common indicators, we need to identify the real risk, to develop the appropriate screening tools in order to be able to screen the population.

- **Apply a multi-scale approach with a new holistic vision of the human body as a complex system** (system biology and medicine).

2. Develop a solid model of risk stratification profile in order to quickly predict and prevent the disease or, at least, to personalize the therapy for each single patient.

Therefore, the following actions should be pursued:

- **Define the risk factors and the protective factors** for which limited information still exists. To do that, we need to move away from current factors based on epidemiological data on general population, towards individual risk factors.

- **Identify new biomarkers and better precursors of disease,** possibly common to all diseases, to have a good risk stratification profile.

- **Create models, based on big data** (biomarkers that are available and new biomarkers that should be implemented), big information, *to make risk stratification***.** These models should allow us to predict whether a single person can have a sudden death or not, as well as to early identify the transitional stage in a risky situation. The *parameters* that should be considered are **simple vital parameters and behavioral changes** that should be **monitored over a long time** frame in order to get a validated model. We need to decide which kind of marker or information should be monitored.

- **Develop new sophisticated diagnostic tools/technologies** that could support the medical practice and be useful to early predict the illness onset and/or to give right indications on personalized therapy. *Digital high resolution of imaging* using sensors able to detect markers in the body, which show the transition from health to disease could be useful and integrated in a future "digital biomarkers set" as the more appropriate technological solution, able to support P4 medical practice.

- **Develop platforms for integration of all data** of each individual, to make them available to medical doctors (MD) of hospitals and cross-linked with family doctors on the territory. MDs need to use these platforms to get a longitudinal view of a person and provide a personalized therapy when needed. The hospital of tomorrow should have a decision support system with a dedicated unit where interdisciplinary teams work together to define personalized therapies for each patient based on his/her data. We can figure-out the **new professional figure** of **"health engineer**", who manages all information and implements technological solutions interacting with doctors. However, this would require a harmonized approach in collecting data, a definition of ethical guidelines to protect the individual from possible abuse or data misuse, as well as guidelines from regulatory agencies.

- **Develop intelligent "electronic records**" able to collect information which is reliable and comparable. We need some more time to organize the algorithms, methodologies to have them more comparable and to have a database that allows doctors to compare patients from all over the world.

- **Assess the influence of nutrition on individual health through a multi-genomics approach.** Currently knowledge gaps exist on the real impact of nutrition on health. Investigating the impact of nutrition on selected healthy groups (i.e children during the first 1000 days of life or population of centenaries) can help to identify the **protective factors** to use as markers to prevent the occurrence of diseases. We need to study the **correlation between genetic profiles and metabolic profiles**. **Microbiome research** focused on understanding which effect the gut microbiota has on our health and well-being, influencing our

metabolism, immunity, and behavior, as well as the effect of nutrition influencing microbiota biodiversity changes, could help to fully understand the pathophysiology that leads to diseases.

- **Map over time the individual response to therapies, the risk of escalation of illnesses and comorbidities.** To reduce the risks associated with therapies, which is less than the risk associated to pathology for individuals, we should know which is the best available therapy and have information on how each individual metabolizes and processes drugs or therapeutic compounds. **Pharmacogenomics,** while evaluating possible therapeutic response in particular pathological conditions (**personalized health**), aims to develop rational means to optimize drug therapy, with respect to the patients' genotype. However **the pharmacogenomic tests are not widely available** and therefore investments in R&D are needed.

- **Monitor the individual in term of environmental factors, lifestyle and behavioral change components** to prevent illness or for a successful treatment. To do this, it is necessary: 1) to create a systemic approach where the public health system is able to actively involve and help the single individual or his/her own family (participatory element) to modify his/her behavior and lifestyle; 2) to develop special sensors inside a device, such as smartphones, that are able to collect individual behavioral data.

3. Individual and social actions

- **Move from the public health recommendations towards individual ones**. First of all, **the general guidelines** of what/how we want to achieve should be re-defined on a personal level. We need to adopt a holistic approach to people's perception of their own health and wellness. As well as their attitude toward this issue, and make sure that we are able to communicate this message to the wider community, also through social media, more effectively than we have been able to do so far. People must be motivated to participate to their own healthy lifestyle, also taking care of their stress management. We need to examine any avenue that could lead to behavioral modification, ranging from chemical intervention to social media intervention.

- **Adopt a social-oriented digital medicine,** taking advantage of persuasive technologies and a new field of computer science as tools to motivate and sensitize people to a healthy lifestyle and to induce behavior changes.

- **Ethical and regulatory issues** have to be adequately addressed, with specific reference to the management of personal data.

Figure 3. Memory picture of the Foresight Workshop conclusion (March 23rd 2016).

This report is dedicated to the memory of Prof. Gerard Siest, who contributed to the success of this Foresight Workshop with his great scientific value and his passionate vision of personalised medicine. We will miss his tireless enthusiasm and his friendliness.

3. ANNEXES

3.1. DISEASE INSIGHTS

CARDIOVASCULAR DISEASES

Section 1. FIGURES ON CARDIOVASCULAR DISEASE WORLDWIDE

Acute Coronary Syndromes (ACS), a common complication of coronary heart disease, is associated with more than 2.5 million hospitalizations worldwide each year. ACS describes clinical disorders ranging from ST-elevation myocardial infarction (STEMI) to non-ST-elevation myocardial infarction (NSTEMI) and unstable angina (UA). It is estimated that a myocardial infarction (MI) occurs every 34 seconds in the US, and that every 83 seconds one person dies from a major coronary event. Cardiologists underline that evidence based medicine provides important advances in Acute Coronary Syndromes (ACS) care (intervention on key life style and demographic risk factors; antithrombotic therapy; statins; revascularization procedures). However the recurrence episodes are still very high, approaching the 25%: the repetition of acute coronary episodes determine progressive impairment of myocardial function leading to chronic heart failure (HF) which represents the most critical condition for cardiologist like a pandemic disease.
The heart failure (HF) is a complicated syndrome in which the heart is unable to perform an adequate perfusion of all the organ. Worldwide, over one million new diagnosis of HF are made every year and 600.000 per year only in Europe. HF accounts for 1-2% of total European healthcare expenditure.
Close to 80% of people with HF are over the age of 65 and one out of five adults over 40 years will have a heart failure in their lifetime, but symptoms are by no means a natural result of ageing. Major risk factors: age, diabetes and obesity. Re-hospitalization is a real issue: It is estimated that 1 out of 4 patients will be readmitted to hospital after care within one month. Furthermore the HF mortality is important, in figures:

- Approximately 1 in 10 patients hospitalised with HF will die in hospital
- Around 1 in 3 will die within 1 year
- Approximately 1 in 2 will die within 5 years.

Section 2. SWOT ANALYSIS

Threats and weakness.

1. Late diagnosis and late management of HF patients by family doctors
2. Lack of education.
3. Lack of networking between the territory infrastructures and hospitals.
4. Re-hospitalization in a short follow up period and unpredictability of the recurrence of ACS and/or myocardial infarction.
5. Few correspondence of preclinical models to the clinical pathological findings.
6. Lack of accessibility and data sharing of large randomized clinical trials results and of collected materials (biomaterials, blood and tissue samples, actual images...).
7. Lack of genomic information and limited knowledge of markers for epigenetic regulation.
8. Un-complete and heterogeneous genomic data and limited knowledge of markers for epigenetic regulation.
9. High costs of heart transplantation, implantation of ventricular assist devices and palliative care.
10. Ethical problem to collect data about a single patient.

Strengths and opportunities

1. Important advances in Acute Coronary Syndromes (ACS) care have been already obtained such as intervention on key life style and demographic risk factors, antithrombotic therapy, statins, revascularization procedures.
2. ACS care is already using components of individualized medicine (risk scores; imaging).
3. For severe HF is available heart transplantation, implantation of artificial heart or palliative care with high cost.
4. Theranostic is already at the core of EUROPEAN research projects (i.e *NanoAthero* project developing nanosystems for targeted imaging and treatment of advanced atherothrombotic disease; *CosmoPHOS-*

nano developing near-infrared fluorescence molecular imaging, endovascular near-infrared targeted photodynamic therapy).

Section 3. STRATEGIC TECHNOLOGICAL AND NON TECHNOLOGICAL SOLUTIONS

Which are the major POTENTIAL solutions in the short-medium term (5-10 years)?

1. Improve the network between the territory and the hospital by:
   - Improving diagnosis in primary and secondary care settings.
   - Ensuring quality education and individual support for patients and their families.
   - Guarantee a network between big hospitals and little hospitals, between hospitals and ambulatory activities, between specialists and general doctors for a more personalized approach to care.
   - Encouraging person-centred approaches to care.
   - Investment in professional capacity.
   - Seamless transition of care (from hospital to home settings).
   - Equitable provision of medicines, devices and care.
2. Support research with a broad interdisciplinary approach through:
   - Improvements in therapy → Mechanical Circulatory Support totally implantable, Application of microRNA, etc..
   - Improvements in diagnosis→the role of the genetic and biotechnology.
   - Identify biomarkers (OMICS and circulating factors) for determining individual risk assessment.
   - Handling the enormous personalized data sets: it is important to handle them really with care in order to integrate the information (platforms and technology for new taxonomy of disease).
   - Developing new platforms and technologies to integrate all collected data from single patient for new taxonomy of disease.
   - New mathematical and computational methods.
   - Adapt clinical trial design.
   - New in *vivo* molecular imaging to follow disease, drug response, drug doses.

3. Characterization of a single patient by a deep and rigorous research method instead of statistical evaluation of the population.

Which are the three major POTENTIAL solutions in the long term (20-30 years)?

1. Identify subjects at risks--- EARLY PREDICTION
2. Prevention, diagnosis and targeted therapy in different scenarios of cardiovascular diseases
3. Identify variables and treatment for native heart recovery
4. Develop mechanical circulatory support devices, with following characteristics: total implantable without cables and batteries outside the body (the main problem for infections) in order to reduce the re-hospitalization of implanted patients; sensorized pumps for heart mechanisms recovery in order to perform a temporary assistance (pump weaning).
5. New tools for the recovery of the native heart before developing a severe degree of disease
6. Create stem cells with a given individual genome for regenerative medicine

METABOLIC DISEASES

Section 1. FIGURES ON METABOLIC DISEASE WORLDWIDE

There are 350 million people on earth with documented diabetes; it is estimated that are just as many who have diabetes and don't know that they have it. The projections by the International Diabetes Federation are that in 2025 there will be 500 million people with diabetes. The most powerful risk factor for human diabetes is obesity. Diabetes prevention is strictly connected to obesity prevention. Prevention is not just something to recommend, it's mandatory because of the cost of diabetes with all the complications: microvascular complications, nephropathy, retinopathy, neuropathy and cardiovascular disease (still today diabetics suffer from cardiovascular 2 to 3 times more than non-diabetics individuals). Among obese people is going up to 50% and in obese children even higher.
Another metabolic syndrome is represented by non-alcoholic fatty liver disease (NAFLD, fatty liver), recognized as a disease until a few years ago. It is characterized by accumulation of fat above 5%, a minimum amount of fat in the liver. Fatty liver is now considered one of the biggest public health challenge facing modern time as it affects up to 20 to 25% European population, with increasing trend. Recent data report about 3 millions of people affected. The prevalence is higher in the USA because they are usually more obese. In patients with 2 type diabetes and especially in obese patients with diabetes the prevalence of NAFLD can increase; in bariatric patient population is usually going up to 90%. After the new therapy for hepatitis C, NAFLD is considered the major liver disease especially because it is progressing to non-alcoholic status hepatitis with inflammation (NASH) and then to fibrosis, to cirrhosis as so to hepatocellular carcinoma. Moreover, people can develop hepatocellular carcinoma, without cirrhosis, due to NAFLD. Causes are considered familiarity but especially insulin resistance, obesity ,type 2 diabetes.

Section 2. SWOT ANALYSIS

Threats and weakness.

1. For prevention of diabetes no much progress. Failure of single gene detection, failure of polymorphism clustering as signal an increased risk of developing diabetes in adults: common variants without possibility of targeting treatment.
2. The other difficulty is screening the diabetes: it is very costly and maybe terribly imprecise.
3. Possibility to cause more harm than benefit in preventing the condition by treating with drugs only people at risk.
4. Treatment of obesity has a higher failure rate than cancer; 90% or 95% of the people that lose weight with low calorie diet will regain weight within six months to one year and frequently go in what's called the yo-yo phenomenon, losing weight and then regaining weight every time with a little bit of an interest superimposed.
5. It is estimated that non-alcoholic fatty liver disease (NAFLD) is affecting about 1/3 of the world population. NAFLD ranges from simple steatosis to more serious conditions as non-alcoholic steatohepatitis (NASH) with fibrosis. Most of these patients are undiagnosed since it would be too costly to screen. Currently no medicines are approved for the treatment of NAFLD; usually patients are given advice to make changes in lifestyle especially diet and exercise.
6. Lack of knowledge of NAFLD, which is underestimated by patients and physicians, despite it is becoming the major cause for liver disease and liver transplantation (given the new drugs approved for the treatment of HCV). Moreover, it is a major risk factor for hepatocarcinoma (HCC) that can occur even in absence of cirrhosis.
7. No regulatory agency BLOT, the FDA or the ENA or any health care system pay in the foresee of the future medicines against obesity (risk factor for both diabetes and NAFLD).
8. Lack of robust and validated diagnostic markers of disease.

Strengths and opportunities

1. Therapy in diabetes with new drugs reached good results.
2. Devices that can read online the glucose concentration in the interstitial fluid and administer insulin (the artificial pancreas was approved by FDA in September 2016).
3. New drugs and surgical approaches by bariatric surgery for the treatment of obesity.
4. Non invasive imaging technique are available for diagnosis of liver fibrosis.

Section 3. STRATEGIC TECHNOLOGICAL AND NON-TECHNOLOGICAL SOLUTIONS

Which are the major POTENTIAL solutions in the short-medium term (5-10 years)?

1. Develop nano-devices that can read the glucose concentration in the plasma and that can release on demand insulin (interventional approach).
2. Look at the extremes of the distribution of Gaussian curve (out-layers) to identify predictive risk factors of diabetes and protective factors.
3. A system medicine that put together human factors, metabolic and physiologic phenotype, environmental factors, big database and nutrition data for personalized healthcare.
4. Technology that allows to change behaviour on a minute-by-minute basis in a non-invasive way that allows people to achieve maximum benefit with minimum effort (smart devices).
5. Develop environmental sensors able to detect toxic compounds in order to reduce risk factors.
6. Increase knowledge and awareness on metabolic diseases and on strategies to prevent and cure them starting from healthy diet and lifestyle. This educational step should start as early as possible, since the incidence of metabolic diseases is increasing in the pediatric population. This should also involve education of general practitioner that should routinely check for most common risk factors of metabolic diseases
7. Define common procedures for prevention and early prediction of metabolic diseases. Develop new risk factor analyses and identify non-invasive, non expensive, widely available biomarkers of risk of disease and of its severity and progression.
8. Need for non-invasive, low cost, widely available, easy to use devices.
9. Improve therapy and diagnosis, as well as knowledge, on NAFLD disease.
10. Improve the knowledge of incidence of exposure to environmental factors, such as pollutants (especially the permanent pollutants), plastics and BPA (Bisphenol A) on diabetes.

Which are the major POTENTIAL solutions in the long term (20-30 years)?

1. Increase the knowledge of relation between metabolic disease and microbiome. Known the role of diet and microbiome in brain-gut-liver axis, as well as inflammasome, which are vital players in innate immunity and are associated with onset and progression of various diseases, including metabolic disorders, multiple sclerosis, inflammatory bowel disease, cryopyrin-associated periodic fever syndrome, as well as other auto-immune and auto-inflammatory diseases.
2. Identification of subgroups of subjects with metabolic diseases that will benefit mostly of drug treatment.
3. Identify factors (also environmental) and mechanisms that are at the basis of the non-genetics obesity syndrome.(including NAFLD).
4. Prevention and early prediction of metabolic diseases.

CANCER DISEASES

Section 1. FIGURES ON CANCER DISEASE WORLDWIDE

Cancer incidence and mortality are on the rise, in particular in low and middle-income countries. Sedentary lifestyle increases the risk of cancer. Increasing trends of certain cancers (i.e colon cancer) in the young population. The increasing burden of cancer related to obesity is alarming.
The cost of cancers was €126 billion in the EU in 2009 and this cost is destined to increase. The management of cancer is extremely expensive. All the advantages in the understanding of cancer biology and new technology have failed to reduce the rising price of commercial drug development. It is estimated that the median cost of a new cancer drug will be $ 100,000 USD per patient per month in 2035.

Section 2. SWOT ANALYSIS

Threats and weakness.

1. Most of the cancer genome unexplored (<2% coding).
2. Poor translation of the acquired knowledge in clinical practice.
3. Cancer treatments are protocol based and follow multi-lines approach (expensive).
4. Non homogeneous response or survival rate to therapy among the same group of cancer patients or between different cancer histotypes. This is due by high complexity derived from genetic characteristics of cancer cells and immunological response induced by cancer. This complexity is patient specific and should be characterized to increase the therapeutic success.
5. Far-from-optimal screening tests for early detection and prevention.
6. Cancer molecular testing based on a handful of markers helpful for directing treatments, which are all protocol-based.
7. Costs of precision medicine.
8. Cancer centres are often not ready to translate the new knowledge into clinical practice.
9. Need for more bio-informatics competences.
10. Lack of ethical regulation on how to communicate molecular analysis results to patient when there is not therapeutic solution.
11. Ethical issue on guarantee new drug and new device to all even if are expensive.

Strengths and opportunities

1. Adequate knowledge of the molecular landscape (exome) of many cancers.
2. High technology improvement.
3. Decreased costs for molecular analyses.
4. Improve treatment by applying a good quality precision medicine.
5. New drugs, in particular immunotherapies, are available.

Section 3. STRATEGIC TECHNOLOGICAL AND NON TECHNOLOGICAL SOLUTIONS

Which are the major POTENTIAL solutions in the short-medium term (5-10 years)?

1. Application of an integrated biomedical anthropological and evolutionary approach to reach the P4 medicine by putting the disease within an evolutionary perspective on the basis of own genes, microbiota, lifestyle an so on. Found solutions on how we can modulate the evolution. *In the last 15-50 years there were tremendous changes of the environment and we adapted to these changes (i.e obesity).*
2. Definition of new pre-clinical models (i.e animal's model that have long term memory of the immunological system and recreate cancer microenvironment) to set up personalized therapy.
3. Definition of new clinical development paths. *Emerging paradigm is the combination of conventional and novel immune-oncology therapy aimed to improve cancer patient survival.*
4. Optimization of molecular diagnostics for prognostic/prevention.
5. Optimization of molecular diagnostics for routine application of personalized medicine. *Actually "Global jungle" in the routine use of molecular diagnostics. The omics analysis is accurate but not accessible to all patients.*
6. To favour an exponential growth in clinical research through new clinical trials. *International clinical trials would allow to treat patients with specific molecular alteration. International consortia should share resources and technologies to increase the quality of analysis and decrease the costs.*

7. Need to change regulatory rules for approval of new therapeutic solutions. The regulatory agencies should adapt to evolution of science. *The new therapeutic solutions often do not follow the classical Kaplan-Meier curve (i.e immunological response is not immediate like chemotherapy) so that statistic parameters of efficacy (i.e curve after the median) should be considered by regulatory Agencies.*
8. To ensure new medicines to all patients independently from the local Health Care system. *New modality to assess price of medicines should be the "value".*
9. To identify molecular predictors of response.
10. To establish profiles useful for chemoprevention.
11. To understand lifetime cancer risk of each person → risk stratification. *There is a terrible lack of knowledge of what is happening in human body. Each person has its own history and - to really prevent and cure the disease - we must not generalize.*
12. To increase the incidence rates by fighting obesity which is key comorbidity risk factor, such as understanding better cancer risk, working on new screening tests, understanding each patient cancer and its targeted treatment, better tracking of response to treatment.
13. To work on big data to understand lifetime cancer risk of each individual.
14. To test new diagnostic screening tools (molecular markers, new imaging technologies) and optimize screening for early detection and cancer prevention. Combination of more diagnostic tests less invasive and more sensitive for better accuracy of prediction. *Actually we have a population screening program which targets 50-69 years old people. We need to extend it to younger people to really prevent cancer.*
15. Point-of care applications (*Tests on Blood, saliva, liquid biopsy markers and circulating tumour cells as well as immunological component).*
16. Large-scale testing of new cancer treatment strategies (organoids 3D culture reconstruction of the whole cancer microenvironment: patient, cancer-driven drug screen, drug-delivering conjugated with imaging technologies etc.)
17. To implement predictors of successful treatments (cell-free DNA, miRNAs others). *Actually cancer risk is manly based on epidemiological predictors (family history, sex comorbidity, lifestyle).*
18. To support the oncologists for correct interpretation of diagnostic/prognostic data to treat patients with personalized therapies (precision medicine): more bioinformatic competences are needed.
19. Better interaction with patients. *Interfacing with the population is needed to better explain the aim and the limit of precision medicine avoiding any personal conflict of interest (i.e you are under the control of big pharma). Medical doctors should discuss with the patient the role of such comorbidities like lifestyle, presence of other pathologies as diabetes and obesity that can increase the risk of cancer.*

Which are the major POTENTIAL solutions in the long term (20-30 years)?

1. Creating immunological response to induce systemic effects. This can allow to fight not only cancer but also other diseases.
2. Develop metabolic therapy: association of completely different kind of therapy targeting microenvironment, inflammation and immunological system due to multifactorial genesis of cancer.
3. Identify the "key marker" that is related to origin of the disease.
4. 1-step test in new-born for lifetime cancer prediction → tailored next generation cancer screening test for high-risk subjects (imaging combined with molecular markers) → tailored chemoprevention.
5. Patient-specific cancer treatment with combined drug and imaging delivery → real-time monitoring of response → molecular markers for long-term follow-up.
6. Reduce the high incidence of cancer and economic impact on society by: Targeting screenings for those individual that are really at risk → reducing the cost of mass screening; Targeting chemoprevention for at-risk subjects → economical impact; Treatment based on each patient's cancer and genome profile → economical impact.
7. Theranostics as a strategic direction of the future in oncology with applications for both cancer prevention and treatment. But to achieve this goal we need more knowledge on basic science and basic information rather than on big technologies that can be developed trying to solve the problems in the next 20 years since they are already available. There is a defective usage of what we know already. The difficulty for theranostics is on how to implement the knowledge we have already and how to identify what is truly missing at this point of time.
8. Educate young people and family on what the risk is and which is the correct lifestyle to prevent cancer disease. We should educate the people to behaviour not only in term of lifestyle but also on how to look at the medicine.

NEUROLOGICAL AND NEURODEGENERATIVE DISEASES

SECTION 1. FIGURES ON NEUROLOGICAL/NEURODEGENERATIVE DISEASES WORLDWIDE

4.9 million affected with Alzheimer disease and 1.2 million with Parkinson disease in Europe, of course can make reasonable for the important cost of bringing them that was calculated in 2010 around 800 billion of Euros. Annually 15 million people worldwide suffer a stroke. 5 million of these die making it the second leading cause of death. Another 5 million are left permanently disable, placing a burden on family and community. Across Europe around 1.3 million people suffer a stroke each year. It was estimated that in 2060 more than 30% in Europe will be more than 65 years old and this will increase the percentage of people, which will develop neurodegenerative diseases.

Section 2. SWOT ANALYSIS

Threats and weakness:

1. Current neurology is mostly focused on the development of drugs, devices and diagnostic tests. This approach is reactive to diseases, only when they manifest. The feeling among the experts is that the field of neuroscience research is 10 year far behind with respect to the other medical fields.
2. Large percentage of population at risk of dementia and stroke due to an increase of aging population. Both cerebrovascular and neurodegenerative diseases are age-related and a two-fold increase of the incidence is expected in the next 20 years together with severe disability and dependency.
3. Absence of specific cure for neurodegenerative diseases, with current therapeutic opportunities limited to extremely restricted time windows. Use of drugs previously developed for different disorders due to the lack of resources for the development of novel and innovative drugs capable to target specifically neurological disorders.
4. Tendency to produce a rational system based on efficiency, calculability, predictability, and control of humans by means of non-human technology: this leads to negative consequences in neurological practice which affect the care for the individuals and the patient-physician relationships, representing the antithesis of P4 Medicine.
5. Lack of clear research priorities with poor integration between basic and clinical research in neurology and absence of longitudinal studies, which could give more information about the nature of history of the disease;
6. Poor collaboration between academia and industry and lack of funding to support public campaigns capable of increasing awareness of the risks of unhealthy life for brain. Most of public funding for research is allocated at national level and not transnationally putting a barrier for inter-disciplinary research.
7. The intensification of human-machine interfaces will become an issue for users and therefore regulators have to work together with experts in radio frequency and sensors.

Strengths and opportunities

1. New emerging fields can offer novel important tools in the prevention of neurodegenerative disorders, for which an intervention on the same risk factors of cerebrovascular diseases (smoking, high intake of salt and alcohol, low level of physical activity, obesity, high blood pressure and cholesterol, diabetes and atrial fibrillation) has been already shown an effective strategy in a significant percentage of individuals:
   - Proteinopathies are emerging as a specific group of neurological disorders previously considered neurodegenerative in nature (Alzheimer's disease, Parkinson's disease, frontotemporal lobar degeneration, progressive supranuclear palsy, corticobasal degeneration, chronic traumatic encephalopathy and Amyotrophic lateral sclerosis) with the possibility of new therapeutic strategies.
   - New specific disorder-associated biomarkers and new therapeutic approaches can be identified by means of a thorough analysis of neuronal network activity which has been associated, when characterised by abnormal oscillatory profiles, with a wide spectrum of neurological and neuropsychiatric disorders, from cognitive impairment of different degree, stroke related disabilities, depression and drug abuse.
2. Autoantibodies binding to synaptic neural antigens (e.g. IgG specific to NMDA receptor or to the astrocytes aquaporin-4 water channel) has elucidated the pathogenesis of several neurological diseases. Molecular characterization of their target antigens, providing highly specific diagnostic tests for disorders

affecting multiple levels of the nervous system, can be the basis for the development of novel therapeutic strategies.
3. To achieve personalized treatment of neurological disorders, the information obtained from functional multimodal brain imaging studies might be used to early detect the pathological condition, develop new therapeutic strategies and choose treatments by predicting response in individual patients.

Section 3. STRATEGIC TECHNOLOGICAL AND NON TECHNOLOGICAL CHALLENGES AND NEEDS

Which are the major POTENTIAL solutions in the short-medium term (5-10 years)?

1. Development of computer based algorithms integrating clinical and electrophysiological data, implementing computer based image analysis, outcome and risk prediction, so as to face the increasing complexity of neurology. Technological solution putting together biomarkers and digital medicine but able to reduce enormous data dimensionality (hypothesis of disease and effective therapy to adopt).
2. Identification of panels of markers for rapid and early diagnosis of neurological disorders as well as for prevention (there is the need to identify reliable biomarker of brain pathological change in healthy individual to protect the neurons before the first clinical signs).
3. Development of strategies aimed at risk factor reduction to prevent stroke and neurodegenerative disorders (how, when and where take action and also what to do).
4. Increase awareness of the public, policymakers, and health professionals about the causes and symptoms of stroke and dementia;
5. Definition of the pathogenic role of lifestyle factors for the physiology of the brain and identification of the actors that maintains the homeostasis in the central nervous system.
6. Education of people to healthy lifestyle since it reflects in healthy brain and could change our risk to develop neurodegenerative diseases like Alzheimer, Parkinson and stroke.
7. Promotion of the integration between basic and clinical research in order to support a more "visionary" research and to go beyond repurposing previously developed therapies in neurology.
8. Look at mechanisms underlying longevity to better face and fight these brain pathologies.
9. Need to understand the function of physiological sleep (low wave sleep and REM sleep). Monitoring the sleep could allow the identification of new protective factors, acting in the cleaning of the synaptic occupancy that could improve the quality of life together with physical activities, lifestyle and healthy nutrition.

Which are the major POTENTIAL solutions in the short-medium term (20-30 years)?

1. To make the human brain interfaceable (neuronal network activity recording, brain stimulation technologies, robotic devices for rehabilitation, etc.). This can be achieved through:
   - providing personalized risk profile and develop individualized therapeutic approaches using the information obtained from brain functional studies and from genetic studies;
   - developing computational approaches to design new molecules in *silico* to precisely target antibodies against CNS antigens;
   - implementing multi modal diagnostic techniques to better understand the dynamic interactions between brain structure and function;
   - developing electromagnetic-dependent pharmaceutical tools ("electromagnetic-ceuticals") to treat neurological disorders by means of peripheral stimulation that could have effect not only on neurological disorder but also on other diseases.
2. Empowerment of associations of patients through a integration with scientific societies and the institutes where research and studies are performed (this will strongly facilitate patients' recruitment for evaluating new treatments in disorders with no cure).
3. The establishment of worldwide collaboration of researchers through International organizations aiming at globalize research funding. Open science and a broad alliance of scientific, clinical, public, and private sectors.
4. Theranostics as potential new strategic direction for the innovative medicine in neurology: for instance, diagnosis and treatment of oscillopathies represent one of the most promising area. It can be hypothesized that new techniques will be developed in the next few years capable of non-invasively recording and modulating neuronal network activities at circuital level and with a closed-loop approach that will help to restore a physiological condition.

3.2. PARTICIPANTS BIO-SKETCHES

Luigi AMBROSIO
Director of Department of Chemical Sciences and Materials Technology, National Research Council of Italy,
"Embracing multidisciplinary foresight"

Doctoral degree in Chemical Engineering (1982) from University of Naples "Federico II'. Adjunct Professor of University of Connecticut, USA (1997-2003) and of University of Naples "Federico II" (1997-2010). Director of Institute of Composites and Biomedical Materials (2009-2012). President of the European Society for Biomaterials (2006-2013). Distinguished Professor at Nanjing Normal University, China. (since 2013). He has been nominated Fellow of the American Institute for Medical and Biological Engineering (March 2001), and Fellow of Biomaterials Science and Engineering (May 2004). Member of the European Commission Advisory Group of the FP7 theme Nanoscience, Nanotechnologies, Materials and New Production Technologies (2006-2008) and Member of High Level Group on Key Enabling Technologies at European Commission (Since 2009). Main areas of interest: design, characterization and processing of polymers and composites for medical applications and tissue engineering.	

Ezio ANDRETA
Project Coordinator of S&T Foresight Interdepartmental Project at CNR

Ezio Andreta, after a degree in Political Sciences at Genoa's University in 1965, completed his studies in Economics and international relations at Lyon's University, and in Economics and monetary problems at the London School of Economics and Political Sciences. In 1972 he joined the European Commission in Brussels where he assumed different responsibilities in matter of energy, international relations, and Research and Innovation. In 1995 as Director of Energy Department, and Director of the Task force "Car of Tomorrow", he was in charge of the "Nanotechnology, Materials and Production" programme and responsible for the negotiations of the EU Delegations in Nanotechnology and Intelligent Manufacturing System. From 2004 member of the Scientific Committees of Lombardia Region (IRER), Scuola Superiore Sant'Anna in Pisa, Fondazione Snaidero, and Magna Carta. From 2006 member of the Scientific Council of the National Research Council of Italy (CNR) and President of the Italian Agency for the European Research. In April 2008 Commissioner of the Italian Innovation Agency and from 2012 adviser of CNR President and coordinator of the Foresight Project. He chaired and participated as speaker in many international meetings, wrote many articles and taught as visiting professor in Italy (Politecnico di Torino e di Milano, Università di Genova, Lecce e Trento) and abroad (Escuela Politecnica de Madrid, and Istituto Panamericano de Desarrollo de Empresa in Mexico City).	

Francesco BALDINI
Senior Scientist Institute of Applied Physics (IFAC) CNR
"Do nothing to others you would not have done to you"

Francesco Baldini graduated in physics from the University of Florence magna cum laude in 1986. Since 1986 he joined the Optical Fiber Group at IROE-CNR in Florence (now IFAC-CNR). Since 1990, his activity has been mainly devoted to the design and development of optical sensors for the detection of chemical and biochemical parameters for clinical applications and of optical nanoprobes for intracellular applications. He is author of almost 200 publications on the subject in International Journals, in scientific books and in International Conference Proceedings. He is/was coordinator responsible of many international and national projects in the field of optical chemical and biochemical sensors. He was President of the Italian Society of Optics and Photonics (SIOF) for the biennium 2015-2016. In 2009 he was nominated fellow of SPIE for "his achievements in biological and chemical sensing in biomedicine".
Main areas of interest: photonics, biophotonics, optical sensing for chemicals and biochemicals in biomedicine.

Daniela BANTI
Technician - Research Support and Executive Assistant to the general management, Institute of Clinical Physiology, Area CNR, Pisa - Italy

Daniela Banti has been part of the Technical Management staff for the Institute of Clinical Physiology – National Research Council (IFC-CNR) since 1982, where she works as referent for the report coordination of the scientific activities. Within this framework, she coordinates the research reports in the field of Science and Biomedical and Health Technologies for both operative and territorial units. Since 1999 she has been the contact point for IFC management of the CNR Institutes using the Internet procedures. In her quality of IFC referent for the Library of the CNR Pisa Area, she is responsible for the management of the document and bibliographical heritage of IFC. Since 2012 she has been member of the "Working Group of the CNR Central Library G. Marconi", for which she works as expert of the libraries of the Scientific Network with regard to the activities for Research Quality Evaluation (VQR). Since 2014 she has been Executive Assistant to the General Management and is responsible for Document Management of IFC. Since 2015 she has been a member of the Scientific Committee within the working group "Health" and she takes part in the "Science and Technology Foresight Project" of CNR. In 2016 she also obtained the qualification "ISO 9001:2015 Risk-based Thinking" qualified Auditor.
Main area of interest: Biomedical Sciences, Digital library Repository, Knowledge infrastructure, Self-Archiving system, DataBase design.

Cecilia BARTOLUCCI
Researcher of Institute of Crystallography (IC) CNR and Coordinator of WG "Food" - Science and Technology Foresight Project
"Duration in Change" (J.W. Goethe)

Since 2013, Coordinator of the WG "Food" within the "Science and Technology Foresight Project" of the CNR, where she holds a position as Researcher at the Institute of Crystallography. She graduated in Chemistry in Rome and, after obtaining a scholarship from the Ministry of Foreign Affairs, started her research activity at the Institut de Chimie Therapeutique in Lausanne, Switzerland. As postdoctoral fellow, with a NATO-CNR Advanced Fellowship, she spent 18 months at the MPI für Medizinische Forschung in Heidelberg, Germany. In 2000 she received a fellowship from the Humboldt Foundation to work as Postdoctoral Research Associate in Protein Crystallography at the MPI für Biochemie, Martinsried, Germany, where she continues to collaborate. Her wide-ranging research interests allowed her to gain experience in many different sectors. From the synthesis, characterization and structure-activity relationship studies of pharmaceutically active compounds; to the crystallography of biomolecules and functional studies; to nutraceuticals and eventually to food, she learned to value a highly interdisciplinary approach. Main areas of interest: Food, Nutrition, Protein structures.	

Fiorella BATTAGLIA
Assistant Professor, Faculty of Philosophy, Philosophy of Science and the Study of Religion. Ludwig-Maximilian-Universität. Munich
"Justice is the first virtue of social institutions" (J. Rawls, A Theory of Justice)

Fiorella Battaglia (1960) studied philosophy at the University of Pisa and at the Humboldt University of Berlin. 2004 she completed her Ph.D. at "L'Orientale" University of Naples. 2005 she completed a master dissertation at National Council Research on ethics and epistemology of environmental epidemiology. From 2006 until 2010 she had a research position at the Berlin-Brandenburg Academy of Sciences and Humanities. From 2007 until 2013 she was lecturer at the Department of Philosophy of the Humboldt University. Since 2007 she is permanent visiting lecturer at the Medical School of the University of Pisa. 2013 she got the National Habilitation as Associate Professor of Moral Philosophy in Italy. Since 2013 she works as an Assistant Professor at the Faculty of Philosophy of the Ludwig-Maximilians-Universität of Munich. She has been PI of the EU-project: "Robolaw. Regulating Emerging Robotic Technologies in Europe". Since 2013 she is PI of the EU-project "Credits4Health. Credits-based, people-centric approach for the adoption of healthy life-styles and balanced Mediterranean diet in the frame of social participation and innovation for health promotion". Since 2015 she is PI of the EU-project "ReCriRe: Between the representation of the crisis and the crisis of representation. How crisis changed the symbolic background of European societies and identities: Implication for policies". Main areas of interest: Normative Ethics. Meta-ethics. Ethical issues of social and technological research and innovation. Philosophy and ethics of emerging technologies.	

Patrick BOISSEAU
VP Healthcare at CEATech, Nanomedicine European Technology Platform

Patrick Boisseau is graduated in biological engineering from the French Elite Schools Institut National Agronomique (1983) and Ecole Nationale du Génie Rural, des Eaux et des Forêts (1985). He holds different positions in academic research, research and development and research management in biological research and later in medical technologies. Patrick Boisseau's current position is VP Healthcare at CEATech, a public non-for-profit Research & Technology Organisation, based in Grenoble, France. His field of technical expertise is drug delivery, medical imaging and innovative medical technologies. He has acquired a large expertise of coordination of numerous EU projects and is currently coordinating EU-NCL infrastructure on nanocharacterisation. He is elected Chairman of the European Technology Platform on Nanomedicine. He is chairing the ESTHER Task Force designing and implementing this European Industry Driven Initiative on Emerging and Strategic Technologies for Healthcare since May 2015. Main areas of interest: Nanomedicine, medical technologies.	

Gabriele BRONZETTI
Director of Institute of Cardiology, University of Bologna and of Operative Unit of Pediatric Cardiology & cardio-surgery, S.Orsola-Malpighi Hospital, Bologna
"We do not invent anything, we discover"

Gabriele Bronzetti received the Diploma degree in Medicine and Surgery from the University of Bologna in 1993, and the PhD degree in Cardiology from the University of Bologna in 1997. He has been awarded a fellowship at the Division of Cardiology University of Liegi in 1997 (July- December 1997) and two Clinical fellowship in Electrophysiology at the Division of Cardiology, Hospital for Sick Children of Toronto, Canada in 2001 and in 2004. He is currently Professor and tutor of Master in Paediatric Cardiology, University of Bologna, and member of Italian Society of Cardiology and Italian Society of Paediatric Cardiology. He is currently Director of both Institute of Cardiology, University of Bologna and of Operative Unit of Paediatric Cardiology & Cardio-surgery, S.Orsola-Malpighi Hospital, Bologna. He also operates as paediatric cardiologist volunteer at the "All souls mission" in Zimbabwe. He is author and co-author of more than 90 indexed paper in peer-reviewed journals and invited speaker at several national and international conferences. In the last 5 years he was invited speaker at the Word Conference on Antiarrhythmic of Heart Rhythm Society as maximum expert on arrhythmias in childhood. His Clinical skills include Cardiac Electrophysiology and Antiarrhythmic drugs. Main areas of interest: Congenital heart conditions in childhood and young; prevention of young unexpected death; sport medicine.	

Enrico CAPOBIANCO
Head of Computational Biology & Bioinformatics, Center for Computational Science, University of Miami
"What's the difference between God and a doctor? God doesn't think to be a doctor"

Holds a Doctorate in Statistical Sciences from University of Padua (Italy). Conducted MPhil at LSE (London, UK), Northwestern University, and graduate studies at UC Berkeley, then postdoc research in computational fields at Stanford University (US) (1994-1998). Held twice a NATO-CNR grant (Stanford, and Niels Bohr Institute & Danish Technical University), ERCIM fellow at CWI (Center for Mathematics and Computer Science) in Amsterdam (NL) in 2001-2. Senior scientist at Boston University, Biomedical Engineering (2004-5), head of methods at Serono (Evry, FR) in 2005, team leader at CRS4 in Sardinia (Italy) in quantitative systems biology (2006-11). Founding PI (2012-5) of the Laboratory of Integrative Systems Medicine at the Institute of Clinical Physiology of CNR, in Pisa (It). Now an associate of CNR. Was CAS research professor in China (2011), ICTP fellow (Trieste, Italy) (2003), visiting professor at Fiocruz in Brazil (2008-10, Program, Capes - FIOCRUZ), and visiting scientist at the Institut des Hautes Études Scientifiques (IHES) in France (2010). Main areas of interest: Systems Medicine, Network Science, Big Data.	

Alicia CASALS
Professor, Head of the Associate researcher at the Institute for Bioengineering of Catalonia (IBEC)
"Sensor based robot control in rehabilitation, assistance, surgery and training."

Background in Electrical and Electronic Engineering and PhD in Computer Vision. Professor at UPC in the Automatic Control and Computer Engineering Department. Head of the research group on Robotics and Computer Vision at the Centre of Research in Biomedical Engineering. The research is oriented to improve human robot interaction through multimodal perception, focused mainly in the area of medical robotics. In this field she is working in robotic systems and control strategies for rehabilitation, assistance and surgical applications. From 2001 to 2008 coordinator of the Education and Training key area within Euron, the Network of Excellence: European Robotics Network, and IEEE-Robotics and Automation Vice President for Membership in the period 2008-2009. Main awards: International Award on Technology, *Barcelona 1992*, *Barcelona City* Award 1998, and *Narcis Monturiol* Medal from the Catalan Government 1999. From 2007 member of the *Institut d'Estudis Catalans*, the Academy of Catalonia. Main areas of interest: Sensor based robot control in rehabilitation, assistance, surgery and training.	

Caterina CINTI
Director of Operative Unit of Clinical Physiology Institute in Siena & Coordinator of WG Health- S&T Foresight Project, National Research Council of Italy (CNR)
"A fact acquires its true and full value only through the idea which is developed from it."
(Justus Von Liebig)

Senior Researcher at the Institute of Clinical Physiology from 1993. Director of the Operative Unit of Institute of Clinical Physiology in Siena Since 2006. Graduated in Biological Science at University of Bologna in 1984, board certificated in Genetic in 1987. Post-doctoral NATO Senior Fellowship in Biotechnology and Molecular Biology, at the Kimmel Cancer Institute, Thomas Jefferson University, Philadelphia, USA from 1993 to 1994. Scientific member of S.H.O. at the Jefferson Medical College, Thomas Jefferson University of Philadelphia, PA, USA from 1994 to 2002 and Adjunct Associate Professor at the College of Science and Biotechnology of Temple University, Philadelphia, PA, USA from 2002 to 2005. Tutor and supervisor of 11 PhD theses, 4 Master theses and 2 Bachelor Theses. Expert evaluator of scientific projects of several international bodies (European Commission, Italian Ministero Università e Ricerca (MIUR), Spanish Ministry of Health and Consumer's Affairs, French National Alliance for Life and Health Sciences-AVIESAN) and Editorial Boards of several peer-review journals. Author of more than 132 peer-reviewed scientific papers of which 80 on ISI journal, along with 9 books and inventor of 3 International Patents. Main areas of interest: development of pharmacologic and biologic cancer therapy, of drug delivery systems; epigenetics; tumor multi-drug resistance; computational system biology.	

Pietro CORTELLI
Full Professor of Neurology, Department of Biomedical and Neuromotor Sciences (DIBINEM), University of Bologna

Pietro Cortelli received the Diploma degree in Medicine and Surgery from the University of Bologna in 1979, the specialization in Neurology, University of Bologna in 1983 and the Ph.D., in Neurological Sciences, University of Verona in 1990. From 2014 Full Professor of Neurology, Department of Biomedical and NeuroMotor Sciences (DIBINEM), University of Bologna. Main areas of interest: 1) genetic and phenotipic prion diseases (Fatal Familial Insomnia, Creutzfeldt-Jakob, Gerstmann-Straussler-Scheinker), Parkinson's disease, Amyotrophic Lateral Sclerosis, Familial Hemiplegic migraine; 2) autonomic nervous system in health and disease with a focus on neurological control of the cardiovascular system; 3) autonomic circadian rhythms in relation to wake-sleep cycle in neurodegenerative disorders; 4) autonomic, clinical and neurophysiological aspects of mitochondrial diseases and primary headache.	

Valentin Alek DEDIU
Group leader, CNR-ISMN , National Research Council of Italy
"Mind your personal magnetism"

Born 19/02/1959 in Drochia, Moldavia, USSR; Master Thesis (1982) and PhD (1989) at Moscow Physical Engineering University. He gave about 60 Plenary, Key Note and Invited Talks at International Conferences and coordinated four European projects. Main areas of interest: charge and spin injection and transport in molecular solids; memristors, resistive bistability, various memory effects; magnetic properties of complex oxides; interfaces between magnetic and molecular solids; nanomagnetism for medical applications; magnetic diagnostics (magnetic lab on a chip); biomaterials.	

Vincenzo DI LAZZARO
Director of Clinical Neurology, Campus Bio-Medico University of Rome (UCBM)
"We need to become persons before becoming doctors"

Vincenzo Di Lazzaro is Professor of Neurology, Medical Director for Clinical Neurology and serves as Director for the Neurology Residency Program at Campus Bio-Medico Medical School. The main areas of research are the study of the physiological bases of recovery in stroke and the development of methods of neuromodulation (both invasive and non-invasive) as potential treatment tools for several neurological diseases, movement disorders and stroke in particular. Editor of Case Reports in Medicine; Editor of Neurology Research International; Editor of Behavioural Neurology; Editorial Board of Brain Stimulation. Main areas of interest: Clinical Neurology and Neurophysiology.	

Giorgio EINAUDI
Scientific Director of S&T Foresight Interdepartmental Project, CNR

Giorgio Einaudi, graduated in Physics, is presently Manager of the Italian Council for Eco-Innovation within the Sustainable Development Foundation and Member of the Board of the S&T Foresight Project. His academic career developed at the Scuola Normale Superiore of Pisa, the University of Florence, the University of Pisa, the University of California, Irvine, the University of Paris, and the Naval Research Laboratory, Washington DC. His research activity is in plasma physics with astrophysics applications. He is author of over hundred papers on refereed international journals. From July 2001 to July 2009 Dr. Einaudi was Scientific Attaché at the Embassy of Italy in Washington, acting to strengthen the S&T relationships between Italy and the USA, and developing his main activity in the fields of energy, environment and space, being an important interlocutor with American institutions as the Department of Energy, the Environmental Protection Agency, NASA, NSF, EPA and OSTP. In the past few years Dr. Einaudi has been advisor to the Italian Ministry of Environment. In particular he has created the Italian Cleantech Network of innovative companies of all sizes to facilitate the visibility of Italian "green economy" in the world. Lately Dr. Einaudi contributed to the launch of the Science and Technology Foresight Project (STFP). Form March 2008 to July 2010 he was Acting Deputy Director of ISGP directed by Dr. Atkinson.	

Abdelhamid ERRACHID EL SALHI
Full professor, University Claude Bernard Lyon1
"Overcome the challenges facing existing diseases"

Abdelhamid Errachid is a Full Professor in Claude Bernard University-Lyon. He has been involved as a principal investigator and team leader in several European Projects under FP6 (DVT-IMP, MAPTech, Nano2Life, Cell-PROM, ARES, VECTOR, SPOT-NOSED), FP7 (SensorART, BOND, SEA-on-a-chip), and H2020 (HEARTEN (Coordinator), MicroMole, DiagCan (coordinator)) as well as NATO (Coordinator), INTAS and TEMPUS International Projects and national Spanish projects (MICROMENCE, MINAHE I, MINAHE II and PETRI). Prof. Errachid is a head of the Micro/Nanotechology group and expert in the field of BioLab-on-a-chip development. Main areas of interest are: Analytical chemistry, Micro & nano-biotechnology for health.	

Eleuterio FERRANNINI
Full Professor of Internal Medicine at the University of Pisa School of Medicine

Ele Ferrannini is Professor of Internal Medicine at the University of Pisa School of Medicine; Chief of the Metabolism Unit of the CNR (National Research Council) Institute of Clinical Physiology, Pisa; and Clinical Professor of Medicine, Diabetes Division, University of Texas Health Science Center at San Antonio, Texas, USA. His professional education includes: degree in Medicine, at the University of Pisa School of Medicine, 1975; Specialty Board Certification in Nuclear Medicine, at the University of Pisa and Diabetes&Metabolic Disease at the University of Torino, 1978; Visiting Scientist at the Karolinska Institute, Stockholm, Sweden (1977-78); and NIH PhD Fellowship at Yale University School of Medicine (1978-1982).
He is a member of several scientific societies, a founding member and President of the Italian Society of Obesity. He was President on the Executive Council of the European Association for the Study of Diabetes (EASD), and has been Editor-in-Chief of the official Journal of EASD (*Diabetologia*, 1994-1997). He is the Chairman of the European Group for the Study of Insulin Resistance and a member of the EASD Foundation.
Main areas of interest: insulin resistance and atherosclerosis; oxidative stress on endothelial function; pathogenesis of the fasting hyperglycaemia of diabetes; autoimmunity in adult-onset diabetes; pathophysiology of insulin secretion; hyperinsulinaemia on autonomic nervous system function; pathogenesis of the insulin, resistance and hyperinsulinism in obesity; coronary atherosclerosis in diabetes; pathogenesis of the microvascular dysfunction and proteinuria in adult-onset diabetes.

Dimitrios I. FOTIADIS
Professor, Unit of Medical Technology and Intelligent Information Systems, University of Ioannina
"To integrate the most recent advances of multi-scale modelling in everyday clinical practice"

Dimitrios I. Fotiadis received the Diploma degree in chemical engineering from the National Technical University of Athens, Athens, Greece, in 1985, and the Ph.D. degree in chemical engineering and materials science from the University of Minnesota, Minneapolis, in 1990. He is currently a Professor of Biomedical Engineering in the Department of Materials Science and Engineering, University of Ioannina, Ioannina, Greece, and an Affiliated Member of FORTH, Institute of Molecular Biology and Biotechnology, Dept. of Biomedical Research. He has coordinated and participated in several R&D funded projects.
His research interests include modelling of human tissues and organs and intelligent wearable devices for automated diagnosis.
Main areas of interest: Biomedical Engineering, Multi-scale modelling, Decision Support Systems.

Claudio FRANCESCHI
Full Professor of Immunology and Director of the Interdepartmental Center for Studies on Bioinformatics and Biocomplexity "Luigi Galvani", University of Bologna.

Full Professor of Immunology at the Universities of Padova (1980-86), Modena (1986-1998) and UNIBO until 2013. Founder and Director of the Interdepartmental Center for Studies on Bioinformatics and Biocomplexity "Luigi Galvani", UNIBO. Director of the Dept of Experimental Pathology, UNIBO (2010-2012). Scientific Director of Italian National Research Center for Aging (INRCA, IRCCS) (1996-2005), a public institution of the Italian Ministry of Health devoted to aging research and care of the elderly. He was coordinator of several European Large Collaborative projects on Aging and Alzheimer disease and WP leader of EU projects on Proteomics and aging, Nutrition and healthy aging, Biomarkers of human aging, and on physical activity and gut microbiome changes lifelong. Main areas of interest: i) immunosenescence; ii) conceptualization of the theories of "remodelling of aging", “inflammaging”; iii) pioneering genetic, epigenetic, metabolomic, metagenomic, glycomic studies on centenarians and their offspring as model of successful aging and longevity; iv) nuclear gene and mtDNA polymorphisms associated to human longevity, Alzheimer disease and type 2 diabetes; v) new biomarkers of aging (i.e. gut microbiota).	

Sandro FUZZI
Research Director at Institute of Atmospheric Sciences and Climate, National Research Council (CNR) of Italy
“Only those who dare fly can fly” (L. Sepulveda)

Research Director of the Italian National Research Council. His main expertise is in the field of global change and the effects on climate, ecosystems and human health. Is active in European programs to transfer research results to policy makers. Has coordinated several national and international projects, among which the European Network ACCENT involving all major European Institutions in global change research. Is member of several International Panels of the European Commission, United Nations Environmental Program and World Meteorological Organization. He has participated to the writing of both the 4th and 5th IPCC Assessment Reports on climate. Dr Fuzzi has been recognised Highly Cited Researcher, among the top 1% most cited scientists worldwide in the field of Geosciences. He is also President of the public-private SME Proambiente, that operates in the field of innovation and technological transfer for environmental surveillance, protection and remediation. Main areas of interest: Atmospheric Sciences, Atmospheric composition change and effects on climate, ecosystems and human health.	

Amalia GASTALDELLI
Head of Cardiometabolic Risk Group Institute of Clinical Physiology CNR Pisa, Adjunct Associate Professor, University of Texas Health Science Center, San Antonio, Texas, USA
"The future is very open and depends on all of us. It depends on what you and I and many other people do, today, tomorrow, and the day after tomorrow" (K. Popper)

EDUCATION: 1990 Laurea in Electronic Engineering University of Padova; 1994 PhD in Biomedical-Engineering Politecnico Milano; 1995 PhD in Human Metabolism, UTMB, USA: PREVIOUS EMPLOYMENTS: 2013-14 Adj Prof. Facoltà di Medicina Scuola Superiore S. Anna, Pisa; 2008-09 Director Mass Spectrometry Lab, Fondazione Monasterio, Pisa; 2006-11 Adj. Prof. Biomedical Engineering, University of Pisa; 1996-2008 Head Mass Spectrometry Lab, IFC-CNR, Pisa; 1992-1995 Visiting Scientist UTMB, Galveston, TX USA CURRENT ACTIVITIES: Chair and founder of the NAFLD-EASD study group; Director of the European Chapter of American College of Nutrition. *Member of:* board of directors of the American College of Nutrition; committee EASL-EASD-EASO for "Clinical Practice Guidelines for the management of NAFLD"; board of the European Group for the study of Insulin Resistance; board of the Centre Européen pour la Nutrition et la Santé in Lyon, France. Main areas of interest: Cardiometabolic diseases, Metabolism, Diabetes, Obesity, NAFLD, non alcoholic fatty liver disease, and nutrition.	

Silvia GIORDANO
Full professor of Histology and Embriology at the University of Torino, Italy; Group Leader at the Institute for Cancer Research and Treatment, Candiolo, Torino, Italy.
"Dreams left in the closet are food for moths"

Dr. Giordano has a longstanding experience in the field of translational oncology. In 1989 she identified and characterized the receptor tyrosine kinase encoded by the MET oncogene and its involvement in human tumors. Recently, her work was aimed at studying the phenomenon of oncogene addiction, the involvement of tyrosine kinase receptors in human tumors, new strategies to target them and the mechanisms of resistance to targeted therapies. She also studied hepatocarcinogenesis and identified genes and microRNAs involved in the first phases of liver cancer development. Recently, she started an innovative research program on gastric cancer, aimed at identifying new therapeutic strategies for this pathology. This project is based on the generation of a platform of patient-derived xenografts, an experimental model that is a valuable tool for personalized medicine strategies. The PI published more than 100 papers in peer reviewed journals, for a total IF of 992 (average IF 9.3). She is president of the Italian Cancerology Society (SIC). Main areas of interest: Molecular Oncology, cancer therapy	

Renata GRIFANTINI
Head Translational Research at National Institute of Molecular Genetics, Milan. Italy
"Unusquisque faber fortunae suae"

In June 2016 she joined the National Institute of Molecular Genetics (Milan, Italy) as Head of Translational Research, leading research projects on the discovery of novel markers and targets for cancer and autoimmune diseases. In her previous employment (2008–2016), she was Research Director at Externautics SpA, a biotech company focused on the development of novel cancer markers and therapeutic targets. She has a multiannual industrial experience in pharmaceutical companies. She was Project Leader at Novartis Vaccines & Diagnostics (2004-2008), and at Chiron Vaccines (1996-2004) (Siena, Italy), leading research on the identification and characterization of vaccines candidates against bacterial pathogens, and in studying the immune response using innovative delivery systems. She was scientist at ENI-Research (1990-1996) conducting research in the biotechnology field. Her competences are in molecular and cellular biology, immunology, microbiology, vaccinology and biotechnology. Main areas of interest: Molecular and cell biology, vaccines, biomarkers and therapeutic targets for cancer and autoimmune diseases.	

Sandra KWEDER
Deputy Director, Office of New Drugs U.S. FDA

Education: Bachelor of Science (B.S.), Biology, General at University of Connecticut (1975- 1979); Health Policy and Administration, University of North Carolina at Chapel Hill (1980 – 1981); Doctor of Medicine (M.D.) at Uniformed Services University of the Health Sciences - F Edward Hebert SOM (1981 – 1984). She was Deputy Director, Office of Drug Evaluation IV Center for Drug Evaluation and Research, FDA from 1997 to 2000 and Deputy Director, Office of New Drugs U.S. FDA from 2000 to present. Main areas of interest: Regulatory Science & Affairs; Drug development; Public Health; internal medicine; policy analysis	

Christina KYRIAKOPOULOU
Senior Scientific officer , European Commission, Health research
"It's far more important to know what person the disease has than what disease the person has." (Hippocrates)

Christina Kyriakopoulou is Scientific officer at the "Innovative tools, technologies and concepts in Health research" Unit, the Health Directorate at the European Commission, Directorate for Health, DG Research and Innovation, European Commission. Christina Kyriakopoulou holds a PhD in biochemistry awarded by the Department of Biology, University of Athens, Greece for research studies related to post-transcriptional regulation of gene expression. She held postdoctora positions at Departments of Medical Genetics and Cell/Molecular Biology at Uppsala Universitity. Since 2003, she works as a Scientific Officer at the European Commission having as her main tasks, the future research policy design, the management and the-impact assessment of R&I projects' portfolio in the area of systems biology and its applications in medical research and clinical practice. Lately, she manages projects developing bioinformatics and computational tools for the integrative analysis of complex/heterogeneous molecular & clinical data to understand disease pathophysiology and enable personalized medicine approaches. Main areas of interest: bioinformatics and systems biology.	

Gabriella LEO
Researcher ISMN – CNR

Gabriella Leo is researcher at the Institute for the Study of Nanostructured Materials (ISMN) - CNR in Montelibretti Research Area (Rome). She holds a degree and a PhD in Physics. She has been member of expert panel for evaluation and review of FP5, FP6 and FP7 research projects. From 2008 to 2013 she has been National Seconded Expert (SNE) at the European Commission contributing to the elaboration and implementation of research and innovation policy initiatives in the field of photonics, to reinforce and coordinate photonics regional innovation clusters and national technology platforms and to promote high-quality Solid State Lighting technology in Europe. She is vice-president and founding member of the Italian technology platform for Photonics CORIFI (COordinamento Ricerca e Innovazione Fotonica Italia). Her research interests concern the investigation of structural, morphological and optical properties of nanomaterials and nanostructures for photonics and sensor applications. Main areas of interest: Physics, Materials Science, Nanomaterials, Nanostructures, Photonics.	

Giovanna LIUZZO
Professor Catholic University of Sacred Heart, Department of Cardiology, Rome, Italy

In 1992, Dr. Liuzzo started her clinical and basic research studies in the field of ischaemic heart disease; from May 1997 to November 1998 she was research fellow at the Department of Internal Medicine – Division of Cardiology and Division of Immunology – of Mayo Clinic (Rochester, Minnesota, USA); in 1999 she obtained her PhD degree at the Catholic University of Rome; from 2000 she is involved in the direction of the PhD's School of Cellular and Molecular Cardiology of the same Institution. She is also responsible of the Molecular Biology Laboratory of the Institute of Cardiology. Her research interest is primarily on the pathogenesis of acute coronary syndromes with particular attention to the role of inflammation, immunity, infectious agents, and their link with plaque rupture and thrombosis. Main areas of interest: Ischemic Heart Disease, acute coronary syndromes.	

Paul LUKOWICZ
Professor/Scientific Director DFKI & TU Kaiserslautern Universityof Technology;
Leader of Embedded Intelligence Research Group/Pervasive Health/Ubiquitous and Wearable Systems

Paul Lukowicz is Professor of Computer Science Deutsches Forschungszentrum für Künstliche Intelligenz (DFKI) and Kaiserslautern University of Technology in Germany where he heads the Embedded Intelligence group. He was previously Professor for Embedded Systems, Faculty of Informatics and Mathematics in Passau and prior to that Full Professor at the University of Medical Informatics, Health Science and Technology (UMIT) in Innsbruck, Austria. He holds an MSc. and a Ph.D. in Computer Science and a MSc. in Physics. His research focuses on context aware ubiquitous and wearable systems including sensing, pattern recognition, system architectures, models of large scale self organized systems, and applications. These include a long history of pervasive health related projects ranging from wearable monitors for cardiac patients, through smartphone based analysis of mood related disorders, to various smart home based AAL approaches. Main areas of interest: Cyber-Physische Systeme, Pervasive Computing, Soziale Interaktive Systemes, Wearable Computing, Ubiquitous Computing.	

Peter B. LUPPA
Head of the Central Medical Laboratory, Institut für Klinische Chemie und Pathobiochemie Klinikum rechts der Isar der TU München, Germany

Peter Luppa is head researcher of both the Central laboratory of the University hospital RDI and the biosensor research group in the institute. He is POCT coordinator of the RDI, Transfusion coordinator and head of the immune-hematological laboratory of the RDI. Educational Background: Study of Chemistry 1974-1980 University of Regensburg; Study of Medicine 1980-1986 University of Erlangen-Nueremberg. Doctoral examination (MD) 1986; Specialization in Laboratory Medicine 1986-1994, University hospital Grosshadern, Ludwig Maximilians Universität Munich; Postdoctoral lecture qualification 1993-1997, RDI, Technische Universität Munich. Peter Luppa is Chairman of the working group POCT of the German society for Laboratory Medicine (DGKL). Main areas of interest: Bio-sensorics and Point-of-Care Testing (POCT); Steroid biochemistry; Autoantibody analytics.	

Arianna MENCIASSI
Full Professor of Bioengineering/Medical Robotics, Area Leader of "Surgical Robotics and Allied Technologies", Scuola Superiore Sant'Anna
"Merging the accuracy of robotics with the potentials of smart and active bio-nano-materials"

Prof. Menciassi obtained the M.Sc. in Physics (Pisa University, 1995) and the Ph.D. in Bioengineering (Scuola Superiore Sant'Anna – SSSA, 1999). She teaches at SSSA and the Pisa University. She carries on an intense research and training activity at high level (master candidates, PhD students, etc.). In 2013-2014, she was Visiting Professor at the Ecole Nationale Superiorieure de Mecaniques et des Microtechniques of Besancon (France) and at the Universitè Pierre Marie Curie in Paris. She coordinates several international projects. She served in the Ed. Board of the IEEE-ASME Trans. on Mechatronics; she is Topic Editor in Medical Robotics of the Int. J. of Advanced Robotic Systems; she is Co-Chair of the IEEE-RAS Tech. Comm. on Surgical Robotics. She is IEEE Senior Member. In 2007, she was awarded with the Well-tech Award (Milan) and the Gonfalone D'Argento (Tuscany Region). Main areas of interest: biomedical robotics, surgical robotics, microsystem technology, nanotechnology, with a special attention to the synergy between robot-assisted therapy and micro/nanotechnology-related solutions.	

Luca PANI
Director General of "Agenzia Italiana del Farmaco" (AIFA)
"Be today the visionary of tomorrow"

Luca Pani, Medical Doctor, specialized in Psychiatry is an Expert in Pharmacology and Molecular Biology, and a Fellow of the National Research Council of Italy who currently serves as Director General of the Italian Medicines Agency (AIFA) and is part of the Faculty and the Department of Psychiatry and Behavioural Sciences of the University of Miami School of Medicine. Luca Pani's professional trajectory has touched several areas of expertise from preclinical study to clinical activity as well as R&D of central nervous system (CNS) drugs, along with his commitment to teaching on experimental and clinical cases. He has attended to national and international regulatory activities for the European Union. During the past decade he has prepared, evaluated and coordinated many national and international research projects and has participated in international bodies and advisory committees worldwide. He is Italian Member of the Committee for Human Medicine Products (CHMP); Member of the Scientific Advice Working Party (SAWP); participant of the Working Party on Central Nervous System (WPCNS); he serves as Chair of the European Union Management Board Telematic Committee (EUMBTC) and Chair of the European Risk Management Strategy Facilitation Group (ERMS-FG) of the European Medicines Agency (EMA) in London (UK); member of the HMA Management Group. Luca Pani is the author of over 140 scientific publications and of several volumes. He has attended more than 1000 conferences, seminars and national and international roundtables as an invited speaker.
Main areas of interest: Clinical Neurosciences and Pharmacology.

Paolo PAOLETTI
CEO of Kesios Therapeutics Ltd, London

Graduated in Medicine at the University of Pisa, Italy. NIH Fellow at the University of Arizona, USA. Professor of Pulmonary Disease at the University of Pisa, Italy. Many research assignments and grants from Italian Research Council. Member of the Executive Committee of European Respiratory Society. **Current Position:** CEO of Kesios Therapeutics Ltd (UK Private Company); 2004 – 2015 Senior executive positions in GSK (President of Oncology up to April 3 2015): **Current Board Positions:** Chairman: Psioxus (UK Private Company); Member: Nucana (UK Private Company); Member: Genmab (Danish Public Company); Member: Forma (USA Private Company).
Special Competences: Extensive experience in Research, Development and Commercialization in the Pharmaceutical Industry. Successfully conducted submissions and approvals of new cancer drugs and new indications in USA and in Europe. Seven new medicines for cancer patients during 10 years in GSK and, one new medicine while in Lilly.
Main areas of interest: oncology and drug development.

Enrico PERNA
Consultant cardiologist at Niguarda Ca' Granda Hospital, Milan, Italy

In 2009 Degree in Medicine, Sant'Andrea Hospital, University "Sapienza", Rome Italy; PhD in Cardiology (Magna cum Laude), Sant'Andrea Hospital, University "Sapienza", Rome, Italy (2015). From 2008 to 2009, he had a Scientific collaboration with "Cardiovascular Research Unit, Division of Cardioliogy and Institute of Physiology, University of Zurich - Irchel, Zurich, Switzerland". Dr. Perna is currently consultant cardiologist, specialist in heart failure, heart transplantation, ventricular assist devices, Niguarda Ca' Granda Hospital, Milan, Italy. His expertise is on Internal Medicine (General Medicine), Cardiology, Cardiothoracic Surgery. Main areas of interest: 1) heart failure, including rare cardiomyopathies, acute myocarditis, and cardiogenic shock of ischemic or non-ischemic aetiology; 2) standardised and personalised approach to medical therapy optimization, patient education, multiparameter prognostic evaluation, and planning of follow-up.	

A. Galvan QUINONES
Chief of Metabolic and Cardiovascular Risk Unit, Fondazione Toscana Monasterio/CNR, Pisa
"The future does not exist so far and if it does not exist, it is not possible to see; however it is possible to predict on the basis of present knowledge, that already exist and can be seen"
(Sant'Agostino, Book XI, Cap. 13, 18.23)

Quiniones Galvan A. is the chief of Metabolic and Cardiovascular Risk factor Unit of Fondazione Toscana G. Monasterio from 2000- to date. He graduated as Medical Doctor at Universidad Nacional Autònoma de Mèxico (UNAM), Mexico City in 1988 and received his PhD degree in Biochemistry and Nutrition at the University of Florence in 1997. He is the author of more than 100 paper in peer-reviewed journals. Main areas of interest: Internal Medicine; clinical obesity and associated conditions; metabolic diseases; personalized therapy; translational and interdisciplinary clinical research; nutrition and obesity; coronary syndrome in diabetic patients.	

Luigi RICCIARDIELLO
Professor of Gastroenterology, Department of Medical and Surgical Sciences University of Bologna
"Take personal responsibility for your life (and health)"

Luigi Ricciardiello is Associate Professor of Gastroenterology at the University of Bologna, Italy. He received his Medicine Degree from the University of Bologna in 1994. In 1997 joined the UC San Diego to perform research on colorectal cancer. From March 2005 to 2009 Prof. Ricciardiello was Senior Research Associate at Baylor University Medical Center in Dallas. He is specialized in Gastroenterology (Italy) and Internal Medicine (USA). His clinical and research activities are related to the prevention of colon cancer. He is the Coordinator of the colon cancer screening program at the University Hospital. He is principal investigator of two investigator grants from the Italian Association for Cancer Research and co-coordinator of the EU-FP7 project PATHWAY-27. He has been nominated Chairman of the National Societies Committee of the United European Gastroenterology starting his tenure on January 2017. He has been invited to lecture and to be Chairman at the major international conferences on gastroenterology. Main areas of interest: Colon cancer prevention and clinical oncology.	

Matteo SANTIN

Professor of Tissue Regeneration at School of Pharmacy and Biomolecular Sciences, University of Brighton and Leader of the Brighton Centre for Regenerative Medicine, University of Brighton.

"Balancing IP exploitation with socially-responsible licensing in areas of research of great public significance and interest"

Matteo Santin received the Honour Degree in Biological Sciences, University of Naples, Italy in 1987, the PhD in Biomaterials, University of Naples, Italy in 199 and PhD in Biomedical Sciences, University of Brighton, UK in 2001. He is currently Leader of the Brighton Centre for Regenerative Medicine and Professor of Tissue Regeneration, School of Pharmacy and Biomolecular Sciences, University of Brighton, UK. He has been reader in Tissue Regeneration, School of Pharmacy and Biomolecular Sciences, University of Brighton, UK from 2006 to 2010 and Senior Lecturer, School of Pharmacy and Biomolecular Sciences, University of Brighton, UK from 2004 to 2006. From 2001 to 2004 he has been awarded a Senior Research Fellow, EPSRC project, Title: Biocompatible coatings for cardiovascular stents, School of Pharmacy & Biomolecular Sciences, University of Brighton, UK. He also obtained research Fellows/Part time PhD student from 1992 to 2001 by School of Pharmacy & Biomolecular Sciences, University of Brighton, UK (BRITE-EuRam III EC Project Lipostin), Department of Pharmacy, University of Brighton, UK (BRITE-EuRam II EC Human Mobility Fellowship), Institute of Human Anatomy, Faculty of Medicine, University of Turin. From 1989 to 1992 he was researcher of Institute of Protein Biochemistry and Enzymology, Consiglio Nazionale delle Ricerche and in 1992 he was also Visiting Scientist, Institute of Materials Science, University of Connecticut, USA. Project title: Interpenetrated polymer network biomaterials.

Main areas of interest: Biocompatibility of biomaterials for soft tissue regeneration; Enzyme-grafting to biomaterials for biomedical and biotechnological applications; Regenerative Medicine/Biomaterials, Tissue Engineering.

Ilaria SANTONI

Research Fellow at S&T Foresight Project at CNR

"Be realistic, demand the impossible!" (Albert Camus)

Dr. Ilaria Santoni graduated in Chemistry at University of Florence in 2001 and was awarded a PhD grant in "Science and engineering of materials" from the same University in 2009. She has worked first on the Scanning Probe Microscopy (SPM) technique then in 2002 she moved in the National Research Council of Italy, Trees and Timber Institute (CNR-IVALSA) where she performed studies about wood chemistry. In 2005 she started the PhD research project concerning factors influencing wood bonding properties. Then she started to work on bio-based adhesives for wood bonding. From 2012 she was involved in study on differentiation of wood species due to provenance and characterization of densified wood and in the analysis of wood volatile organic compounds (VOC) related to air indoor quality. In 2014 she start a fellowship for manager in technology transfer and from 2015 she is involved in the Foresight Project at CNR, supporting to the activities defined by the project coordinators in the thematic areas: Food, Health, Energy and Material.

Main areas of interest: highly interdisciplinary topics ranging from wood chemistry, adhesives and material chemistry, engineering, biology, forest science, technology transfer and foresight issues.

Gérard SIEST

President of European Society of Phamacogenomics and Personalized Therapy (ESPT)

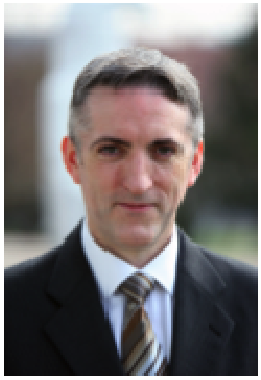
"La liberté de choisir est un facteur essentiel de la condition humaine mais qui ne permettrait que des choix capricieux si elle n'était orientée par une vision de l'avenir" René Dubois (Choisir d'être humain).

Pharm.D., PhD specialization in Biochemistry, Haematology, Bacteriology, Immunology. Gerard Siest is Professor of Molecular Biology and Biochemical Pharmacology at the Faculty of Pharmaceutical Sciences, University Henri Poincaré Nancy 1 (Emeritus). He was Director of the postgraduate course in Biochemical Pharmacology (1977-2003) and Founder and member of Directing Group of DU "Thérapie Personnalisée – Pharmacogénétique". Prof. Siest is a member of the Board of the International Society of Pharmacogenomics (ISP) (since 2002), Editor in Chief of Drug Metabolism and Drug Interactions (since 2010) and Editor in Chief of Drug Metabolism and Drug Interactions (DMDI) (till July 2015). He is also member of the Editorial Boards of: Pharmacogenomics (since 2005); Personalized Medicine (since 2006); International Journal of Clinical Pharmacology and Toxicology (IJCPT) depuis 2013; Pharmacogenomics and Proteomics (since 2014); Practical Laboratory Medicine (since 2014). Prof. Siest is President of the European Society of Pharmacogenomics and Personalised Therapy (ESPT) (since 2011), Member of the « Agence Européenne du Médicament » (EMA), London - CHMP Pharmacogenomics Working Party (since 2014), Doctor Honoris Causa from Laval and Krakow Universities and member of the Royal Academy of Medicine in Belgium. He was recipient of 27 awards from 16 different countries. Main areas of interest: pharmacogenomics and drug metabolizing enzymes and transporters; cardiovascular biomarkers and systems biology for personalized health for cardiovascular drugs; pre-analytical variations of proteomic biomarkers and reference values.	

Stephen J. TAYLOR

Director of Marketing, Communications and Business Development, AREA Science Park Trieste

"The future is already here, it's just not evenly distributed"

Stephen Taylor has over twenty five years-experience as a Director and Senior Consultant, helping major firms and government agencies in Europe and North America to access the latest knowledge and expertise for analysis and planning for new business, market research, new product development, and technology commercialization. His collaboration with AREA Science Park (Trieste) started at the beginning of 2009 and in September of the same year he was appointed as Director of the Technology Transfer Department to optimize strategic activities for technology transfer. Since January 2010 he sits on the board of Innovation Factory S.r.l., the in-house incubator of AREA Science Park, with specific responsibility for business competitiveness and internationalization and in May 2011 he was named CEO. In 2015 he became Director of Marketing, Communications and Business Development of AREA Science Park. He is Specialist in Foresight and Technology Road-mapping. Main areas of interest: Technology Transfer, Valorisation of Research, Pre-incubation, incubation and acceleration of technology-based Start-ups.	

Luisa TONDELLI

CNR Senior Scientist, Head of Unit for Research Internationalisation at CNR Department of Chemical Sciences and Materials Technology.

***"The future is uncertain but this uncertainty is at the very heart of human creativity"* (Ilya Prigogine)**

PhD in Biochemistry, Master Degrees in Industrial Chemistry and Biotechnology. Member of the Executive board and co-chair of Health Working Group within S&T Foresight Project (CNR). Italian National Expert in Horizon 2020 Nanotechnology, Materials, Biotechnology and Production (NMBP) Programme Committee and Sherpa of the High Level Group on Key Enabling Technologies (European Commission). 2007-2011: Seconded National Expert at DG Research (European Commission) - Research Programme Officer in Nanotechnology and Advanced Materials Units of the Directorate for Industrial Technologies and Communication Officer. 1986-2007: Research activity in Bioorganic Chemistry and Biomaterials Science: synthesis and characterization of nucleic acids derivatives as potential antitumor and antiviral agents, development of innovative polymeric nanoparticles for in-vivo delivery of biomolecules for therapeutic and vaccine applications. Co-author of 4 EP/WO patents and more than 100 papers and communications on international peer-reviewed journals and conference proceedings. Main areas of interest: European strategies for Materials Science Research and Innovation.	

Maria Giovanna TRIVELLA

CNR First Investigator/Head of UOS IFC-CNR Milano Niguarda, Head of Experimental Laboratory Pisa

"From the guidelines era to the precision medicine, towards health frontiers"

Medical Doctor (1976 Pisa University), Cardiologist. Awarded by the European Science Foundation for the Exploratory Workshop "Molecular signaling in cardiovascular and oncological disease: similar and shared pathways", Pisa July 2008. Participant in the bilateral project FIRB Italy–Canada, IFC-CNR e IBD-NRC, "New imaging techniques for the understanding of cardiac disease mechanisms and their management". Participant to the ARTreat Project, Information and Communication Technologies (ICT) FP7-224297 for Large-scale Integrating Project (IP), "Multi-level patient-specific artery and atherogenesis model for outcome prediction, decision support treatment, and virtual hand-on training". Coordinator of a Large-scale Integrating Project (IP): "SensorART - A remote controlled Sensorized Artificial heart enabling patients empowerment and new therapy approaches" (FP7-ICT-248763), 2010-2014. Participant to Micro-VAST Project "Microsystems for VAscular diagnosticS and inTervention", Fondazione CARIPI. Participant to ENCODER Project "Engineered Nanostructures for Cellular imaging and for intracellular delivery of Optically active Drugs for cardiac hypertrophy", within the CNR Nanomax Flagship Project. Participant to SMART HealthyEnv Project "A Smart Monitoring System for a Healthy ENVironment ", Tuscany Region. Research Unit responsible, CNR project on ICT application for Health and Society (e-SHS), 2014-2015. Application specialist and Ethical&Privacy Issues Manager in H2020 HEARTEN project "A co-operative mHEALTH environment targeting adherence and management of patients suffering from Heart Failure". Main areas of interest: cardiology; translational and interdisciplinary research; experimental medicine; cardiovascular research; pathophysiology; validation of medical devices, sensors and actuators.	

3.3. EXPERTS' CONTRIBUTION TO THE PREPARATION OF THE WORKSHOP

Fiorella BATTAGLIA

Assistant Professor, Faculty of Philosophy, Philosophy of Science and the Study of Religion. Ludwig-Maximilian-Universität. Munich.
Responsible of research and innovation ethical issues.

"Justice is the first virtue of social institutions" John Rawls, A Theory of Justice

1. State-of-the-art on "Theranostics for P4 Medicine" and the current socio-economic situation.

Feasibility/Ethical Sustainability and Legal and Political Enforceability. From an ethical point of view it's not the feasibility of emergent technologies, which is most important, but their compliance with moral beliefs and regulation. Life Sciences research yields constant progress in the understanding of the structure and function of the human body. This knowledge is fundamental for the development of new diagnostics and treatments for patients and for the increasing of a healthy life for everyone. Furthermore, Life Sciences research has implications for politics of health. Investigating the ethical, political, and social aspects of research and recent advances in the field is of major importance. This knowledge helps to ensure medical methods and findings are utilized in a valuable way for our society.

Often we are dealing not only with existing applications but also with visions. What is wrong with visions? There should be further ethical investigation about what it means to deal with not yet existing innovation. A strong interdisciplinary and societal effort is required. In order to ensure that there will be an implementing process for the development of P4 Medicine, there has to be cooperation between those who develop the technologies, clinicians, industry, researchers from STS, and ethicists exploring the normative dimension. The political and technical feasibility, on the one hand, and the enforceability of the law, on the other, follow different paths of rationality. Technology must be made accessible to everyone in order to allow an improvement of the human condition. Changing what it means to be human is not just a matter of technological progress but also of human intentions, beliefs and actions.

2 Long-term future needs, bottlenecks, knowledge gaps and future actions that should be adopted in the development of P4 Medicine.

The need for an analytical and case-by-case approach. Facing the great number of potential applications of P4 Medicine and further, the variety of features these exhibit, make a dealing with P4 Medicine as a homogenous field impossible. The move from one particular method to a common objective does not help to develop a general approach. There should be an adaption of a case-by-case approach in order to carry out an investigation, which can be exhaustive and precise, but also gives room for further generalization, at the same time.

Legal conditions need to be created in order to ensure equal accessibility to innovations. Such a path is not characterized by paternalism, but rather by a civil rights underlining model.

If an innovation is considered as "desirable" by society, supporting policies for industrial research must be ensured. An insurance as such could help to provide the necessary conditions for the development of supporting policies.

Privacy and security issues need to be properly considered. The collecting, storage, and access to data have to comply with the EU-Legislation

3. Actions that should be addressed for Social Acceptability of future P4 Medicine

We need to deal with ethics earlier. This means a development of innovations in the medical field, has to ensure an acceptance through society at an early stage. Technological innovation must go hand in hand with social innovation. The high societal relevance of health research is underlined by continuously high public interest and ongoing public discourse on this topic.

There is no gap between two cultures: science and society need not be bridged. Rather science and technology are rooted in a tradition that demands that scientific theories fulfil certain definite humanistic requirements. These different dimensions of the human life-form should keep communicating in order to allow a development of responsibility within science (research ethos) and responsibility towards society.

Instead of talking about social acceptability we should rather talk about measures to strengthen autonomy, justice and dignity. This approach would implement one of the principles of the RRI: the co-creation of knowledge. This is not so far from one of the 4 pillars of P4Medicine: the participatory pillar.

Enrico CAPOBIANCO

Head of Computational Biology & Bioinformatics, Center for Computational Science, University of Miami.

"What's the difference between God and a doctor? God doesn't think to be a doctor"

1. State-of-the-art on "Theranostics for P4 Medicine" and the current socio-economic situation.

Big Data are currently a solid perspective for only part of the biomedical community. This is due to the fact that on one side computational and data scientists are very much engaged with Big Data, from genomics to electronic health records, and develop methodological tools, data repositories and warehouses and decision support systems of clinical use. On the other hand, clinical specialists and biologists tend to consider Big Data a sort of cloud whose contents are not distinctly clear. This limitation calls for further integration between the disciplines, and for the search of a new communication language. Teams of experts work now more than in the past together, but additional efforts are requested to improve the synergy.

Research grants are consistently stimulating the recalled integration, and this seems a trend destined to continue.

2 Long-term future needs, bottlenecks, knowledge gaps and future actions that should be adopted in the development of P4 Medicine.

Big Data (5-10 years scenario).

A computer-assisted clinical decision making context is based on a few assumptions:

1-Every patient is one sample, and the information embedded is relevant in a population context more now than in the past, due to the role of experimental omics and electronic health records

2- Each patient, each disease, each diseased cell are different, according to personalized and precision medicine principles, and linked to lots of generated data that need to be put in a context, possibly a model designed to learn and generalize (predictive modeling).

3 - Newly designed smart tools are necessary for assembling evidences and connecting data. This calls for novel inference tools, data-driven and model-free or agnostic.

Novel data visualization solutions will allow Big Data to unleash its true impacts linked to the integrated approaches in biomedicine, involving structured vs unstructured data, lossless compression, cloud systems, health ecosystems.

Deep phenotyping (10-20 years scenario)

Need to develop suitable analytical backbone by identifying Decision Support Systems tools for efficient communication between computational and clinical scientists and physicians. A productive data utilization will complement doctors' experience to the benefit of patients.Knowledge from symptoms data and evidences multitude need to be better connected to be effective in clinical care.

Translational Health (> 20 years scenario)

1-Integrative medicine is the expected benchmark, leveraging over digital health and next generation medical tools (patient-centered DB resources, inference signatures allowing profiling, risk assessment and predictive interventions).

2-Electronic Health Systems will represent complex junctions of phenotypes, and repurposing these phenotypes will be central to Precision Medicine.

3- Big Data will yield a new disease taxonomy inspired by genotype-phenotype relationships, but will also expand knowledge beyond symptoms and test data due to the integration of heterogeneous information.

Nonetheless, treatment of biases and confounders, design of flexible clinical decision support systems (i.e. enabling automated covariate selection), elaboration of new social network metrics (i.e. allowing sensitivity analyses and ad hoc propensity scores), remain challenges destined to become soon either strengths or weaknesses of new scientific thinking.

3. Actions that should be addressed for Social Acceptability of future P4 Medicine

I envision the following actions, and related consequences.

1-Team Work at the labs and outside the labs: better synergy between clinics, academics and industry.

2-Science Focus (not only business): big challenges need big ideas and cross-contamination between disciplines.

3-Public Awareness: data transport from industry to individuals and consumers (healthy or not), and increasing role of Socials.

4-Data Liquidity: digital biomarkers (metadata) and patient avatars (supermodels).

Alicia CASALS

Professor, Head of the Associate researcher at the Institute for Bioengineering of Catalonia (IBEC)

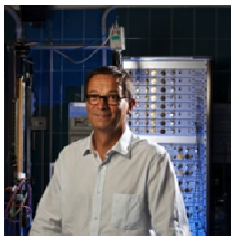
"Sensor based robot control in rehabilitation, assistance, surgery and training."

1. State-of-the-art on "Theranostics for P4 Medicine" and the current socio-economic situation. Robotics has applicability in health, in areas like diagnostic, surgery, rehabilitation and assistance in daily living. Strengths: Robotics is a mature technology, able to provide the accuracy that human hands lack. Robotics can also bring the physical support necessary in rehabilitation and provide a better complementarity to the performances of the monitored person. Robotics benefits from the advances in Artificial Intelligence and Big Data to improve its performance. Weaknesses: Still heavy equipment, burden set up, administrative and legal obstacles, including patents. The technical weak point is registration, the fact of having to relate robot coordinates with the user and objects or organs. Uncertain data obtained from biological and physiological signals. Technological limits to fit application requirements. The need to deal with no predictable events, in real time. Opportunities: Much effort in robotics: reaching the target, the position, measuring for monitoring /control... can be shared both in therapy and diagnosis. As intensive domestic automation has brought technology at home, medicine and health will be achievable in the future for Daily Living Assistance. Threats: The use of technology at home, in daily life, can become obsessive (as happen with games). Lengthening life further than the point it can't provide fullness living.

2 Long-term future needs, bottlenecks, knowledge gaps and future actions that should be adopted in the development of P4 Medicine. We can distinguish the contribution of robotics in surgery-treatment and in rehabilitation-assistance. In the next 5-10 years it is expected a significant advance in the development of new and lighter robotic systems for rehabilitation and for monitoring the user. For this, it is necessary to progress in the concept of soft robotics including materials, actuators, batteries and sensors, achieving more power, flexibility, miniaturization, kinematic architectures, etc. User engagement is also a key factor which requires intelligent and friendly interfaces: In rehabilitation this could be serious games (cognitive, motivation) or compliant devices and cooperative control strategies for human-robot physical interaction. The former implies user's motivation and involvement. In surgical robotics surgeon-system efficient interaction can pass through the availability of augmented reality for situation awareness or for higher levels of cooperative control, meaning more robot adaptability to the context. Dealing with big amount of data (big data) corresponding to a complex reality can bring access to results obtained in similar situations that can be rare, only occurring in special cases, as for illnesses affecting 1 out of 1000 people or so. The need of efficient computational techniques, better algorithms and strategies, since problems as registration for navigation in surgery should be solved in real time. Translational medicine should start to be compulsory so as to see the interaction between therapies, treatments and patient attitude, being robotics part of them. Conclusion: Current developments are still big and too expensive to spread its use (i.e, the Da Vinci surgical robot that costs $2 Million). Next 10-20 years: Progress in miniaturization and nanotechnology should help to give a new jump to personalized medicine through for instance, sending a drug to the adequate part or organ of the body. Improvement of navigation techniques, external monitoring, tracing, will help to perform better surgery and expand its reach. Besides the availability of new devices, the decrease of the cost of this technology will facilitate its expansion. Over 20 years: While current devices introduced into the body are externally guided (magnetically), future nanodevices entering into the body will be guided by their own nanocomputers, which intercommunicated will form a cooperative net for efficient treatment. The continuous changing and advancements in technology should also lead to more flexible regulation that adapts to the new contexts. For instance, in surgical robotics much evaluation on animal experimentation are required, while much more can be learnt and evaluated in specific laboratory environments with repetitive trials, quantitative measuring and programming progressive level of difficulty and possibility of separating problems. Global policies and technology should advance together.

3. Actions that should be addressed for Social Acceptability of future P4 Medicine. The application of robots in medicine is continuously growing even considering the difficulties in continuously adapting to the levels of uncertainness that physical and cognitive interaction with humans implies, as well as to changing conditions. For its acceptance, technology should engage the user either for its efficiency, ease of use, its size and appearance or its cost. The four P conditions are essential in assistive robotics, in rehabilitation and in robotic surgery. Robot designers should be humble and honest in the sense of trying to look for simple systems as much as possible and avoid unnecessary equipment, against what marketing interests might look for. Legal and public policies should facilitate the deployment of robotics technology that follows ethical principles, making sure that it is at the user's reach when needed.

Pietro CORTELLI



Full Professor of Neurology, Department of Biomedical and Neuromotor Sciences (DIBINEM), University of Bologna.

1. State-of-the-art on "Theranostics for P4 Medicine" and the current socio-economic situation.

For all the most common neurodegenerative disease (ND) age is its major risk factor. Despite this evidence, the relationship between cellular/molecular alterations in physiological ageing and those underpinning Parkinson Disease (PD) pathogenesis are unclear. We hypothesize that ND might be consider as a sort of segmental ageing. At least in part, progressive decline of neurological fitness and a degree of physiological ageing with anatomo-pathological signs of neuronal degeneration in the brain characterize both elderly with and without clinical sign of PD. Parkinsonism has an incidence of 18.6 %. However, an anatomo-pathological investigation on subjects without PD (mean age 88.5 yrs.) who donated their brains showed: i about 1/3 of cases had mild or more severe nigral neuronal loss; ii. about 17% had Lewy bodies; iii.10% of the brains showed both nigral neuronal loss and Lewy bodies (*Buchman et al, 2011*). Thus, there is an apparent continuum between healthy ageing and neurodegenerative age-related motor disorders resulting from the combined effects of ageing and genetic and environmental risk factors (lifestyle/nutritional/environmental determinants, exposure to toxicants). This calls for challenging work to be done to identify the proper conceptual and structural framework to study ND. Outside such a framework the application of OMIC technologies is probably useless and the P4 medicine will remain a chimeras.

2 Long-term future needs, bottlenecks, knowledge gaps and future actions that should be adopted in the development of P4 Medicine.

The main scientific question answer to drive significant advances in the P4 medicine of neurodegenerative disorders is to why is advancing age the most important risk factor for developing idiopathic AD, PD, and other cognitive and motor diseases? This very simple question poses the study of neurodegenerative disorders (ND) into a new rationale that starts from the hypothesis that the environment feeding ND onset and progression is the elderly physiology. This new perspective assumes ND as totally embedded within the basic molecular and cellular mechanisms of the ageing process, *e.g.* accumulation of senescent cells and the low grade, chronic inflammatory status named "*inflammation" ("neuro-inflammaging"* in the brain), among others (*Franceschi et al., 2000; Cevenini et al., 2013; Vitale et al., 2013; Chinta et al., 2013*).

To achieve a significant advance in the P4 medicine in ND, OMIC technologies has to applied be on very informative cohorts of patients and controls that maximise the differences between groups and that allow to pose ND OMIC characterisation in the frame of ageing physiology. Such human models could be:

i) Twin models of ND (concordant and discordant)
ii) well charcterized cohorts of de-novo patients, recruited at the time of the diagnosis
iii) the identification of cohorts of probants at high risk to develop ND to identify early risk bio-markers
iv) longevity cohorts to be used as gold standard references and to identify protective factors

3. Actions that should be addressed for Social Acceptability of future P4 Medicine

There is the need to generate tools that allow the maximal access of present and past datasets in the respect of person's privacy. Equally urgent is the need to move significant advances in generate legal and technical tools that allow an higher integration between private profit subjects and public ones as it is rather unreal that P4 medicine, once realised, will be cost effectively distributed to the general population only by public health care systems.

Vincenzo DI LAZZARO

Director of Clinical Neurology, Campus Bio-Medico University of Rome (UCBM).

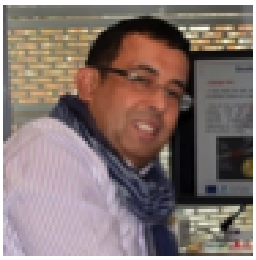
"We need to become persons before becoming doctors"

1. State-of-the-art on "Theranostics for P4 Medicine" and the current socio-economic situation. The growth in the elderly population is paralleled by a substantial increase in the number of patients with neurological disorders because of the high incidence of both vascular and neurodegenerative diseases over the age of 65. At present, no cure is available for most of the degenerative diseases, first of all Alzheimer's disease, and the current therapeutic opportunities are restricted to an extremely restricted time window for cerebrovascular diseases. Thus, a large percentage of the world population is at risk for dementia, severe disability and dependency. On the other hand, the current global financial crisis has a negative impact on research funding. However, recent advances in the knowledge of the mechanisms of degenerative diseases (e.g. prion-like mechanisms), together with the impressive amount of new data on the mechanisms of inflammatory disorders (also the discovery of new inflammatory disorders previously considered degenerative in nature) and the emergence of new therapeutical approaches (e.g. electroceuticals and focused ultrasound) pave the way to innovative treatment for several neurological disorders presently considered with no cure. Recent studies have also shown that even disorders that were considered not preventable (first of all Alzheimer's disease) can be prevented in a significant percentage of individuals through an intervention on several risk factors, but these interventions have not been implemented. Finally, new diagnostic tools have been developed with the identification of new biomarkers of neurological disorders (e.g. antibodies against neural antigens) and the introduction of new imaging techniques (e.g. PET studies for amyloid detection in the brain). But, again, these new tools have not completely developed and are largely underused.

2 Long-term future needs, bottlenecks, knowledge gaps and future actions that should be adopted in the development of P4 Medicine. The main present obstacles in neurological research are represented by: the limited amount of funding for this specific area of medicine; the extreme parcelization of the studies in neurological field, we still have a large number of studies involving a few patients with no possibility to draw any definite conclusion. This is due both to the limited resources but also to the limited number of neurological network worldwide that can implement larges studies; the lack of integration between basic and clinical research, thus some advancements in basic knowledge do not have an effect on clinical research and, also, some clinical studies do not have a strong rationale provided by basic research; limited information about ongoing research available to patients and their family, this impairs the rate of recruitment in the studies and make it difficult to complete those studies in a reasonable time interval.

3. Actions that should be addressed for Social Acceptability of future P4 Medicine. One key feature could be the empowerment of associations of patients promoting an integration of these associations with scientific societies and the institutes were research and studies are performed (Universities and research institutes). The ongoing studies and the future directions of the different sub disciplines of neurology should be made available for the public access through the media with regular reports from scientific societies. The emerging areas of research in Neurology are represented by: diagnosis and treatment of neuroimmunological disorders; characterization of biological basis of neuropsychiatric disorders, this is an emerging field that requires attention because some organic diseases mimicking psychiatric disorders have been identified in recent years; change the perspective form the current disease targeted intervention to patient targeted intervention by the characterization of different phenotypes of the same disorder (e.g. motor neuron disorders, multiple sclerosis), this process can be implemented by charactering genetically the patients and by developing new biomarkers of ne urological diseases. This is relevant also because genetic characteristics might influence also the response to treatment; implement neuro-modulation techniques capable to make the human brain interface in order to make it possible to send information in the brain even in the presence of disorders of the senses and let information out of the brain even in the presence of movement disorders; to develop models of the brain reflecting the human connectome; to develop physical therapies (e.g. magnetic and electric fields, ultrasounds) for neurological disorders.

Abdelhamid ERRACHID EL SALHI



Full professor, University Claude Bernard Lyon1.

"Overcome the challenges facing existing diseases"

1. State-of-the-art on "Theranostics for P4 Medicine" and the current socio-economic situation.

Theranostics is a combination of diagnosis and therapeutics and is focused on patient-centered care. Theranostics provides a cost-effective specific successful treatment protocol. It deals with the custom made treatment plan based on uniqueness of every individual thus resulting in right drug for the right patient at the right time. Pharmacogenetics, proteomics and biomarker profiling forms the backbone of theranostics. Thus, theranostics is a holistic transition from trial and error medicine to predictive, preventive and personalized medicine leading to improved quality care of pharmacotherapy. However, the weakness is the following: it must have a strong interaction with the Lab-on-a-chip bio-analysis in order to obtain a more efficient pharmacotherapy.

2 Long-term future needs, bottlenecks, knowledge gaps and future actions that should be adopted in the development of P4 Medicine.

The most important future action that should be adopted in the development of P4 Medicine is the management. The future success of approach will depend the standardization of data inputs and, indeed, participation of patients willing to share personal data, development of the necessary technological infrastructure, training of personal and of course establishment of appropriate regulatory mechanisms.

Citizens need to be confident about the responsible, transparent and accountable management of ethical, legal and social concerns

3. Actions that should be addressed for Social Acceptability of future P4 Medicine

Citizens and patients must increasingly taking advantage of social media and new technologies to share information about their own health and lifestyle. They must take responsibility for their own health through active monitoring, prevention measures and even direct treatment choice.

Dimitrios I. FOTIADIS

Professor, Unit of Medical Technology and Intelligent Information Systems, University of Ioannina.

"To integrate the most recent advances of multi-scale modelling in everyday clinical practice"

1. State-of-the-art on "Theranostics for P4 Medicine" and the current socio-economic situation.

Strengths: Theranostics in P4 medicine is especially relevant in the field of multiscale modelling for diseases simulation. Specifically, multiscale modelling addresses all different aspects.
Predictive: Multiscale models are able to simulate future conditions and predict future outcomes
Preventive: Since by predicting future progression and outcomes helps towards prevention
Personalized: The data needed for multi-scale models are patient specific
Participatory: The medical professional and the patient can both design therapeutic strategies based on the preventive and predictive strategy.
Weaknesses: Still, very few multi-scale models have been tested and validated in large scale clinical trials, making their adoption difficult.
Opportunities: There are plans to perform large scale validation, as it has been shown that multi-scale models can provide cost effective solutions for P4 and social impact.
Threats : The patient specific data needed to simulate the multi-scale models are usually costly, threatening their wide usage.

2 Long-term future needs, bottlenecks, knowledge gaps and future actions that should be adopted in the development of P4 Medicine.

Short term Needs .
The need for large-scale clinical studies. In order to achieve the acceptance of the development of P4 Medicine platforms and tools, besides the validation with a large number of well characterized patients and to validate its utility in clinical practice, large-scale studies are required.

Short-medium-long term Bottlenecks
Lack of incentives to Healthcare system and towards the application of the developments in P4 medicine in the clinical practice. In order to avoid this, evidence that shows increased efficiency vs remuneration will be provided.
Missing regulations for the take up of new developments. For this, documented recommendations to regulatory bodies, taking into account the European guidelines and identified limitations as well as medical software directives should be provided.

Medium-long term Future actions
In order to maximize the impact of the recent developments in P4 Medicine, they should receive the CE marking and be characterized as medical software and/or other relevant safety standards; these processes require long time and as such, should be performed in the medium and long term.
What can be performed in the short term, among other are: integration of data and models, formulation of decision support systems, 3D visualization tools, set of cloud environments, HCI user interfaces, small scale validation, cost effectiveness analysis and assessment of behavioral, ethical, legal, social and regulatory implications).

3. Actions that should be addressed for Social Acceptability of future P4 Medicine

In order to address social acceptability for P4 Medicine in the future, several actions are required to address the 4P dimension
Large scale clinical trials of models/tools/algorithms used in order to validate in a wide population their efficacy
Dissemination of the validation results and raise awareness in all different stakeholders, from micro level (patients and patients' associations), to meso level (medical experts and healthcare organizations) and to macro level (regional, national and international health authorities)
Costs: Reduction of the costs of the patient specific examinations that are needed for simulating the models/tools/algorithms
Public health policy: Compensation of new examinations required and informed decisions for introducing P4 medicine tools in everyday clinical practice as well as in the healthcare authority level

Amalia GASTALDELLI

Head of Cardiometabolic Risk Group Institute of Clinical Physiology CNR Pisa, Adjunct Associate Professor, University of Texas Health Science Center, San Antonio, Texas, USA.

"The future is very open and depends on all of us. It depends on what you and I and many other people do, today, tomorrow, and the day after tomorrow (K Popper)"

1. State-of-the-art on "Theranostics for P4 Medicine" and the current socio-economic situation.

Strengths: opportunity to early identify/prevent the progression of disease by having immediately the most appropriate treatment.

Weaknesses: initial cost. Early markers of disease are often not available. Very often tests are expensive and thus not performed since the disease might be at early stage and not yet threaten. Need to educate MDs.

Opportunities: to have better treatments, prevent progression of diseases, better quality of life and public and private economical advantage in the long term

Threats: Move the attention from treatment to prevention. Since at the beginning the cost is high and the economic advantages are seen in the long term, it might not be considered a priority. If there is no collaboration between politics and researchers it will never be put in place.

2 Long-term future needs, bottlenecks, knowledge gaps and future actions that should be adopted in the development of P4 Medicine.

The EU has already identified personalized medicine as a priority for the best heath care of this millennium. However, I think genomics is not the answer to every question because most of the diseases are multifactorial. On the other hand, some environmental issues should be taken into account: Type of food, use of some type of fats (hydrogenated oils, palm oil etc), sedentarity due to use of elevators and cars, chemicals in food and packaging that act as endocrine disruptors.

Education of people and MD should be planned together with screening for disease prevention.

3. Actions that should be addressed for Social Acceptability of future P4 Medicine

Move the attention from treatment to prevention and education to healthy lifestyle.

Silvia GIORDANO

Full professor of Histology and Embriology at the University of Torino, Italy; Group Leader at the Institute for Cancer Research and Treatment, Candiolo, Torino, Italy.

"Dreams left in the closet are food for moths"

1. State-of-the-art on "Theranostics for P4 Medicine" and the current socio-economic situation.

Strengths: We now know that cancer is a gene disease and we know the alterations that characterize many forms of cancer. Moreover, in recent years, technology has deeply improved, thus allowing many discoveries. Weakness: Our analyses focus only on a minor part of the genome, leaving most of it unexplored. In everyday life, much of what we know is not used in clinical practice. Opportunities: To improve treatment by applying a good quality precision medicine. Threats: Costs of precision medicine are very high. Knowledge is often not applied in clinical practice. Cancer centres are often not ready to translate the new knowledge into clinical practice. The NHS often does not allow treating patients with the correct molecular therapy. There is the need of more bio-informatic competences. Lack of an adequate ethical regulation for the report of the molecular analyses is also a threat.

2 Long-term future needs, bottlenecks, knowledge gaps and future actions that should be adopted in the development of P4 Medicine.

We have to change the paradigm of cancer treatment to correctly apply precision medicine to cancer patients. Many clinical trials are still designed using old schemes, without a correct preselection of patients and thus with a high risk to waste drugs that are potentially useful but have been tested in the wrong context. This is negative both in prospective terms and in terms of costs. Moreover, the NHS system often does not allow providing the correct treatment to patients. This is a serious bottleneck. Big "umbrella" international trials should be designed to allow treatment of patients with specific molecular alterations for which an effective drug is available but not yet approved for that specific indication. Big international consortia should be created in order to share resources and technologies, in order to increase the quality of the analysis and to decrease costs.

3. Actions that should be addressed for Social Acceptability of future P4 Medicine

More efforts should be done to better explain the aims and the limits of precision medicine not only to patients but to the whole population which is often exposed to inappropriate information. This means that exaggerated optimism should be avoided in the divulgation of results. Moreover, appropriate information could:

1) convince the non-experts that this kind of research is not under the control of pharma, trying to drive the clinic; 2) make clear that the decision to apply or not a therapy depends only on the presence of a particular molecular context.

Peter B. LUPPA

Head of the Central Medical Laboratory, Institut für Klinische Chemie und Pathobiochemie Klinikum rechts der Isar der TU München, Germany.

1. State-of-the-art on "Theranostics for P4 Medicine" and the current socio-economic situation. Point-of-care testing (POCT) is a laboratory medicine discipline that evolves rapidly in analytical scope and clinical application. At present, POCT ranges from basic blood glucose measurement to complex viscoelastic coagulation assays. POCT shortens the time to the clinical decision-making about additional testing or therapy, as delays are no longer caused by transport and preparation of the clinical samples, and the biochemical test results are rapidly available at the point of care. Improved medical outcome and lower costs may ensue. For this thesis, however, evidence is still missing. For improving the current socio-economic situation throughout the European countries, this is urgently needed.

2 Long-term future needs, bottlenecks, knowledge gaps and future actions that should be adopted in the development of P4 Medicine.

The POCT process is truly innovative in healthcare, since it offers new possibilities for prevention, diagnosis, and monitoring of diseased subjects. As Price and St. John (2014) pointed out, while underlying analytical technologies hold some clever inventions, "genuine innovation can only come about if the invention is applied in a useful way" within the healthcare system to deliver an enhanced value for the patient. But it should be recognized that for POCT an additional principal catalyst for the innovation process is the patient himself, which reinforces the importance of POCT. Consequently, the benefits of a POCT process management are only to be reaped if cooperation with the core competences of the central laboratory exists. If there is complementary understanding between POCT specialists and laboratory experts, a reconfiguration of clinical pathways can significantly improve the overall patient outcome. A good example of this improvement is the self-testing of glucose or PT/INR by diabetics or patients under anticoagulation. These subjects use the self-monitoring to adjust treatment. There are studies available, which show that a better disease management improves outcomes in a way that has not been possible before the advent of the respective POCT technologies. Innovation in healthcare means novel ways for care, being delivered to the patient. In the context of many health challenges in developing countries, it becomes apparent that POCT most likely offers such changes. The transforming effect of POCT can be verified by the fact that the increasing number of malaria tests has already reduced significantly inappropriate anti-malaria treatment during the last decade. The role of the central laboratory, however, is still very important, even when POCT is applied. Test results alone are useless, as laboratory experts play an important clinical role for the support of the physicians as consultants in hospitals and for outpatient areas. They provide helpful advice for the interpretation of results, comment on pre- or post-analytical errors, recommend follow-up tests, and provide as POCT coordinators the quality management of the patient-near testing. What makes POCT attractive, is that there has been a 2-step paradigm shift occurring in the last decade: 1. POCT was originally a supplement of the central laboratory and defined as hospital bedside biochemical testing with a limited test portfolio. Now, POCT is often used as the sole diagnostic approach in developing countries without a central laboratory infrastructure. 2. An additional shift arises from the insight that until today laboratory medicine focused on measuring a high number of parameters in the human body with sophisticated methodologies, whereas POCT analysis has a restricted number of parameters with robust devices for many subjects that are self-determined customers or indigent patients in developing countries.

POCT is a type of sustaining technology, to be defined as "disruptive innovation", a term first generated by Christensen et al (2009). Besides genetic testing, promoted to the general public and matrix-assisted laser desorption/ionization time-of-flight mass spectrometry for the rapid identification of bacteria and fungi, POCT was also identified as a disruptive innovation with the potential to offer healthcare solutions with new performance metrics. There are also several limitations for the further evolution of POCT. First, in industrialized nations with central labs, the application of POCT is self-limiting and depends on establishment of new and reliable parameters, which, in clinical disciplines, remain elusive. Second, a global problem for the dissemination of POCT is that reimbursement systems often can't keep up with the technological changes in clinical diagnostics and, thus, hinder the further evolution. Third, further limitations for the development of novel POCT were caused by the market failure of non-invasive devices, having been under development for decades.

3. Actions that should be addressed for Social Acceptability of future P4 Medicine. The POCT market in the EU has an annual turnover of more than 3.5 billion Euros, with the home care sector accounting for a major market share. During the last decade, the market size for POCT grew constantly by more than 10%, which can be partly explained by the new trend towards quantified-self measurements by laypersons. As promoted by pharmaceutical services, an increasing demand for direct-to-consumer (DCT) testing is currently underway, where the subject is no longer a patient but a consumer. Moreover, concerns about health have become integral parts of normal life. The "Quantified Self" movement mirrors this new normality. Healthy individuals measure many aspects of their daily life to gain new insights from this data and reach self-defined goals. These analyses rely on measurements from activity trackers or wrist-bands. However, there is a growing demand to also include biochemical markers. Due to their ease of use, POCT seems to be pre-designated to fulfil this need. The testing process chain: patient – doctor – laboratory – doctor – patient is shortened to patient –laboratory – patient. This conceals many dangers for the patient, such as poor control of appropriateness and preanalytical requirements, as well as test panels, which are based on unsupported scientific data. POCT experts should ensure that this development should be controlled in a coordinated way.

Arianna MENCIASSI

Full Professor of Bioengineering/Medical Robotics, Area Leader of "Surgical Robotics and Allied Technologies",Scuola Superiore Sant'Anna.

"Merging the accuracy of robotics with the potentials of smart and active bio-nano-materials"

1. State-of-the-art on "Theranostics for P4 Medicine" and the current socio-economic situation. In relation to this area, a very brief SWOT analysis is reported below. STRENGHTS: 1) very active field of research and development, with the involvement of companies and end-users; 2) many research avenues to be discovered, giving the possibility to pursue basic research for disruptive innovation as well as incremental developments. WEAKNESSES: 1) missing key technologies (in terms of powering, communication, signal processing, etc.) hamper the development of P4 Medicine solutions; these key technologies are not covered by traditional efforts in Theranostics; 2) missing of standardization in evaluating research outputs and missing of clear pathways (in terms of costs and time) for clinical translation. OPPORTUNITIES: 1) growing interest in the field from end-users, stakeholders and new generations (many students worldwide decide to study biomedical engineering and biomedical robotics). THREATS: 1) failure of some key technologies and not fulfilment of people expectations could decrease the confidence of end-users for Theranostics.

2 Long-term future needs, bottlenecks, knowledge gaps and future actions that should be adopted in the development of P4 Medicine. Theranostics for personalized/precision medicine can be perceived and approached under different perspectives. From the robotics viewpoint, there are some issues to be taken into account when defining future scenarios: nowadays, for any specific anatomy, any specific age and any specific condition of patients, it is possible to select the most adequate/acceptable/safe diagnostic solution; patient screening is becoming more and more common and early disease detection is more and more possible. Consequently, we need therapeutic solutions which are acceptable for a-symptomatic patients, which are able to treat early diseases at the level of few cells, which are very targeted and with limited side effects. On the other hand, with the aging population, we need more and more therapeutic solutions for chronic patients which could be adopted for many years with a limited burden for people, for the healthcare system and for the society. In this scenario, we are assisting to a growing quest for miniaturization and natural access to the targeted pathologies. This quest will lead to the development of diagnostic and surgical tools to be delivered with an endoluminal and transluminal approach - such as endoscopic capsules, injections, inhalation - and to be controlled, steered and propelled by remote operation schemes from outside. In addition to the traditional control of remote devices into the body, external sources have been used for stimulating internal devices and triggering some therapeutic effects from outside, in a non-invasive way. These external sources can be based on magnetic fields, ultrasound waves or laser beams, which can directly deliver their energy to the target area or which can activate responsive (bio)materials inside the body. The quest for targeted therapy has opened new opportunities for robotic technologies, which can be used more and more as controllers for the delivery of drugs embedded in nanobiotech vectors and as solutions for making therapy really localized in the area of interest, enabling on-demand release kinetics and eliminating (or strongly limiting) side effects. Exploring the above mentioned opportunities requires many interdisciplinary competences and shared methodologies, such as: identification of the unmet medical needs for specific anatomies/pathologies. Robotics is fundamental for many therapies, but the time and costs of robotic diagnosis/therapy/surgery must be accurately considered before embarking a robotic approach; merging the typical accuracy and reliability of robotics with the potential of smart materials, drug delivery, nanomedicine, for a concrete and ultimate targeting action; defining from the beginning the testing methodologies, protocols to carry out studies and to evaluate their outputs, pathways to preclinical and clinical studies; allocating resources for developing fundamental technologies, which could solve many problems for personalized and targeted therapy/diagnosis. E.g.: the lack of efficient power sources with miniature size is the real bottleneck for the development of wireless in-body tools for therapy/diagnosis. On the other hand, typical efforts for theranostic and personalized medicine consider these technologies as something already available per se (even if it is not like this).

3. Actions that should be addressed for Social Acceptability of future P4 Medicine. The social acceptability of P4 Medicine is related to some objective and subjective considerations. P4 Medicine social acceptability depends mainly on: 1) the cost effectiveness of the process going from research to clinical application and validation. Keeping time and cost under control, without generating anticipate expectations in people, is one of the most important issues; 2) the reliability of the P4 Medicine results, especially in terms of predictive/diagnostic medicine; 3) the proved effectiveness of personalized treatment in comparison with traditional treatment; 4) the clear and transparent methodology for patient recruitment for specific therapies: in many cases the potentials of P4 Medicine are presented without specifying that the patients who could benefit from the P4 solutions are a sub-set of the overall patients; 5) the education to correct prediction and prevention, for fighting the psychological barrier which links them to the fear of diseases.

Luca PANI

Medical Doctor, specialized in Psychiatry is an Expert in Pharmacology and Molecular Biology, and a Fellow of the National Research Council of Italy. Director General of the Italian Medicines Agency (AIFA). Faculty member of Dept. Psychiatry and Behavioural Sciences, Univ. Miami School of Medicine, USA.

"Be today the visionary of tomorrow"

1. State-of-the-art on "Theranostics for P4 Medicine" and the current socio-economic situation.

Theranostics is a combination of diagnostics and therapy. There are 3 different scenarios for a Theranostic: development of a therapeutic product and then of a diagnostic one; diagnostic product followed by a therapeutic one; co-development of the two, made possible by nanoparticles. What is exciting is the opportunity to have a real-time evaluation at the same time of the delivery of the drug. The weakness of this new approach of treatment may be represented by the lack of knowledge of the regulators with respect to theranostics. Another important challenge is for sure the assessment of short and long term toxicity. From an economic point of view, beyond undisguised medical benefits that can be provided by theranostics, also new industries can expect economic benefits from research in this field. Moreover the personalization of medicine can be seen as cost saving for Health Systems; so despite an uncertain cost of these new technologies, savings can still be predicted in long term.

2 Long-term future needs, bottlenecks, knowledge gaps and future actions that should be adopted in the development of P4 Medicine.

An important future need is the clarification of the approval process for combined products of theranostics. Moreover an important definition should be given, whether or not we are talking about drugs or medical devices. Another big challenge for regulators is that of achieving the appropriate knowledge of these technologies in a short period of time, in order to assess and evaluate the dossier of upcoming products. This implies the drafting of specific guidelines and specific training courses for the assessors. The Pharmaceutical companies should therefore start an early dialogue with the regulators in order to accelerate the whole process.

3. Actions that should be addressed for Social Acceptability of future P4 Medicine

Together with efficacy of new treatments there is a growing tendency to consider the social acceptability. This new patient-centred approach for the development of innovative medicines is fundamental especially for some diseases for which there is no strong evidence of efficacy, at least not enough data to support it and for sure not definitive.

In those case, when proposing a Theranostic, the patient's preferences should carefully be considered and expert physicians should explain the different therapeutic options. It must be clear that there are unknown risks and other unknown factors.

A. Galvan QUINONES

Chief of Metabolic and Cardiovascular Risk Unit, Fondazione Toscana Monasterio/CNR, Pisa.

"The future does not exist so far and if it does not exist, it is not possible to see; however it is possible to predict on the basis of present knowledge, that already exist and can be seen" (Sant'Agostino, Book XI, Cap. 13, 18.23)

1. State-of-the-art on "Theranostics for P4 Medicine" and the current socio-economic situation.

STRENGHTS: 1) Increased knowledge about causes and effects of obesity 2) Increased medical, public and political perception of the importance of obesity and related disorders as a crucial disease and not as a " simple associated condition". 3. Increased perception of the economic burden of obesity.
WEAKNESSES: 1. Complexity and great heterogeneity of the cause (s) and clinical effects of obesity 2. Persistence in clinical grounds, of the application of common and scarcely evidence-and-scientific-based (presumptions) for the study of the pathophysiology, diagnosis, treatment and prognosis of obesity and related disorders 3. Common transference of the responsibility (guilt) of the disease to the patients and families. 4. No clear nor immediate political and managing perception about the enormous impact of obesity on social health systems.
OPPORTUNITIES: 1) The increased prevalence of human obesity and related disorders offers a vast field of opportunities for investigate, at the population, clinical and laboratory level, the causes, effects, potential treatments and prognosis of obesity and related disorders. 2) Interdisciplinary interactions, including educational, genomic, proteomic pharmacological and nutraceutical developments for the cure of obesity and related disorders.
THREATS: 1) Fragmentation of medicine 2) Continued use of "presumptions" and conceptual generalizations about obesity 3) Lack of a clear perception of the long term effects of obesity and related disorders.

2 Long-term future needs, bottlenecks, knowledge gaps and future actions that should be adopted in the development of P4 Medicine.
According to the WHO, by 2015 near 2 billion adults, >18 years were overweight, with 600 million of obese. Overall, about 13% of the world's adult population (11% of men and 15% of women) were obese in 2014. The worldwide prevalence of obesity more than doubled in 35 years form 1980 and 2014. Obesity is not only a high-income country problem: overweight and obesity are now on the rise in low- and middle-income countries. In developing countries the rate of increase of childhood overweight and obesity has been more than 30% higher than that observed of developed countries.
Potential scenarios: It has been well described in trend analysis the scenario for the next 5 years:. Obesity will be present in 3 out of 4 Americans by 2020 and trend analysis shows a similar curve in nearly all European, Latina-American and even asiatic countries. If no solution will be found and this trend continues, many of our own descendants will be probably obese-overweight in the next 10-20 years.
Potential strategies:
a) Combine obesity-prevention policies like health promotion campaigns (elementary schools), taxes, subsidies, and government regulations, with individual approaches. The family doctors can be at the center of the ecosystem together with their patients in order to maintain implemented, specific information and monitoring. Dissemination work of the meaning of 4P medicine and associated theranostics activities must be done at different levels and for different stakeholders, including governments, universities, industry, health systems and social networks.
b)Multidisciplinary teams must be prepared by university and master courses: investigators (young an seniors) able to understand different cognitive levels (from the lab to clinical and social level) together with a strong specific, background preparation should be selected and inserted in training in order to educate highly trained individuals with specific characteristics, without risk of fragmentation of medicine. We can learn from the experience of some sub-specialties, such as Cardiology and Tropical Medicine, that has been associated with significant improvements in the managing of heart and transmittable diseases respectively.
c) Basic and clinical research must be strongly encouraged at multidisciplinary level; universities and research centers. government and industry must actively participate in this process.

Luigi RICCIARDIELLO

Professor of Gastroenterology, Department of Medical and Surgical Sciences University of Bologna.

"Take personal responsibility for your life (and health)"

1. **State-of-the-art on "Theranostics for P4 Medicine" and the current socio-economic situation.** Besides great efforts in understanding the biology of cancers, recent trends show that the incidence and mortality are on the rise, in particular in low and middle-income countries. Increasing trends of certain cancers are rapidly rising in the young population, which is not the target of screening programs. The cost of cancers has been estimated at a whopping €126 billion in the EU in 2009, that inevitably will lead in the future to few resources to manage and treat cancer patients. Also, the increasing burden of cancer related to obesity is alarming since obesity (especially in young subjects) is becoming one of the strongest risk factors for subsequent cancer development. The management of cancer is extremely expensive because of the nature of the disease and the cost of treatments. At this moment we have far-from-optimal screening tests for early detection and prevention (with significant economic burden), while cancer molecular testing (based on a handful of markers) are helpful for directing treatments which are, though, all protocol-based. Recent advances in cancer research have provided new drugs, in particular immunotherapies, for poorly-responding cancers. Yet, the use of these molecules follows steps that involve different lines of therapies. Thus, for both cancer prevention and treatment a need for a more precise/personalized approach must be envisioned in the near and long-term future.

2 Long-term future needs, bottlenecks, knowledge gaps and future actions that should be adopted in the development of P4 Medicine. First: This is not related to technology; but we need to make sure that the societal trends can change for our children's children in the very next future. Meaning, the alarming trends in cancer incidence and mortality (some of them seen in our country) need to change. Only a quick implementation of cancer prevention programs/campaigns at the national and/or regional levels aimed at primary prevention and early detection is likely to have a major impact in reducing the projected burden. And this will have a huge impact on the economy with resources that can be shifted in the future toward a precision/personalized medicine. Second: precise/personalized cancer screening/diagnosing. There is an urgent need to develop molecular tests for screening/diagnosing. One example for all: FIT for colorectal cancer. It is the screening method used in most European countries including Italy. It has a very low sensitivity but good specificity: it can hardly diagnose someone with adenomatous polyps, the precursor lesion leading to invasive cancer. The test needs to be repeated every two years, with important economic burden related to second level test capacities (colonoscopy). Right now we have 50% of uptake of the screening within the target population → 6% are FIT positive → only 33% have adenomas or cancer → 66% are negative. So we need better screening tests. We have fecal DNA testing (the first report is dated 1992) which was approved last year in the US but the sensitivity for adenomas is low. Circulating free-cell DNA can be found in premalignant carriers or in early cancers (the so called liquid biopsy). So finding carriers with specific pre-malignant features can be key for early treatment and prevention of further malignancy.Also we need to know more about those 33%. Why are they positive? What is their specific lifetime risk? Do we have information that couple DNA profile, lifestyle, environment etc. that can lead to a specific risk? We have increasing colon cancer cases in young subjects outside the target population: thus knowing a person lifetime risk can be extremely important in order to direct that subject to specific tests for that specific cancer (through the establishment of algorithms). Omics approaches can help us understanding possible risk stratifications. Thus, in the mid-term we need to implement highly precise tests that can help identifying those at very high risk of developing cancer. Tests that can be performed in 30 years by the primary care physician or the patient himself allowing to establish whether the patient is at high risk, and direct him/her to next generation, molecular-based screening tests. Third: precise/personalized chemoprevention. Tumors can be prevented with the use of drugs or even natural compounds/dietary approaches. For example, we know that long-term use of baby aspirin protects toward the development of colon cancer, but the drug can have important side effects. We now understand that not all aspirin takers are protected, because specific genome profiles confer resistance to aspirin treatment. Thus, omics can provide to each subject a profile of possible specific genes that can confer sensitivity or resistance to potentially preventive treatments, targeting those who can really benefit from them. Also, omics will provide clues on each person real risk related to specific lifestyle adoption, thus providing the subject a knowledgeable approach to primary preventive measures through the diet and activity. Fourth: precise/personalized treatment. In 2016 we are able to collect a cancer tissue from a patient and reproduce it (as a 3D culture, called organoid) in the lab. This is a huge step forward, since we can combine the genetic profile of a subject with the molecular features of his/her cancer. Importantly, we could test multiple agents directly on the organoid and see which combination works better. In the midterm/30 year future, we won't have cancer protocols, but treatments that will be specifically tailored on the patient's cancer and his/her genetic background. This will avoid the wasting of resources and the administration of potentially harmful (rather than beneficial) treatments. And through nanotechnologies, cancer-directed drugs will be precisely delivered to tumor cells and the effects on the patient monitored real-time through advanced imaging technologies.

3. Actions that should be addressed for Social Acceptability of future P4 Medicine. 1) Establishing the usefulness for the population (for screening tests and prevention) and patients (for treatments). This will come from for serious, reliable, large-scale data that will meet social acceptability. Showing clear benefit from new technologies must be science-based. 2) Making drugs more affordable, reducing waste of resources, with case-based treatment. 3) New screening technologies must be cheap and easy to reach everyone, reducing disparities across regions, simple to administer and with a fast turnaround. 4) Increasing the engagement between patients and providers, by providing real-time information on patient status, advancements and results. Empowering the patients is key.

Matteo SANTIN

Professor of Tissue Regeneration at School of Pharmacy and Biomolecular Sciences, University of Brighton and Leader of the Brighton Centre for Regenerative Medicine, University of Brighton.

"Balancing IP exploitation with socially-responsible licensing in areas of research of great public significance and interest"

1. State-of-the-art on "Theranostics for P4 Medicine" and the current socio-economic situation.

Currently, R&D in Theranostics has failed to provide a systematic programme for applications in Medical Devices and Regenerative Medicine. Only sporadic evidences have been provided linking novel biomaterials able to act simultaneously as therapeutics and diagnostics. These include for example new biospecific contrast agents for clinical imaging where the conventional contrast agents have been functionalized with molecules enabling biospecific recognition for some pathological conditions. Scaffolds have also been magnetized that could be useful not only for tissue engineering, but also to monitor the regeneration of the tissue and the degradation of the implant.

It is conceivable that most of the life style disease (cardiovascular and osteochondral-pathologies, diabetes, etc) can benefit from early diagnosis and treatments by the means of biomaterials able to support cell-based therapies or drug delivery while being monitored with imaging and sensing methods. The availability of these biomaterials will enable the personalized treatment of each patient mainly through minimally-invasive implantation procedures based on the injection of biomaterials or nanoparticles.

2 Long-term future needs, bottlenecks, knowledge gaps and future actions that should be adopted in the development of P4 Medicine.

It is likely that such a novel class of biomaterial will be regulated in a more stringent manner by the new regulatory framework and need higher level of investments. This will be a bottleneck for the development of new products alongside a lack of communication with investors and biomedical or pharmaceutical companies. A mapping of the available technologies and expertise should be performed in the next 5 years and their integration favoured through strategies of Open Innovation within 10 years where companies with complementary expertise are coordinated to the development of new products and IP protected through joint ventures. New products could indeed emerge in the long term that are based on the merging of existing technologies.

3. Actions that should be addressed for Social Acceptability of future P4 Medicine

It is necessary to establish a strong PPI agenda and include representative of the public and patients in key panels and committees. There is a need to address IP issues linked to new technologies of impact on problems of large societal scale such as diabetes where public/private enterprises should absorb the risk and ensure the widespread access of the developed technology leveraging private interests with strong claims of public-interest.

Gérard SIEST

President of European Society of Phamacogenomics and Personalized Therapy (ESPT).

"La liberté de choisir est un facteur essentiel de la condition humaine mais qui ne permettrait que des choix capricieux si elle n'était orientée par une vision de l'avenir" René Dubois (Choisir d'être humain).

1. State-of-the-art on "Theranostics for P4 Medicine" and the current socio-economic situation.

ESPT has decided not to use the word theranostics which was in the first name of ESPT. Patients were not understanding what it is.

We prefer to use pharmacogenomics which give the best examples of personalised medicine, term too largely used in scientific meetings, papers… but its exact definition is vague and unclear. The current definition proposed by the E U commission seems the most appropriate "medical model using molecular profiling for tailoring the right therapeutic strategy for the right person at the right time and / or to determine the predisposition to disease and / or to deliver timely and targeted prevention".

Laboratory medicine, laboratory diagnostics is playing a preeminent even predominant role which is probably much larger than that of any branch of science and medicine.

2 Long-term future needs, bottlenecks, knowledge gaps and future actions that should be adopted in the development of P4 Medicine.

- Real personalized medicine is not dealing only with the control of our personal health but also it should correspond to modification of our life style and a new definition and proposition of the society involvement.
- Education of clinicians and patients are required.
- Research should be done for mastering new technologies.

But simultaneously we should be careful with all the "*phraseologie methodologique*" which are used without also clear definition and being an "*effet de mode"*

- o systems
- o models
- o structures
- o functional
- o information

and are not based on enough serious researches and trials.

3. Actions that should be addressed for Social Acceptability of future P4 Medicine

- We need to demonstrate personal benefit in place of clinical benefit.
- We should abandon the biostatistics risk prediction models
- We should replace the traditional diseases classification particularly the chromic ones.
- We should train the patient to collect with high quality the phenotypes which are necessarily in addition to the "omics" (questionnaires, events collections, focus on laboratory quantitative phenotypic data.
- The patient is part of the strategy and not only a consumer of technology.
- The familial aspect has also a great importance.

Maria Giovanna TRIVELLA

CNR First Investigator/Head of UOS IFC-CNR Milano Niguarda, Head of Experimental Laboratory Pisa.

"From the guidelines era to the precision medicine, towards health frontiers"

1. State-of-the-art on "Theranostics for P4 Medicine" and the current socio-economic situation.

STRENGHTS: 1) very active field of clinical research and patient care, with application of different implantable and wearable medical devices; 2) experimental models of pathophysiological conditions to mimic human diseases.

WEAKNESSES: 1) complexity for clinical data sharing procedures; 2) different database for multiple protocols in different institutions; 3) property of data of medical doctors, hospitals, manufacturers; 4) ethical issues for genetic/epigenetic data; 5) high costs; 6) difficult utilization of analytical methods produced for humans in the animal samples.

OPPORTUNITIES: 1) with the patient in the centre, in a vision of precision medicine, specific data collection and optimization of sharing data; 2) interdisciplinary interactions.

THREATS: 1) overcoming the barriers of clinical arena; 2) fragmentation of medicine.

2 Long-term future needs, bottlenecks, knowledge gaps and future actions that should be adopted in the development of P4 Medicine.

As indicated above, fragmentation of medicine and excessive compartmentalization of specialization areas can constitute the most critical limits for a real 4P medicine application.

The exponential acquisition of knowledge elements within a single specialty could further increase the critical situation for creating a real active and competent medical team in order to have a feasible 4P program. Furthermore, the technological innovation of ICT tools oblige to organize a dedicated effort in training health professionals as well as patients.

The family doctors can be at the centre of the ecosystem together with their patients in order to maintain implemented, specific information.

Dissemination work of the meaning of 4P medicine and associated theranostics activities must be done at different levels and for different stakeholders.

Multidisciplinary teams must be prepared by university and master courses: versatile researchers able to listen and understand different languages together with a strong specific, background preparation should be selected and inserted in training.

A systems biology and medicine roadmap must be defined and prepared by a given specific program in order to reinforce their knowledge.

From my point of view, also the order of the 4 P must be changed: Personalised, Participatory, Preventive, Predictive.

3. Actions that should be addressed for Social Acceptability of future P4 Medicine

Strong political actions for clinical sharing data from one side and for "technological" cultural programs from the other side must be required.

Dissemination activities to reassure people about "new" therapeutic and diagnostic tools must be actively made, by a program of continuous information of advantages together with a clear picture of the risk assessment→ transparent and responsible research platform.

3.4. LIST OF PARTICIPANTS

Name	Surname	Affiliation	Email
Luigi	Ambrosio	National Research Council - CNR, IT	direttore.dsctm@cnr.it
Ezio	Andreta	S&T Foresight Project, National Research Council - CNR, IT	andreta@libero.it
Daniela	Banti	S&T Foresight Project, National Research Council - CNR, IT	daniela.banti@cnr.it
Cecilia	Bartolucci	S&T Foresight Project, National Research Council - CNR, IT	cecilia.bartolucci@cnr.it
Fiorella	Battaglia	Ludwig-Maximilian-Universität. Munich, DE	fiorella.battaglia@lrz.uni-muenchen.de
Daniele	Biglino	S&T Foresight Project, National Research Council - CNR, IT	daniele.biglino@ic.cnr.it
Patrick	Boisseau	Nanomedicine European Technology Platform	patrick.boisseau@cea.fr
Gabriele	Bronzetti	University Hospital Policlinico Sant'Orsola-Malpighi, IT	gabronz@hotmail.com
Enrico	Capobianco	Centre for Computational Science - University of Miami, USA	ecapobianco@med.miami.edu
Alicia	Casals	Universitat Politècnica de Catalunya, ES	alicia.casals@upc.edu
Caterina	Cinti	S&T Foresight Project, National Research Council - CNR, IT	caterina.cinti@cnr.it
Pietro	Cortelli	Dept. Biomedical & Neuromotor Sciences, Univ.Bologna, IT	pietro.cortelli@unibo.it
Luca	De Biase	Sole 24 Ore – Nova, IT	luca.debiase@ilsole24ore.com
Valentin Alek	Dediu	S&T Foresight Project, National Research Council - CNR, IT	v.dediu@bo.ismn.cnr.it
Vincenzo	Di Lazzaro	Campus Bio-Medico University Hospital, IT	v.dilazzaro@unicampus.it
Giorgio	Einaudi	S&T Foresight Project, National Research Council - CNR, IT	einaudi5250@gmail.com
Abdelhamid	Errachid	Inst.Analytical Sciences, Claude Bernard Univ. Lyon 1, FR	abdelhamid.errachid@univ-lyon1.fr
Eleuterio	Ferrannini	Department of Internal Medicine, University of Pisa, IT	ferranni@ifc.cnr.it
Dimitrios	Fotiadis	Dept. Materials Science & Engineering – Univ. Ioannina, EL	dimitris.fotiadis30@gmail.com
Claudio	Franceschi	University of Bologna, IT	claudio.franceschi@unibo.it
Sandro	Fuzzi	S&T Foresight Project, National Research Council - CNR, IT	s.fuzzi@isac.cnr.it
Amalia	Gastaldelli	National Research Council – CNR, IT	amalia@ifc.cnr.it
Silvia	Giordano	University of Torino Medical School, Torino, IT	silvia.giordano@unito.it
Renata	Grifantini	INGM, National Institute of Molecular Genetics, IT	grifantini@ingm.org
Sandra	Kweder	Food and Drug Administration, USA	kweder@cder.fda.gov
Christina	Kyriakopoulou	DG Research - European Commission	christina.kyriakopoulou@ec.europa.eu
Gabriella	Leo	S&T Foresight Project, National Research Council - CNR, IT	gabriella.leo@ismn.cnr.it
Giovanna	Liuzzo	Università Cattolica Sacro Cuore - Milan, IT	giovanna.liuzzo@gmail.com
Paul	Lukowicz	Institute of Pervasive Technologies, DFKI GmbH, DE	paul.lukowicz@dfki.de
Peter	Luppa	Inst Klinische Chemie und Pathobiochemie, Univ.Munich, DE	p.luppa@tum.de
Arianna	Menciassi	Department of Biorobotics, Scuola Superiore S. Anna, IT	arianna@sssup.it
Luigi	Nicolais	University of Naples, IT	nicolais@unina.it
Augusta Maria	Paci	S&T Foresight Project, National Research Council - CNR, IT	augustamaria.paci@cnr.it
Luca	Pani	M. Miller School of Medicine, University of Miami - US	lpani@med.miami.edu
Paolo	Paoletti	Kesios Therapeutics, UK	paolo.paoletti.priv@gmail.com
Enrico	Perna	Niguarda Hospital Ca' Granda, IT	enrico.perna@ospedaleniguarda.it
Luigi	Ricciardiello	Dept. Medical Science & Surgery, Univ. Bologna, IT	luigi.ricciardiello@unibo.it
Matteo	Santin	School Pharmacy & Biomolecular Sciences, Univ. Brighton,UK	m.santin@brighton.ac.uk
Ilaria	Santoni	S&T Foresight Project, National Research Council - CNR, IT	ilaria.santoni@ic.cnr.it
Gerard	Siest	University of Lorraine, Nancy, FR	
Stephen	Taylor	Area Science Park, Trieste, IT	stephen.taylor@areasciencepark.it
Luisa	Tondelli	S&T Foresight Project, National Research Council - CNR, IT	luisa.tondelli@cnr.it
Maria Giovanna	Trivella	S&T Foresight Project, National Research Council - CNR, IT	trivella@ifc.cnr.it

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