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*The Oncologist* 2012, 17:e26-e32.

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Disclosures: Ruxandra Draghia-Akli: Inovio (OI, IP). The other authors indicated no financial relationships.

(C/A) Consulting/advisory relationship; (RF) Research funding; (E) Employment; (H) Honoraria received; (OI) Ownership interests; (IP) Intellectual property rights/inventor/patent holder; (SAB) Scientific advisory board

Translating Cancer Discovery into Cancer Cure: A Priority for European Union Research

Cancer remains one of the major public health challenges worldwide. Significant efforts and investments in cancer research over the last decades have resulted in remarkable advances in controlling and curing cancer, with steadily decreasing age-standardised mortality rates for several cancers [1], underpinned by better prevention, earlier diagnosis, and more effective treatment approaches.

Yet, in the foreseeable future, cancer will remain a formidable social and economic challenge, including in Europe. Projections for 2012 indicate that 3.2 million people in Europe will be diagnosed with cancer, with 1.2 million dying from this disease [2], elevating cancer above cardiovascular disease as the primary cause of adult mortality in a number of European countries [3]. The ageing of the European population, together with lifestyle factors including obesity, alcohol consumption, physical inactivity, and smoking, underpin this rising trend.

In recent decades, the European Union (EU) has played an important part in steering coordinated efforts and investments in cancer research and innovation. The principal aim of the Sixth Framework Programme for Research and Technological Development (FP6, 2002–2006) was to bring basic knowledge into clinical practice by translating the wealth of information generated from genomic research [4]. The Seventh Framework Programme for Research and Technological Development (FP7, 2007–2013) built on this platform, permitting the development of innovative solutions to stratified prevention, diagnosis, prognosis, treatment, and quality-of-life regimens, by supporting and promoting more personalised cancer medicine approaches [5]. This evolution was mirrored by a quantitative increase of the EU overall effort on cancer research, as well as a diversification of its support mechanisms. Under FP6, more than 100 multidisciplinary transnational research projects were funded for a total of €485 million [6]. Since its start in 2007, FP7 has dedicated over €1.1 billion to cancer research, using a variety of funding mechanisms including collaborative research, frontier research, mobility programmes, public-private partnerships, and coordination of national research activities to strengthen the innovative translation of research discoveries to clinical application.

Collaborative Research: Stronger Together

By bringing together excellent research teams from different countries with complementary skills, collaborative research projects enhance the capacity to address complex diseases such as cancer and provide innovative solutions that can directly influence patient care. In cancer research, 148 projects of this nature have been implemented so far under the Cooperation programme of FP7, with a total budget of €680 million (64% of the overall funding).

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projects enhance the capacity to address complex diseases such as cancer and provide innovative solutions that can directly influence patient care. In cancer research, 148 projects of this nature have been implemented so far under the Cooperation programme (Fig. 1A) of FP7, with a total budget of €680 million (64% of the overall funding) [7].

Representing 16% of the entire Health theme’s budget [8], these projects address a series of topics that range from aetiology of cancer to cancer survivorship, thus covering the entire spectrum of cancer research represented by the Common Scientific Outline classification system in cancer (Fig. 1B) [9]. The three best-funded categories—cancer causes and mechanisms, cancer diagnosis, and cancer treatment—represent 80% of the budget. One third of the budget (€190 million) has been committed to investigating causes and mechanisms underlying cancer initiation, development, and progression, metastasis, infectious agents, genomic instability, through to molecular mechanisms relevant to preclinical drug discovery. An increasing number of projects focus on personalised cancer medicine approaches in one or two cancer indications (Fig. 2).

Successful examples of how collaborative programmes in fundamental research can provide added value include CancerPathways [14], a €3 million-funded project that, by studying Drosophila signalling, developed models for high-throughput screening and candidate cancer drug testing, an RNAi library, and a comprehensive set of open-access bioinformatics tools and databases, such as NEXT-RNAi, web-cellHTS2, imageHTS, and FLIGHT [15–17]. It also elucidated new members of the Ras-MAPK signalling pathway [18], thus identifying the potential for new druggable targets.

Cancer outcomes critically depend on the stage at which the disease is detected, with early detection underpinning higher cure rates. Thus, accurate indicators of early disease are crucial diagnostic tools for the cancer physician. A total of €385 million (50% of the budget) have been devoted to early diagnosis, prognosis, and personalised treatment strategies for patients, with funded projects developing diagnostic and prognostic biomarkers, facilitating early detection of drug resistance, identifying novel drug targets, and producing clinically annotated databases and associated interpretative technology.

In this context, the ADAMANT project (€3 million) identified novel angiogenesis markers and produced human monoclonal antibodies that target proteins expressed only in the tumour neovasculature and stroma [19]. A number of the anticancer products developed through this collaborative programme are now entering clinical trials, including Tenapet, a vascular targeting antibody specific to tenasin C that is currently being tested in phase II trials in solid cancers [20–22].

Similarly, the INFLA-CARE project (€12 million), which focuses on the role of inflammation in cancer, has developed novel mouse models of hepatocellular carcinoma and colitis-associated cancer, as well as novel therapeutic approaches including synthetic compounds, immunotherapy, and immune status-tailored chemotherapeutic strategies for gastrointestinal stromal tumours [23], which are likely to influence clinical practice [24–27].

Support for investigator-driven clinical trials is also an important innovative hallmark of FP7. Since 2010, the health programme has devoted €75 million to support 41 cancer clinical trials, mostly phase II treatment trials validating biology-driven, targeted cancer therapies for rare and uncommon cancers. One such example is the EUROSARC project within an integrated translational trial network (€6 million), addressing soft-tissue and bone sarcomas [28]. These trials could only be conducted at an EU-wide level to guarantee the accrual of sufficient patients in a reasonable time frame, something that would not be feasible from existing national pools.

Moreover, efforts in prevention research (€30 million) have addressed infectious agents, nutritional, environmental, and socioeconomic factors, with a view to developing cancer risk reduction approaches for breast, head and neck, liver, cervical, and gastric cancer.

Finally, €24.5 million are devoted to 11 projects focusing on research into cancer control and survivorship issues. The issues addressed range from the search for molecular markers underpinning complex symptoms such as depression, cachexia, and pain to the implementation of large-scale prospective studies on long-term side effects in childhood and adolescent cancer survivors.

**Public-Private Partnerships: Championing Innovation at the Academia-Industry Intersect**

Fostering innovation in health care is a difficult and articulated process, due to the escalating costs and the long time frame for product development and regulatory approval. These issues are particularly pronounced for cancer drug development and therapeutic interventions, with overall attrition rates ranging from 74% to 95% [29, 30] and the largest percentage of phase III submission failures (23% for the 2007–2010 period) [31]. This reflects an urgent need to develop stratified medicine strategies to improve patient outcome in terms of economic and health care challenges. On the other hand, development of new therapies and interventions in this area represent a major growth market for industry and small and medium enterprises (SMEs), with one-third of all drugs in the pipeline of the pharmaceutical sector related to cancer [32]. Congruent investments and partnerships at EU level are therefore required.

To harness the strengths and potential of both the private and public sector in this area, the Innovative Medicines Initiative (IMI) was launched in 2008 as a large-scale public-private partnership between the European Commission and the European pharmaceutical industry, represented by its umbrella organisation, the European Federation of Pharmaceutical Industries and Associations (EFPIA) [33]. Endowed with a total budget of €2 billion, IMI aims to speed up the development of and access to better and safer medicines for patients. In IMI projects, partners from pharmaceutical companies that are members of EFPIA collaborate with researchers from SMEs and academia, as well as regulators and patients’ representatives. EFPIA companies contribute with their own resources (in-kind contribution);
the other partners are funded through the IMI Joint Undertaking with Framework Programme support. To date, €78 million (of which €38 million is from FP7) have been devoted to the identification of novel cancer biomarkers for drug efficacy/safety and the elucidation of both the beneficial and the unwanted effects of drugs.

For instance, the project OncoTrack [34, 35], coordinated by Bayer HealthCare Pharmaceuticals and the Max Planck Institute for Molecular Genetics, is using large-scale genomic analysis as a basis for rational selection of novel biomarkers for the early diagnosis of colon cancer. Similarly, the QuIC-ConCePT project, coordinated by the European Organisation for Research and Treatment of Cancer, aims to identify specific imaging biomarkers to improve cancer drug development [36]. The MARCAR project has developed an efficient method to identify epigenetic changes underpinning nongenotoxic carcinogenesis [37, 38]. In a very short time, IMI has established itself as a best practice model to reinvigorate drug development.

Public-Public Partnerships: Maximising the Coordination of Cancer Research Efforts at the European Level

Despite an average annual expenditure of approximately €150 million since FP6, EU efforts represent only 3.5% of the total expenditure of cancer research in the EU’s 27 member states [39], showing that the bulk of research in this field is funded at the national level. The European cancer research arena is a vibrant example, contributing significantly to the international peer-reviewed literature, translating research discoveries into tangible patient-oriented benefits, and providing added value through coordinated approaches. However, it is characterized by a significant degree of fragmentation and diversity (e.g., multiplicity of support mechanisms, funding bodies, barriers between disciplines, suboptimal critical mass). The necessity to better coordinate cancer research throughout Europe, which requires a strong commitment from the scientific community, is now largely recognised. Support of this coordination at the EU level has
represented an increasingly important objective of the EU research and innovation policy in the last 10 years.

Since the Fifth Framework Programme for Research (FP5, 2002–2006) [40], the EU has been funding initiatives tailored to this purpose, such as the mapping of national cancer funding resources across Europe [41] and the Eurocan Plus study, aimed at identifying the needs and potential benefits of a pan-European coordination of national cancer research activities [42].

Under FP7, approximately €31 million have been directly employed to facilitate cross-border collaborations amongst cancer centres; to empower coordination of national and regional cancer registries to optimise the use of cancer registration data for the improvement of cancer control; and to link cancer translational research programmes undertaken in member states.

The European Research Area Network of Cancer Registries project EUROCOURSE [43] (EU contribution €2 million) is tackling fragmentation and streamlining cancer data collection in member states by linking national and/or regional cancer registries and enabling exchange of technical expertise, sharing of best practices, and development of robust recommendations. Its efforts are based on longstanding national and EU initiatives and close collaboration with the International Agency for Research on Cancer (IARC).

The Eurocan Platform project (€12 million) has brought together 28 leading cancer centres and organisations who are joining efforts in the establishment of a shared platform for translational cancer research to speed biomarker validation and early clinical trials in melanoma, breast, lung, head and neck, and pancreatic cancers [44]. Linking 25 national and regional programs in translational cancer research, the European Research Area Network on Translational Cancer Research (TRANSCAN) project intends to establish a sustainable mechanism for continued cooperation and joint implementation on agreed-upon areas of action [45]. The first joint transnational call for proposals, focused on the validation of biomarkers for personalised cancer medicine, was launched in December 2011 and closed in July 2012.

Finally, to support member states in their efforts to develop national cancer control strategies, the EU launched in 2009 the European Partnership for Action Against Cancer (EPAAC) [46], which brings together member states, cancer associations, industry, academia, and patient advocacy groups. Led by the National Institute of Public Health in Slovenia with a €3 million budget, EPAAC aims to provide a framework for identifying and sharing information by linking capacity and expertise in cancer prevention and control. It has also set the goal of achieving coordination of one third of cancer research from all funding sources by 2013. Its first efforts towards developing high-quality national cancer plans and establishing a single European Cancer Information System (ECIS) for the provision of accurate, quality-assured cancer statistics could provide a sustainable solution for harmonising, improving, and using population-based cancer information in Europe.

Going Beyond Europe: Developing Global Partnerships in Cancer Research and Cancer Care

In 2008, an estimated 12.7 million new cancer cases and 7.6 million cancer deaths occurred [47]. With cancer becoming an increasing public health burden in developing countries, global coordination efforts are required if research is to help meet the challenge of reducing its morbidity and mortality. One such example is the commission’s participation in the €250-million

Figure 2. Number of funded Seventh Framework Programme for Research and Technological Development projects by cancer indication in relation to their incidence and 5-year median survival rates in Europe [2, 10–13]. Only collaborative projects with an exclusive focus on one or two cancer indications are shown.

Abbreviation: Merkel, Merkel cell carcinoma.
International Cancer Genome Consortium (ICGC) [48] initiative through its CAGEKID [49] and BASIS [50] projects. The ICGC will provide a comprehensive description of genomic, transcriptomic, and epigenomic changes in 50 different tumour types and/or subtypes of clinical and societal importance across the globe.

Fundamental Research: Better Understanding Fuels the Translation Pipeline

Another important source of EU funding comes from the bottom-up programmes of the European Research Council [51] and Marie Curie Actions [52], which focus on basic fundamental research and career development fellowships, respectively. In these schemes, applicants freely choose their subject of research. Approximately €332 million (441 projects) have been devoted to cancer research through these schemes, reflecting the importance of new discoveries to inform our understanding of the multitude of molecular causes and mechanisms that drive cancer initiation and progression. It is encouraging to note that 15% of the funds allocated by the scientific panels of these bottom-up programmes have been devoted to cancer research. This is very much in line with the commission’s strategic top-down approach under the Health theme (16%, see above), demonstrating that top-down schemes can strategically complement investigator-driven bottom-up approaches.

Opportunities for Cancer Research in the Health-2013-Innovation Calls for Proposals

The last calls for proposals in FP7, published on July 10, 2012, offer substantial opportunities for translational cancer research addressing important unmet clinical needs. A budget of €72 million is proposed within the FP7-Health-2013-Innovation call, to be allocated to the following areas:

1. Investigator-driven treatment trials to combat or prevent metastases in patients with solid cancer.
2. Strengthening the cancer patient’s immune system.
3. Investigator-driven supportive and palliative care clinical trials and observational studies.

In addition, several cross-cutting topics provide further funding opportunities for cancer research:

5. Genetic determinants of diseases and ageing processes.
6. Understanding and controlling pain.

Finally, the FP7-Health-2013-SMES-For-Innovation call for proposals offers opportunities to valorise innovative solutions obtained within projects supported by FP6 and FP7 in the area of health, including cancer, by calling for applications that establish proof of concept and validation of results, being led by SMEs, and bridging the gap between successful prior research and the earliest stage of a marketable innovation. Full information on all of these opportunities, including details on how to apply, is available at the Research and Innovation Participant Portal [53].

The Future of EU Cancer Research

In November 2011, following an extensive consultation exercise, the European Commission presented its proposals for Horizon 2020 [54], the next Framework Programme for Research and Innovation (2014–2020). It is designed to trigger sustainable growth, create new jobs, and address the major societal challenges considered beyond the scope and resources of any one country to tackle.

Horizon 2020 will feature a number of improvements. With a proposed budget of €80.8 billion over 7 years, corresponding to an increase of almost 50% as compared to FP7, it will unite all EU funding in research and innovation in a single programme for the first time and support every stage of the innovation ecosystem “from research to retail”. Great efforts have also been made to cut red tape to allow companies, universities, and institutes in all EU countries and beyond to get easier access to Horizon 2020 funding. The programme proposes a more straightforward and user-friendly design, a single set of simpler rules for participation with just two funding schemes, and a shorter time to grant period to get funded projects operational as rapidly as possible.

The final shape and budget of Horizon 2020 is currently subject to the view of the legislators in the Council (the EU member states) and the European Parliament. The legal provisions of the new programme are expected to be ready during 2013, and the first application round for funding should be launched in early 2014. A budget of nearly €8.5 billion for the 2014–2020 period is proposed for the “Health, demographic change, and well-being” theme, making it the largest of Horizon 2020’s societal challenges. Horizon 2020 will concentrate on those research areas that require trans-European cooperation to address today’s most pressing health challenges, will ensure well-being for European citizens, and will help keep Europe’s health care sector at the forefront of innovation and economic development.

Adapting to an ageing population, pursuing the path to more personalised medicine, harnessing and encouraging private sector capability, coordinating national efforts, and expanding global cooperation are but some of the most important features that EU health research will need to embrace if it is to deliver its full potential in this decade [55]. These areas also resonate strongly with the cancer research and cancer care communities as they strive to reduce both the incidence and mortality of this disease, effecting cures when possible and making cancer a chronic disease.
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EDITOR’S NOTE:
As Máire Geoghegan-Quinn, Commissioner for Research, Innovation and Science, launches the funding call for proposals under the European Commission’s (EC) Seventh Framework Programme for Research and Technological Development (FP7), European Perspectives examines the role that the European Union plays in supporting excellence in research and innovation in cancer and how this role can contribute to both the health and the wealth of the European citizen. In the concise review by van de Loo et al., “Emphasising the European Union’s Commitment to Cancer Research: A ‘Helicopter View’ of the Seventh Framework Programme for Research and Technological Development,” the value of strategic investment in cancer research and innovation is outlined, emphasising how a co-ordinated research policy and funding approach has underpinned successful collaborative efforts across the European cancer research continuum, leading to advances in prevention, diagnosis, prognosis, and cure for the cancer patient.

The investment has been significant; over €1.1 billion has been dedicated to cancer research since FP7 was originally launched in 2007. Discrete funding mechanisms have empowered all sections of the cancer research community, supporting frontiers (basic) science, underpinning clinical and translational research and promoting the highly relevant academia–industry intersect. The principles of coordination and cooperation have allowed the assembly of effective transnational research consortia, leading to demonstrable “added value” and providing solutions in complex diseases such as cancer that cannot easily be achieved at the national/local level. In the article, European Perspectives also looks forward to the Horizon 2020 Framework Programme for Research and Innovation (2014–2020), the proposed successor to FP7, which, if ratified by the EU member states and the European Parliament, will see an investment of €80.8 billion in research.

Accompanying this article, European Perspectives interviews Dr. Conor O’Carroll, Director of the Research Office at the Irish Universities Association and a recognised expert on European research policy and funding (http://sto-online.org/european_perspectives). The interview explores what FP7 has achieved, its relevance to the cancer community in Europe, and the significant opportunity that Horizon 2020 represents. Future issues of The Oncologist (European Edition) will include an interview with Commissioner Geoghegan-Quinn.

A budget of nearly €8.5 billion for the 2014–2020 period is proposed for the “Health, Demographic Change and Wellbeing” theme of Horizon 2020. Cancer will soon surpass cardiovascular disease as the major cause of disease-related mortality in Europe. It represents one of the key “societal challenges” as envisaged by Horizon 2020—thus it is critical that the European cancer community unites to ensure that the research priorities (and associated funding) in Horizon 2020 reflect this increasing disease burden.