INTERNATIONAL HUMAN EPIGENOME CONSORTIUM

Chair of the Executive Board **Dr Eric Marcotte** introduces IHEC, an organisation dedicated to providing free access to high-resolution reference human epigenome maps, with the larger goal of understanding the role of the epigenome in health and disease

The International Human Epigenome Consortium (IHEC) has a long-term goal to understand the extent to which the epigenome has shaped human populations over generations and in response to the environment. Why is an organisation like IHEC essential for the advancement of epigenomic research?

Like a number of other international consortia in the genomic space, IHEC is tackling the broad questions around what regulates our genome, and the implications this has for explaining human health and disease. This requires coordination on a large scale, especially in terms of what constitutes a proper reference epigenome, and what cell and tissue types provide the most relevant and useful resources. This simply cannot be done in isolation by standalone projects in individual countries. Any one country lacks the necessary resources to tackle these challenges in a comprehensive fashion. There is a great strength that comes from bringing together complementary expertise in a collaborative consortium, with the potential for far greater impact than an equivalent number of individual projects.

Epigenetic mechanisms provide a compelling model for how environmental influences can modify the expression of the genome, in a long-lasting way. The overarching objective of IHEC is to help address fundamental questions around how the environment interacts with the genome during development to influence health and disease.

What are IHEC's specific goals within this overarching objective of understanding the role of the epigenome in human health and disease?

IHEC has been coordinating the production of at least 1,000 reference epigenomes from healthy and diseased human cells, as well as a limited number of relevant model organisms. For this initial phase, the focus is on key cellular states, such as 'stemness', immortality, proliferation, differentiation, senescence and stress response. Each reference epigenome consists of high-resolution maps of DNA methylation and key regulatory histone modifications, with corresponding information about the type and expression level of all transcribed genes.

The hope is that this information will be used by researchers as a starting point for more detailed human health and disease studies. A key feature is that the data produced is quickly made freely available to the larger research community. There is also no needless duplication of effort; the coordination allows us to ensure that an appropriately diverse collection of cells and tissues are explored, with appropriate scientific overlap.

Can you discuss the benefits that the Consortium brings to the wider research community?

Our reference epigenome standards (particularly our assay, data and metadata standards) provide a 'gold standard' for those looking to engage in state-of-the-art epigenomic analyses. By focusing on key cellular states, we have the potential to unlock basic mechanisms for understanding the integration of environmental influences. We have created a common baseline platform across diverse cells and tissues that will be highly relevant for more advanced targeted studies. In addition, all of our data are rapidly released into public archives, easily accessible from a common IHEC Data Portal with sophisticated search and visualisation functions.

IHEC is able to provide this coordination in a remarkably efficient way. As a largely virtual organisation, all of the work is distributed, with member countries sharing resources and activities. There is little additional overhead for the coordination, as the individual Consortium members voluntarily fill in all the necessary functions. And we can easily integrate new members seeking to expand epigenomic analyses in new directions.

The structure of IHEC facilitates interaction and development of new joint initiatives between the global community of researchers and funding agencies. This helps foster the development of new epigenomics tools and methods – including associated data analysis and bioinformatics strategies – that will benefit the more detailed health and disease analyses to come.

How is the Consortium structured and governed?

IHEC is based on a distributed organisational model, similar to that used successfully in a number of international genomic projects. It relies on the close interaction of funders, though the Executive Committee (EXEC), and leading researchers through an International Scientific Steering Committee (ISSC). EXEC provides oversight and the setting of general goals, while ISSC establishes and sets guidelines, standards and the specific goals of the Consortium. There are also a number of working groups to address key issues and activities of IHEC, and which integrate stakeholders and research leaders from across the broader communities. This is an important mechanism to bring all the necessary expertise into the Consortium.

What does your role as Chair of EXEC encompass?

As Chair, my main role is to facilitate discussions and decision making within IHEC, and to promote outreach to other consortia and new potential members. This is conducted jointly with the Chair of ISSC – currently Dr Henk Stunnenberg (Radboud University, the Netherlands), a leading researcher in the field and Head of one of the IHEC production centres (European Commission BLUEPRINT project). I am supported in my role through the distributed IHEC model, where various member countries provide additional resources. For example, there are secretariat functions performed by staff at the National Institutes of Health (NIH), and our core communication group is embedded within the DEEP consortium in Germany. Even the annual meetings rotate among the member countries, to help even out the overall costs and contributions of each.

IHEC is composed of several international research projects. How are these projects contributing to the IHEC's major goals?

The member nations support IHEC by directly funding epigenomic data production and analysis centres in their own countries. These affiliated projects form the backbone of IHEC, as all their efforts are aligned within the common standards and goals established by the overarching consortium. The members also collectively come together to set the IHEC standards. This is a key feature of the Consortium – the voluntary commitment to coordinated activity is what allows it to have a greater impact than the sum of its individual research components.

Several member countries also support additional projects – individually or through multilateral partnerships – to improve epigenomic technologies, investigate epigenetic regulation in disease processes

IHEC 2014 Annual Meeting, Vancouver, British Columbia, Canada

GLOBAL COLLABORATION

IHEC was built from a number of established national epigenomic initiatives, most notably in North America and Europe. Current IHEC members include:

- Canadian Institutes for Health Research (CIHR)
- European Commission (EC)
- German Federal Ministry of Education and Research (BMBF), represented by the Project Management Agency within the German Aerospace Center (PT-DLR)
- Japan Science and Technology Agency (JST)
- Korea National Institute of Health (KNIH)
- US NIH Roadmap Epigenomics Program and the ENCODE Project – National Human Genome Research Institute (NHGRI)

In addition, there are associate members or observers from:
- Italy (European Institute of Oncology – IEO, FIRC Institute of Molecular Oncology Foundation – IFOM, Italian Institute of Technology – IIT, Center for Genomic Science)
- France (National Research Agency – ANR)
- UK (UK Funders Alliance, Medical Research Council, Biotechnology and Biological Sciences Research Council – BBSRC, Cancer Research UK, and the Wellcome Trust)
- Australia (National Health and Medical Research Council – NHMRC)

and explore broader gene-environment interactions in human health. By virtue of the relationships established through the Consortium, novel forward-looking funding opportunities have been developed that are open to the broader community, designed to build on previously supported mapping studies.

IHEC held its Annual Meeting and Science Day in Vancouver, Canada, from 6-8 October 2014. What were your highlights from the Meeting? Can you provide an overview of the Science Day event?

As a virtual organisation, the annual in-person meetings are critical for IHEC. This is where we collectively take stock of all of our activities and collaboratively look forward to plan the next steps. Highlights for me from last year's meeting were the rapid progress in overall IHEC data production, and the high scientific impact of recent publications from IHEC-affiliated projects. But particularly gratifying was how quickly IHEC members were able to develop and launch the Data Portal, which offers a sophisticated set of tools for the epigenomic research community to view and access all IHEC data.

The open Science Day is another core function, designed to engage the broader research community. We are consistently able to attract an extremely high calibre of international and domestic research leaders each year, providing overviews of how epigenomic data can be applied in various health fields. We look forward to continuing this very popular outreach activity at our Tokyo meeting in 2015.

Can you describe your vision for the future of IHEC? What are its core goals for 2015?

Although IHEC is currently focused on reference epigenome mapping, that is just the starting point to help address the ultimate question of the role of the epigenome in human health. The steps we have taken to date have at their core an appreciation of the fundamental information we need to advance in that direction (ie. understanding key cellular states, considering sex and gender differences, the effects of ageing, potential gene-environment interactions, etc.). We have made tremendous progress on our initial mapping goals, which are advancing even more rapidly than expected. The question now is how to integrate all that we are doing, assess what remains to be done and develop a plan to move forward collectively toward that larger transformational goal on human health.

Toward that end, ISSC is currently integrating all the future direction perspectives put forward at our last annual meeting. Among our priorities for 2015 is to develop a collective IHEC position document on our next set of goals. But in general terms, I think central to moving forward is embracing the characteristics that make these sorts of international consortia so successful: research excellence, voluntary participation with high-level national support, meaningful cooperation and coordination, and integrative analyses of comprehensive datasets. As IHEC expands and integrates new members into the consortium, I'm confident that our successes and ultimate impact will only continue to grow.

www.ihec-epigenomes.org

IHEC
International Human Epigenome Consortium