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News & Views

Turning the Stockholm Declaration into reality: Creating a world-class infrastructure for cancer research in Europe

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Europe needs to be better organised. That is the now-unanimous conclusion of the continent's cancer community, after years of debate about possible ways to tackle bottlenecks and barriers in research. A process of review and analysis of the situation in Europe, begun in 2004 by then-EU Commissioner for Research Philippe Busquin, has provided a concrete proposal to focus the frustration shared by all. But to move this plan forward and smooth the flow of new treatments and diagnostics from laboratories to patient care, scientists are having to learn some political lessons.

The movement now absorbing the cancer-research community started with a project funded out of Europe's last framework programme—the main mechanism through which EU centrally held research monies are distributed—to identify the barriers hindering cancer-research advances. Dubbed the EUROCAN + Plus project, the 4-year-long analysis, which published its final report this year ([EurocanPlus, 2008](#)), considered all aspects of research funding, organisation, infrastructure, and coordination in Europe. “The main outcome of which,” explains EUROCAN participant and *Molecular Oncology* editor-in-chief, Julio Celis, “has been to structure the cancer community in a way that hasn't been done before.”

However, it took a determined group of cancer research professionals representing 16 of the largest and most successful cancer centres in Europe, to come up with a solution to EUROCAN's many grievances. Outlined in a document labelled The Stockholm Declaration ([Ringborg, 2008](#)), these cancer leaders proposed an innovative platform for translational research in Europe to link large comprehensive cancer centres (CCCs) and basic/preclinical cancer centres across the continent in a network to produce the critical mass necessary to deal with increasingly complex biological and clinical questions and harmonise methods, infrastructure, and regulations to make cross-border investigation less burdensome. The

platform is expected to support the cancer “dream teams” of the future.

1. Networking cancer centres

The Declaration calls for an immediate action to create the network to achieve greater cooperation and harmonisation across the EU. Three novel notions are its main tenets: the concept of the patient at the centre of cancer research; the need for all stakeholders to join forces and resources to fight cancer; and the necessity for the cancer community to speak with a single voice in order to tackle political powers in a strategic way. “The Stockholm Declaration signalled a paradigm shift that was catalysed by the commitment and shared vision of basic and clinical researchers,” explains Celis.

Reasons why such a plan is needed are not in dispute. The direction of basic research is towards answering ever more complex questions about the nature of biological systems and the interaction of molecules within their physiological environment. Complex systems and complex questions require huge computational power, sophisticated modelling frameworks, and the computational methods to pull all the information together into dynamic predictions of biological behaviour.

According to Yosef Yarden, of the Weizmann Institute in Israel, basic research such as this needs collaboration because the next developments will come from integrating molecular discoveries into their system context. And advances in clinical research, whose major goal is tailored therapy, need ever greater numbers of patients for clinical trials, close links between physicians and laboratory scientists, and a continual dialogue between the laboratory and clinic.

These demands mean there is an urgent need for bigger centres. But, says Yarden, scientists and managers at existing

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centres cannot meet the challenges alone because “ever-increasing costs of basic research, skilled manpower, large teams and instruments mean all institutions face the problem of matching the modernisation, frequent upgrading of machinery (for example, the necessity to replace mass spectrometers every 3–4 years) and recruitment of young scientists to meet the challenge.” The only logical solution is for large centres to work together to push forward research.

Martine Piccart, a breast cancer specialist and head of the European Organisation for Research and Treatment of Cancer (EORTC), concurs. She says one of the most important goals of advancing cancer research in Europe is to guarantee the best medical practice, to identify overtreatment, undertreatment or wrong treatment, and to provide patients more rapid access to new developments. However, with the ultimate goal as the implementation of tailored personalised therapy—“the right treatment for the right patient at the right time”—more intensive cross-talk with basic scientists is essential.

She explains that clinical trials need to change from the traditional method of comparing two drugs and adopting the better performing one into clinical practice. “We need to be able to say that molecular signature 1 will do well with the old drug, molecular signature 2 will need the new drug, and molecular signature 3, doesn’t respond to any and needs new ones,” she explains. Achieving this kind of clinical precision requires new clinical trials focusing on the co-development of drugs and biomarkers. And these, in turn, require sharing of biomarker data and tumour samples between centres and networks of institutions to conduct trials of sufficient size and statistical power—all suggestions put forward in the Stockholm Declaration. And, adds Piccart, an important part of these new clinical trials is the involvement of industry to develop innovative compounds and draw in funding for large studies (Figure 1).

Therefore, better interaction across centres, countries, and disciplines in Europe is necessary for clinical scientists seeking to apply the best treatments. It is necessary for basic scientists seeking to understand the true biological context of their findings. It is necessary for industry to most efficiently develop and test new, more advanced treatments. It is necessary



Figure 1 – Martine Piccart described the new interdisciplinarity that is essential to reach the goal of truly personalised medicine.

for academia to raise the quality of work in Europe, and scientists produced by Europe. And, ultimately, it is necessary for societies seeking to reap the economic and social benefits of all these efforts to help Europeans live longer healthier lives.

Ulrik Ringborg, Head of the Cancer Centre Karolinska in Sweden, and one of the main proponents behind The Stockholm Declaration says: “Collaboration between individual research groups is no longer the solution. We need also collaboration between centres to guarantee infrastructure support, critical mass of expertise and resources.”

2. Initiating political change

With such a strong consensus on their side, the cancer-research community is now looking at ways to move forward their platform idea. A meeting¹ held last month in Paris, sponsored by the Danish Cancer Society, the Initiative for Science in Europe (ISE) and UNESCO, marked the first step in moving the Stockholm Declaration into reality. The location, at the headquarters of UNESCO in Paris, had a historical significance for the group of cancer leaders and interested politicians gathered. It was in the UNESCO building in Paris that, 5 years ago, discussions on the now-established European Research Council (ERC) began to take form. That landmark change to the way European science is funded has since become a beacon of hope for Europe’s scientists: in contrast to the pervasive disillusionment many felt with the existing structures, increasingly bureaucratic and subject to political whims, the establishment of this independent agency shows that things scientists want can be achieved.

“With the ERC, we have an example of a democratic commitment which has been realised because of the determination of the scientific community to create a new entity,” explains Busquin. “There was a need to create a structure to stimulate research, something not set out in European treaties because research is designed to finance the competitiveness of European businesses.”

However, rather than just being an important victory, there was a lesson for scientists in the establishment of the ERC too. To change things in Europe requires not only a good idea and logic on your side (the history of communal European science is littered with examples of rational proposals that got nowhere), but it also requires scientists to take on the political establishment and do things their way. Winning support from policymakers, presenting ideas at the right time, and understanding the delicate negotiation process is what makes some ideas succeed where others fail.

3. Winning external support

Busquin presented the audience of 150 scientists, clinicians, politicians, managers, patient organisations and industry representatives in Paris with an insider’s view of how to win the support of the European Commission (EC) (Figure 2). First, he

¹ The meeting at the UNESCO headquarters was organised by Julio E. Celis, Luc van Dyck, Maciej Nalecz, Ulrik Ringborg and Thomas Tursz.



Figure 2 – 150 scientists, clinicians, politicians, managers and patient and industry representatives met at the UNESCO building in Paris last month.

explained, scientists must frame the challenge in such a way that it targets the specific responsibilities of the EC, as separate from the national responsibilities. When talking about research on health, that is a particular problem because health and the outcomes for patients of research are not strictly the concern of the EU, Busquin says. Research, by contrast, and its potential to boost the economy in Europe, is a European competence over which Commissioners have the power to legislate and allocate funding.

He explains that this division of responsibilities led to some of the widely acknowledge problems with the Clinical Trials Directive, which has actually hindered clinical researchers in their work. “The directive on clinical trials had some inherent weaknesses and has been hotly debated,” says Busquin. “Since this was not a direct concern of the EU, the directive was an initiative of the pharmaceutical industry and as a result there are potential problems encountered in its implementation.”

Adds Busquin: “It is not just a question of obtaining the support of Euro MPs, it is a matter of passing to a higher level of collaboration. Industry has agreed to work hand in hand in technical spheres, co-financing some research programmes upstream, as is happening with [a recent European project] the Innovative Medicines Initiative. These involve in particular the biomarkers issue. It would be impossible for the Member States themselves to provide the necessary infrastructure,” he explains.

It is essential to win the support of other stakeholders, outside the Commission, adds Busquin, listing Member States, funding agencies, the European Parliament, civil society, medical and scientific organisations, universities, research centres, hospitals, ethical and legal bodies, and the private sector as examples. But perhaps the biggest realisation dawning on the cancer community as a result of the Stockholm group’s agenda is that key to any of these scientific changes should be the focus on the patient. Sandy Craine, a representative of the European Cancer Patient Coalition, the association of patient groups in Europe, told delegates in Paris that: “Informed patients are a reality today,” adding “If the scientific

community can work with informed patients we can move your work forward much quicker, and we can see a real effect on the outcomes of your actions.”

4. The right instrument

But even with all stakeholders on board, the idea may still not get funding. So, scientists must also choose the right instrument to take this idea forward in political circles. This means looking at possible opportunities for existing funding and essentially piggybacking on a current initiative to add more cancer-specific recommendations. “As always the question in Europe is where does the money come from?”, explains Busquin. “It is all about creating the appropriate dynamics, the momentum. We need to avoid giving the impression that Europe is richly endowed with resources. It can catalyse, but the real funds have to come from the Member States.”

With this in mind, The Stockholm Group recognised that the main issue with creating a platform to support better translational research in Europe is infrastructure. Research infrastructures have the potential to help to structure communities, help the exchange of best practices and to promote interdisciplinarity. Better translational research requires better technical platforms for genomics, proteomics, metabolomics, imaging, functional genomics, and bioinformatics; screening facilities for new anticancer agents; libraries of siRNAs and cDNAs; biobanks with harmonised procedures and regulations; and common career structures in cancer centres. Most infrastructures for translational research are available in Europe, but they are not organised, coordinated with other facilities, or formalized in a way that they can be accessed by scientists or most efficiently contribute to the common goals.

Ringborg links this idea to the concept of the CCC, the essence of the Stockholm Declaration. The CCC is a very important concept because it is a unique structure with critical mass of expertise and resources in which cancer care and prevention are integrated with research and education for translation cancer-research linking research and innovation, he explains. Europe has many strengths: strong basic and preclinical research; state of the art technological platforms; nationwide patient registers; biorepositories; frameworks for biomarker validation for clinical use in place; and an established clinical trials infrastructure. So taking these existing assets to another level requires not a massive overhaul, but a little bit of funding, some specific planning, and a lot of motivation.

The European Strategic Forum for Research Infrastructures (ESFRI) could be one of the initiatives to help move the Stockholm proposal forward. As an organisation, it brings together representatives of ministers of the 27 member states, nine associated states, the EU Commission, and a mix of scientists and administrators. ESFRI’s aim is to develop a long-term vision and support an EU policy in pan-EU research infrastructures and bring initiatives and projects to a point where joint decisions are possible (Figure 3).

The roadmap of the ESFRI (2008) is a major instrument through which new or upgraded research infrastructure projects obtain seed funds. In order to become part of this scheme, proposals for infrastructural projects need to be presented by Member States or international organisations. What



Figure 3 – An existing European initiative to improve infrastructures in Europe, the ESFRI, could be one route through which the Stockholm Declaration is enacted.

is more, there has to be a scientific case evaluated by peer review; it must be a major or cutting edge facility for the scientific community; must be multiuser and based on open competitive peer reviewed access, and it must be of pan-European global interest. All these criteria fit the translational research platform proposal of the Stockholm Group.

Another mechanism for helping to promote the platform idea is the development of Joint Programming ([Communication from the Commission to the European Parliament, 2008](#)) between Member States, whereby national research councils align their research priorities and make joint awards to enable cross-border collaborations and large coordinated research projects. Taking these two mechanisms together would tackle the platform issue from both ends. However, warns Busquin, success of even these projects ultimately depends on governments being convinced to fund infrastructures in the long-term, because sustainability needs not just start-up funds but sustainable contributions to enable the continuous maintenance and upgrading that world-class infrastructures require ([Figure 4](#)).

5. Timing is crucial

To move this idea forward now, timing is crucial because political agendas, budget priorities, and subjects of interest are fixed years in advance in European political circles, and with the next Framework programme not up for discussion until 2012, there is only a small window to obtain funding. According to Busquin, there are financial perspectives to be discussed in 2009, “So the cancer-research community has chosen a very opportune time to come together.” But, he warns, “We need to move quickly with specific request for types of funding.” That is the next step the Stockholm Group together with the European Cancer Organisation (ECCO), the Organisation of European Cancer Institutes (OEI), and the EORTC must now take.

But it is now clear that the platform has hope because of a fortunate coincidence of priorities. At the same time as the cancer-research community in Europe is uniting around



Figure 4 – The panel debates how best to improve coordination of cancer research in Europe.

a common notion of what is required to push forward cancer research, there is also a growing interest among the EC of the strategic importance of infrastructural issues to science and economy. What is more, the Commission is starting to look at ways to realise the long-discussed idea of a true European Research Area, to make Europe the knowledge-based economy the Lisbon agenda of 2000 pledged to pursue.

This interest at Commission level has produced mechanisms through which cancer researchers’ aims of a platform for cancer research could easily and quickly become a reality. And with their new experience of manipulating policy for their ends, a skill learned from the ISE in its quest to promote the creation of the ERC, the cancer community is learning how to take advantage of this interest. For Celis, these positive signs give hope that the Stockholm proposal will become one of those concepts, like the ERC, that scientists will look back on as a success. “We live in interesting times. What we need is to find a way to channel all of this momentum in a way that will be productive,” he says.

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