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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

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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, pharmaceuticals, 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) Next-Generation Sequencing (NGS), Next Generation Interference (e-health, computerization / standardization), trans-omics imaging & quantitative multi-scale power. 3) DEVELOPMENT OF <i>IN-VITRO/IN-VIVO</i> 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) CONVINCING 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	<ol style="list-style-type: none"> 1. X PUBLIC / PATIENT INVESTMENT (group sensitive science). 2. X INFORM POPULATION on nanomedicine. 	<ol style="list-style-type: none"> 1. XXXXXXXX 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. 	<ol style="list-style-type: none"> 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			<ol style="list-style-type: none"> 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).

<p>ENABLING TECHNOLOGIES</p>	<p>1. XX OMICs PROFILE of physiopathology cancer and neurodegenerative diseases:</p> <p>A) X next-generation Sequencing (NGS) TRANS-OMICS imaging + quantitative multiscale power.</p> <p>B) X next-generation Interference (e-health, computerization /standardization of protocols for data and validation).</p> <p>2. X CLINICALLY REFLECTIVE IN VITRO /IN VIVO MODELS for nanotoxicology.</p> <p>3. DEVELOPMENT OF NANO-ELEMENTS tool box.</p> <p>4. BIOMARKERS OF ORGAN REJECTION.</p>	<p>1. XXXXX EXPANSION OF SMART PHONES-BASED PoC TESTING (glucose etc).</p> <p>2. XX SMART T-SHIRT TO DETECT MARKERS (i.e. cardiac stress condition and heart reaction) EARLY DETECTION PREVENTION.</p> <p>3. X FLEXIBLE, INDUSTRIALLY, FEASIBLE PLATFORM/ TECHNOLOGY enabling MINIMALLY INVASIVE THERANOSTICS (e.g. nanosized materials).</p> <p>4. X CONVINCING SOCIETY TO CHANGE TECHNOLOGIES (e.g. glucose).</p> <p>5. BLOOD TESTS for Alzheimer.</p> <p>6. TRANSPLANTATION IMMUNOSUPPRESSANT DOSAGE.</p> <p>7. SMART DECISION SUPPORT SYSTEMS for therapy.</p> <p>8. WIRELESS COMMUNICATION with theranostic nanostructure.</p> <p>9. Mini-RNA FOR THERANOSTICS (e.g. diabetes).</p> <p>10. MONITORING DRUG AND MULTIPLE DRUGS IN SINGLE TESTS TO AVOID TOXICITY AND OPTIMIZE EFFICACY.</p> <p>11. PERSONALISED THERAPY FOR CARDIAC DISEASE (non invasive cardiac cell therapy in cat-lab).</p>	<p>1. X TISSUE SPECIFIC SYNTHETIC extra-cellular matrix and growth factors analogues.</p> <p>2. BIORECOGNITION PROGRAM for enabling technologies (contrast agents ecc).</p> <p>3. Effect on health of use of NANOPARTICLES IN COSMETICS (like asbestosis).</p>
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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 (<i>Coordinator ST&B Foresight Project, CNR, Italy</i>)
11:15	Introduction	Caterina Cinti (<i>Topic Coordinator ST&B Foresight Project, CNR, Italy</i>) and Stephen Taylor (<i>Director of Technology Transfer, AREA Science Park, Trieste, Italy</i>)
11:45	Nanotechnology	Fabio Beltram (<i>Scuola Normale Superiore, Pisa, Italy</i>)
12:00	Nanomagnetics	Mike Coey (<i>Trinity College, Dublin, Ireland</i>)
12:15	Point-of-care	Larry Kricka (<i>University of Pennsylvania, USA</i>)
12:30	Q&A	Discussion session
13:00		Lunch break
14:00	Tissue regeneration	Matteo Santin (<i>University of Brighton, Brighton, UK</i>)
14:15	Artificial organs & surgery	Antonio Amodeo (<i>Ospedale Pediatrico Bambin Gesù, Roma, Italy</i>)
14:30	Q&A	Discussion session
15:00	System biology & medicine	Enrico Capobianco (<i>Centre of Computational Science, Miami, USA</i>)
15:15	EU health foresight	Susanne Giesecke (<i>Austrian Institute of Technology, Wien, AT</i>)
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 (<i>Moderator: Stephen Taylor</i>)	
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	
<p style="text-align: center;">SHORT TERM VISION (5-10 years)</p> <p>a) Which are necessary steps in the evolution of the longer term solutions?</p> <p>.....</p> <p>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?</p> <p>.....</p>	<p style="text-align: center;">LONG TERM VISION (> 10 years)</p> <p>.....</p> <p>.....</p>

2. STATE OF THE ART	
<p>STRENGTHS</p> <p>.....</p> <p>.....</p>	<p>WEAKNESSES</p> <p>.....</p> <p>.....</p>
<p>OPPORTUNITIES</p> <p>.....</p> <p>.....</p>	<p>THREATS</p> <p>.....</p> <p>.....</p>

NAME

AREA OF EXPERTISE

RESEARCH FIELD

ANNEX III - List of participants to the Workshop:

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

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