Raising hematology's European voice: the importance of calling yourself a hematologist

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When asked about one's profession, the answer will reveal to the listener(s) a whole set of social markers. Socio-economic status indicators like education and income will become apparent. But also less tangible characteristics, such as political lenience, cultural tastes, and sometimes even personality traits are assumed in reaction to your response. Regrettably, not many people will think anything when the response is "hematologist".

Compared to other medical specialities, the discipline of hematology is little known to the public, and in particular to stakeholders in politics. This may have detrimental effects on strategic issues, including regulatory affairs and the presence of hematology on the European research agenda. Research in hematology has been seminal in introducing novel diagnostic techniques such as the "-omics"; the first whole-genome sequencing of a malignancy concerned a hematopoietic tumor, an acute myeloid leukemia.[1] Sound evidence of targeted therapy in oncology comes from groundbreaking hematologic research on leukemias and lymphomas that has changed the natural course of the disease. Following the discovery of the underlying genetic abnormality, the first targeted therapy was developed for acute promyelocytic leukemia,[2] and the first application of small molecule inhibitors (imatinib in chronic myeloid leukemia) and monoclonal antibodies (alemtuzumab in chronic lymphocytic leukemia, rituximab in lymphoma) were in hematologic malignancies.[3-8] Pivotal contributions have come from hematologists in advancing stem cell research, the impact of which greatly exceeds its disciplinary confines.[9-11]

Still, most people are not aware of these facts. As for the reasons why our medical speciality is so little known one can only speculate. We suggest it may be caused by the scope of hematology, spanning a broad area that includes benign clinical hematology, such as thalassemias and aplastic anemia, myeloid and lymphoid malignancies, plasma cell disorders, stem cell transplantation and highly specialized treatment modalities such as gene therapy, advanced diagnostic laboratories, thrombosis and hemostasis, and transfusion medicine. So when asked, we tend to call ourselves leukemia doctors, blood clotters, stem cell specialists, or the like; not hematologists.

We should. Because identifying ourselves as hematologists will contribute to advancing the European research agenda towards our discipline.

The European Hematology Association (EHA) is undertaking a long-term strategic approach to raise the voice of hematology in Europe. Having grown into the largest European membership organization for hematologists, with an annual congress that attracts more than 9,000 delegates and a journal, *Haematologica/The Hematology Journal*, that is the primary general hematology journal on the continent, EHA has become the representative of hematology and hematologists in Europe. Advocating the interests of hematology, EHA focuses on public research funding and the regulatory environment of clinical trials in Europe.

Towards the achievement of these goals, EHA has launched several initiatives (Table 1). The first has been to embed its political ambitions in its organizational structure: an Advocacy and Political Affairs Committee was installed, and human and financial resources were made available. Steps were and continue to be taken to ally with other stakeholders whose goals (partly) coincide with those of EHA, such as patient organizations, other healthcare professionals in the field of hematology, the pharmaceutical industry, regulatory authorities, other medical speciality organizations, national societies of hematology in Europe, cooperative study groups, and scientific working groups. In addition, we have responded to several consultations of the European Commission and the European Medicines Agency, and have taken part in or co-organized several meetings at and around the European Parliament.

One important dossier concerns the revision of the Clinical Trials Directive (CTD). The Directorate-General for Health and Consumers of the European Commission issued a concept paper outlining the Commission's intentions towards revising the CTD.[12] The Commission acknowledges the shortcomings of the current directive, most prominently illustrated by the 20% drop in applications for clinical trials in the EU over the last four years, from 5,028 in 2007 to 4,193 in 2010, and the concomitant drop in the number of trial participants from approximately 500,000 to 400,000 over the same period.

Under the current directive, a multi-national trial, even when it has a single protocol, must be submitted to and assessed by the competent authorities and ethical committees in each of the EU member states in which the trial is taking place. What is more, the authorization procedures of the member states are taking place in complete isolation from each other. This makes for an unnecessarily cumbersome, long and expensive process. These problems will only be

Table 1. EHA's main Advocacy and Political Affairs activities.

January 2010	Response to the European Commission's Public Consultation Paper 'Assessment of the Functioning of the Clinical Trials' Directive 2001/20/EC
June 2010	Establishment of the EHA Advocacy and Political Affairs Committee
November 2010	Adoption by the EHA Board of the Advocacy and Political Affairs Program
January 2011	Membership of the European Public Health Alliance
January 2011	Membership of the Alliance for Biomedical Research in Europe
March 2011	Response to the European Commission's Consultation on the Recognition of Professional Qualifications
May 2011	Response to the European Commission's Public Consultation on the Concept Paper 'Revision of the Clinical Trials' Directive 2001/20/EC
May 2011	Response to the European Commission's Consultation on the Common Strategic Framework Programme Green Paper
August 2011	Conference 'Haematology and the Next European Decade: a stakeholders meeting' co-organized with the European Cancer Patient Coalition at the European Parliament
September 2011	Response to the European Commission's Consultation on Modernising the Professional Qualifications Directive
November 2011	Invited speaker at the Workshop on Personalised Medicine, organized by the European Cancer Patient Coalition at the European Parliament

exacerbated as national trials lose relevance in the advent of personalized medicine. Increasingly, diseases will be further subdivided into sub-entities rendering them, in fact, rare diseases. This seriously limits the capability of clinical study groups to find enough eligible participants in a single country to recruit into a trial sample in any reasonable time frame. As a result, more and more trials are expected to be performed multi-nationally, with all its consequences. Therefore, EHA has repeatedly made the case to the European Commission to introduce a single submission system, to harmonize the assessment procedure, and to centralize approval of clinical trials.

In addition, the increased bureaucratic burden and increased costs have, in the context of limited public funds, had an even more negative effect on the ability to conduct academic trials. Contrary to its initial goal to increase patient safety, the CTD actually worsened the situation for patients in terms of clinical trials designed to assess the effect and best practice in the use of licensed drugs. For instance, post-authorization academic trials may reduce toxicities and costs by combining new off-label drugs at lower doses. Also, the absence of a risk-based approach to patient safety ignores the willingness of patients with life-threatening diseases to offset the risks associated with the experimental drug with the risk of dying.

Another important dossier concerns the European public research agenda. The Seventh Framework Programme (FP7) for Research and Innovation of the European Commission has produced a startlingly low number of hematologic research projects. So far, only five hematologic research projects[i] appear to have been awarded funds in the Health Programme of FP7.[13] Two other projects[ii] may be considered related to hematology. Hence, of the € 6.1 billion that is allocated to research in health, only € 56.6 million has been spent on hematologic and related projects. That is less than one percent of the health research budget.

Yet, the most prevalent disease in the world is a non-malignant hematologic disease. The World Health Organization states in the latest update of the Global Burden of Disease that "at any given moment, more individuals have iron-deficiency anemia than any other health problems. Even in high-income countries, iron deficiency is common".[14] Likewise, a number of highly prevalent non-malignant diseases, which include anemias, coagulation disorders, and hemophilia, are investigated by hematologists treating pediatric or adult patients. The impact, for instance, of symptomatic venous thromboembolism (VTE) was estimated in a study of six EU countries[iii] (with a combined population of 310.4 million) to reach numbers of over 761,000 per year and the number of VTE-related deaths to exceed 370,000.[15]

Worse, none of the projects that have received funding from the FP7 Health Research Programme of the Commission address hematologic malignancies, while blood cancers are among the most devastating diseases known to medicine. Combined, the mortality of leukemia, Hodgkin's and non-Hodgkin's lymphomas, and multiple myeloma ranks third after lung cancer and colorectal cancer. In the European Union member states alone, more than 95,000 people die each year of hematologic cancers.[16] Given the nature and epidemiology of the diseases, they are most prevalent among some of the most vulnerable European citizens: children and the ageing.

The European Commission is, in the context of the Multiannual Financial Framework of 2014-2020, rolling out budget proposals for each sector, including Research

[i] *BLUEPRINT - A BLUEPRINT of Haematopoietic Epigenomes; ACUSEP - Integrated whole blood coustophoresis and homogeneous nucleic acid detection cartridge for rapid sepsis diagnostics; SYBILLA - Systems biology of T-cell activation in health and disease; TREC - Building research capacity of blood transfusion services in Africa; STEMEXPAND - Stem cell expansion - expansion and engraftment of haematopoietic and mesenchymal stem cells.*

[ii] *DIATOOLS - Tools for minimally invasive diagnostics; PROACTIVE - High throughput proteomics systems for accelerated profiling of putative plasma biomarkers.*

[iii] *France, Germany, Spain, Italy, Sweden, and the United Kingdom.*

and Innovation. Horizon 2020, as the successor of FP7 is called, was proposed to the European Parliament and the Council on November 30, 2011.[17] The 'societal challenge' of Health, demographic change and wellbeing has been allocated € 8.6 billion; up from € 6.1 billion in FP7. EHA welcomes the proposed increase. But in relative terms, as a percentage of the total budget for Research and Innovation, the budget has remained roughly the same. Together with the Alliance for Biomedical Research in Europe, of which EHA is a member, we will keep pushing for a budget increase for health research now that the proposal is in co-decision procedure of the European Parliament and the Council. Most importantly, EHA will keep advocating for funding of hematologic research.

In advocating the causes of hematology and its practitioners, EHA is often hampered by a lack of understanding of what hematology is. Whereas in academia and the medical communities hematology is a respected discipline, politicians, civil servants and the public are rarely aware that the speciality of hematology even exists. And if they do, our speciality is fragmented into malignant diseases (an appendix to oncology) and benign diseases like anemia or blood coagulation; and many of the diseases we treat and explore are subsumed under 'rare diseases'. Before being able to make political claims, we need to raise political and public awareness that ours is a comprehensive discipline of excellent reputation.

Here is where you come in. When asked about your profession, consider responding with a proud "hematologist", possibly extended with "specialized in...". Try to reveal to your patients and to your friends and acquaintances that you are part of a long and impressive tradition of specialists in blood diseases. If hematologists themselves identify with their speciality and will promote its existence and its unity, we will be in a position to represent and advocate your interests effectively.

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