European Science Foundation Policy Briefing

ESF Scientific Forward Look on Nanomedicine

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The European Science Foundation acts as a catalyst for the development of science by bringing together leading scientists and funding agencies to debate, plan and implement pan-European initiatives.

Foreword

Recent years have witnessed an unprecedented growth in research in the area of nanoscience. There is increasing optimism that nanotechnology applied to medicine will bring significant advances in the diagnosis and treatment of disease. However, many challenges must be overcome if the application of nanomedicine is to realise improved understanding of the patho-physiological basis of disease, bring more sophisticated diagnostic opportunities and yield more effective therapies. Both the optimism and the challenges have prompted governmental science and funding organisations to undertake strategic reviews of the current status of the field [1-4], their primary objectives being to assess potential opportunities for better healthcare as well as the risk-benefit of these new technologies, and to determine priorities for future funding.

In 2004, the European Science Foundation launched its Scientific Forward Look on Nanomedicine. I am pleased to see the successful conclusion of this foresight study, which has been the first such exercise focused on medical applications of nanoscience and nanotechnology. The Forward Look involved leading European experts and led to a definition of the current status of the field and debates on strategic policy issues. This Policy Briefing concentrates on the forward-looking recommendations and in doing so provides only a very brief summary of the in-depth discussions which will be fully presented in a detailed report. Implementation of these recommendations should ensure continuing European leading-edge research and development in nanomedicine, resulting in reduced healthcare costs and the rapid realisation of medical benefits for all European citizens. ESF will commit itself to taking the initiative and facilitating the relevant bodies, including ESF Member Organisations and the European Commission, for actions based on these recommendations.

Bertil Andersson
ESF Chief Executive

Introduction

The Medical Standing Committee of ESF (EMRC) initiated the Scientific Forward Look on Nanomedicine with the aims of:

- defining the field and reviewing the current state-of-the-art
- identifying Europe's strengths and weaknesses
- delivering recommendations on
  - future research trends
  - organisational and research infrastructures at both the national and European levels to support coordinated scientific activities
  - mechanisms to facilitate effective dissemination of information to the general public and policy makers.

The ESF Forward Look on Nanomedicine was conducted through a Steering Committee, a series of five specialised workshops involving small groups of experts from academia and industry (1-5 March 2004) and a final Consensus Conference (8-10 November 2004) attended by more than 70 representatives from academia, industry, private foundations and governmental agencies supporting scientific research.

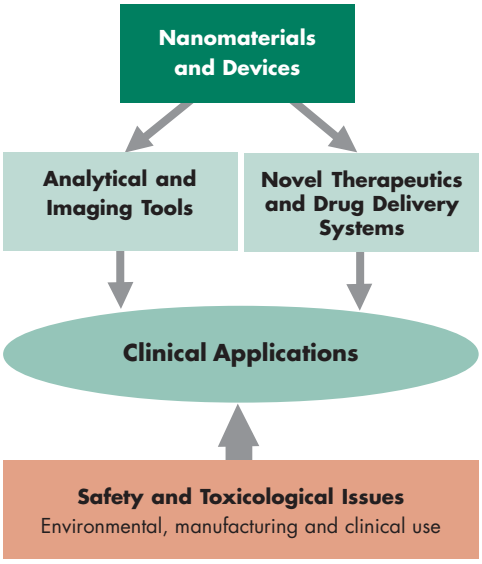

Figure 1. Nanomedicine: towards improved healthcare

The full report and the recommendations of this Forward Look will be published separately. The purpose of this Policy Briefing is to provide a brief scientific background on nanomedicine, and an overview of the principal observations and recommendations.

Background

Nanomedicine uses nano-sized tools for the diagnosis, prevention and treatment of disease and to gain increased understanding of the complex underlying pathophysiology of disease. The ultimate goal is improved quality of life.

The aim of nanomedicine may be broadly defined as the comprehensive monitoring, repair and improvement of all human biological systems, working from the molecular level using engineered devices and nanostructures to achieve medical benefit. In this context, nanoscale includes active components or objects ranging in size from 1 nm to 100s of nm. Also of relevance are nano-interactions within the framework of a larger device.

The key elements of nanotechnology (Fig.1) applied to nanomedicine are:

- the use of analytical tools and devices to bring a better understanding of the molecular basis of disease, patient predisposition and response to therapy, and to allow imaging at the molecular, cellular and patient levels.
- the design of nano-sized multifunctional therapeutics and drug delivery systems to yield more effective therapies.

Underpinning these fields is basic research in the areas of materials science and device fabrication (the "tool box") as well as safety and toxicological issues in respect of environmental impact and manufacturing procedures. Transfer of nanomedicine into routine clinical practice requires a multidisciplinary approach and relies upon careful consideration of clinical, ethical and societal perceptions.

Statements and Recommendations

1. Scientific Trends

Nanomaterials and Devices

Europe is particularly strong in the areas of physical and chemical assembly of nanostructures, and colloid and polymer chemistry for drug delivery. As a principle, future research in nanomaterials and devices should establish application-focused projects making use of recent developments in nanomaterials science.

General directions should be:

- optimisation of existing technologies to specific nanomedicine challenges
- development of new multifunctional, spatially ordered, architecturally varied systems for targeted drug delivery
- enhancement of expertise in scale-up manufacture, characterisation, reproducibility, quality control and cost-effectiveness.

Specific developments should include:

- new materials for sensing of multiple, complicated analytes for *in vitro* measurement
- new materials for clinical applications such as tissue engineering, regenerative medicine and 3-D display of multiple biomolecular signals
- telemetrically controlled, functional, mobile *in vivo* sensors and devices
- construction of multifunctional, spatially ordered, architecturally varied systems for diagnosis and combined drug delivery (theranostics)
- advancement of bioanalytical methods for single-molecule analysis.

Nanoimaging and Analytical Tools

European companies are pioneering imaging technique development including design of contrast and imaging agents. The ultimate goals of nanoimaging and analytical tools are the detection of pathological processes at their earliest stage and the monitoring of the effectiveness of therapies.

Specific developments should include: short term

- use and refinement of existing nanotechniques in normal and pathological tissues for the understanding of initiation and progression of disease

- development of novel nanotechniques for monitoring in real time cellular and molecular processes *in vivo* and for molecular imaging to study pathological processes *in vivo*, with improved sensitivity and resolution
- identification of new biological targets for imaging, analytical tools and therapy
- translation of research based on molecular imaging using nanoscale tools from animal models to clinical applications
- closing of the gap between molecular and cellular technologies and clinical diagnostic nanotechnologies.

Specific developments should include: longer term

- development of a multimodal approach for nanoimaging technologies.
- design of non-invasive *in vivo* analytical nanotools with high reproducibility, sensitivity and reliability for use in pre-symptom disease warning signal, simultaneous detection of several molecules, analysis of all sub-cellular components at the molecular level, and replacement of antibodies as detection reagents by other analytical techniques.

Novel Therapeutics and Drug Delivery Systems

European scientists and companies have pioneered the design and development of many of the first generation nanomedicines including liposomes, nanoparticles, monoclonal antibodies and polymer-drug conjugates. Europe has particular strengths in the research areas of tissue engineering, regenerative medicine and stem cell research.

Specific developments should include: short term

- application of nanotechnology to develop multifunctional structured materials with targeting capabilities or functionalities allowing transport across biological barriers
- nanostructured scaffolds (tissue engineering), stimuli-sensitive devices and physically targeted treatments
- a focus on cancer, neurodegenerative and cardiovascular diseases and on local-regional delivery (pulmonary/ocular/skin).

Specific developments should include: longer term

- synthetic, bioresponsive systems for intracellular delivery of macromolecular therapeutics and bioresponsive/self-regulated delivery systems (smart nanostructures such as biosensors coupled to delivery systems).

Clinical Applications and Regulatory Issues

Europe has harmonised the regulations related to medicines across European countries, exemplified by the activities of the European Medicines Agency (EMEA). Further development of appropriate regulatory requirements, approval processes and organisation is essential to facilitate the safe and swift introduction of future nanomedicines into clinical practice, and to influence basic, translational and clinical research in the field.

General directions should be:

- disease-oriented focus for nanomedicine development in specific clinical applications
- case-by-case approach for clinical and regulatory evaluation of nanomedicines
- highly prioritised communication and exchange of information among academia, industry and regulatory agencies with a multidisciplinary approach.

Toxicology

Europe already has an excellent reputation in the areas of toxicology of inhaled ambient or occupational fine/ultrafine particles.

General directions should be:

- improved understanding of toxicological implications of nanomedicines in relation to material properties and proposed use
- thorough consideration of the potential environmental impact, manufacturing processes and ultimate clinical applications in toxicological investigations for nanomedicines
- risk-benefit assessment for both acute and long-term effects of nanomedicines with special consideration on the nature of the target disease.
- a shift from risk assessment to proactive risk management at the earliest stage of the discovery and development of new nanomedicines.

2. Research Strategy and Policy

Organisation and Funding

The rapidly growing investment in nanotechnology research and development at national and European levels, and indeed globally, was greatly welcomed. However, organisationally, activities in the field of nanomedicine in Europe are currently fragmented, a situation also seen in current funding mechanisms. This can inhibit attainment of the critical mass and the multidisciplinarity needed for effective research and development. It was noted that the multidisciplinary objectives of nanomedicine are difficult to achieve on a virtual scale, especially considering the medical interface and need for innovative clinical trials.

Recommendations:

- improved coordination and networking of research activities and a diverse range of funding sources at the EU, national, and regional levels
- creation of new nanomedicine-targeted funding schemes to better facilitate both transdisciplinary and interface research that is critical for success in nanomedicine
- establishment of European Centres of Excellence in the field of nanomedicine
- modification of funding mechanisms for basic technological research to permit academic-group-only applications
- development of funding procedures with sufficient scale and scope, e.g. with longer term funding rather than continuous short-term funding cycles, to enable research for seriously tackling goal-oriented problems.
- Establishment of economic and social benefits of nanomedicine and communication of them to stakeholders and the public.

Exploitation

European scientists often lack the ability to harness the entrepreneurial, commercially driven research necessary to enable rapid exploitation. To win and maintain a leading position in nanomedicine it is essential that Europe improves technology transfer and shortens timelines from research to market.

Recommendations:

- establishment of a scheme supporting academic/commercial ventures, such as a European version of the Small Business Innovative Research Program of the US National Institutes of Health
- involvement of clusters or highly selected teams, chosen for personal excellence or track record
- establishment of more manufacturing sites with 'Good Manufacturing Practice' designation to support small and medium enterprises for transferring projects more rapidly into clinical development.

Interdisciplinary Education

The European education and training scene (including programmes such as the Marie Curie scheme) is a considerable background strength. Up to master's level, the general standard of university education in Europe, in physics, chemistry, biology, pharmacy and medicine, is amongst the best in the world. However, in the emerging field of nanomedicine there is a significant need for interdisciplinary education and exchange specific to this new discipline at multiple levels.

Recommendations:

- establishment of formal interdisciplinary training courses, mainly at the undergraduate level, covering basic scientific disciplines such as molecular biology, colloidal chemistry, cell physiology, surface chemistry, and membrane biophysics
- institution of new programmes, at master's or early postgraduate level (with combined medical and scientific training), to support the rapidly developing field of nanomedicine
- encouragement of more interdisciplinary MD/PhD degree programmes, with some provision for nanoscience, to provide core scientific training for both scientists and clinicians in the longer term.

Communication

Despite the growing national and European emphasis on transdisciplinary research and development activities, there are still considerable challenges for communication in multidisciplinary research. The current highly focused training in different scientific disciplines in Europe tends to lead to a restriction of productive communication across disciplines. The scientific community needs to make a paradigm shift regarding attitudes to interdisciplinarity.

Recommendations:

- promotion of more truly transdisciplinary conferences focusing on the specific themes of nanomedicine to facilitate better communication between research disciplines.
- encouragement of goal-oriented research partnerships between large medical centres and university research groups.

At the level of political bodies and policy makers, scientifically qualified politicians are not common while regional, national and EU programmes seldom show alignment. Challenges of communication are thus significant. Serious effort needs to be made in addressing politicians by opinion leaders in nanomedicine.

Recommendation:

- clearer articulation and better communication of the benefits of embracing nanomedicine and the threats from inaction: the benefits consisting of employment potential and meeting the medical needs of the ageing population; and the threats including missed economic opportunities.

Communication with the general public is equally important and challenging. The word 'nanotechnology' was popularised initially through science fiction. The general public do not often realise the potential benefits of nanomedicine yet can quickly grasp concerns relating to the safety of nanotechnology.

Recommendations:

- engagement of the scientific community in regular dialogue with the general public in order to discover likely public concerns early, and continuation of dialogue to address and alleviate public concerns by the presentation of clear facts
- supply of non-specialist information on potential benefits of nanomedicine to the general public in a timely fashion, with the emphasis on the fact that nanomedicine is based on mimicking the elegance of nature.

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ESF Forward Look on Nanomedicine

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Consensus Conference:

The Conference took place at Le Bischenberg (France), 8-10 November 2004, with more than 70 representatives* from academia, industry, private foundations and governmental agencies supporting scientific research, co-sponsored by Philips Medical Systems and Schering.

Scientific Workshops:

The workshops were held in Amsterdam (Netherlands), 1-5 March 2004, with more than 35 representatives* from academia and industry. Scientific sub-areas within nanomedicine which had been identified by the Steering Committee (Analytical Techniques and Diagnostic Tools, Nanoimaging and Manipulation, Nanomaterials and Nanodevices, Drug Delivery and Pharmaceutical Development, and Clinical Applications and Toxicology) were investigated in these workshops.

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*The list of all participants contributing to the ESF Forward Look on Nanomedicine will be included in the full report published separately. ESF takes sole responsibility for all content of the resulting reports of this foresight exercise.

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By drawing on the advice and expertise of the ESF's membership, the briefings aim both to provide information and to promote discussion.

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