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EpiGeneSys Network of Excellence

The EpiGeneSys Network of Excellence expects to have more than 100 member laboratories by autumn of 2012. EpiGeneSys (www.epigenesys.eu) brings together epigenetic and systems biology researchers looking for new ways to advance the understanding of human disease and improve human health. The scientific objective of the network of researchers is to use a systems biology approach to define epigenetic mechanisms quantitatively in space and time.

Funded by the European Commission from 2010 to 2015, the EpiGeneSys Seventh Framework Programme (FP7) project currently unites researchers working in 68 laboratories in 14 countries across the globe. The four main areas of research include the study of the dynamics of epigenetic regulators, investigation of the relationship between the genotype and epigenotype, the study of how cell signaling impacts the epigenome, and development of a computational framework for epigenetics and systems biology.

Two rounds of competitive recruitment for 18 new scientific members with less than 3 years of independent research experience have just ended; the most recent additions to the network will be announced later this summer. New recruits receive 150,000 Euros of funding for a 3-year period. Two open calls for participants have also added associate members who collaborate with the network but do not receive direct funds.

Training and education play important roles in EpiGeneSys. Five annual meetings and at least 17 workshops are planned as part of the project. In addition, two courses on systems biology will bolster the knowledgebase in the epigenetics community; the first course took place on 3–6 June 2012 at the Weizmann Institute in Israel.

EpiGeneSys has a mission to communicate science to the public in an interesting and accessible fashion and to awaken the interest of students in research. The web site (www.epigenesys.eu) is therefore structured to cater for the public and scientists.

EMBO Member *Geneviève Almouzni* (Centre national de la recherche scientifique, Institut Curie) is the Scientific Coordinator of EpiGeneSys, and *Asifa Akhtar* (Max Planck Institute of Immunobiology and Epigenetics, Freiburg), *Wolf Reik* (Babraham Institute, Cambridge), and *Eran Segal* (Weizmann Institute of Science, Israel) are Deputy Coordinators.

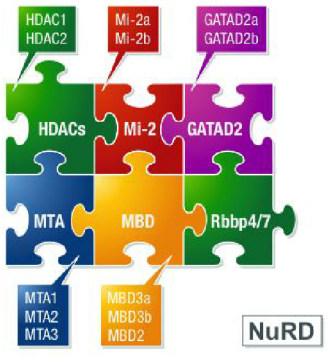
The fate of stem cells in four dimensions

An ambitious new project, 4DCellFate (www.4dcellfate.eu), will study the roles of the Nucleosome Remodeling and Deacetylase (NuRD) and Polycomb Repressive (PRC) complexes in regulating differentiation in embryonic stem cells.

The goal of 4DCellFate is to create a "four-dimensional map" across space (the genome and cell) and time (during differentiation) of the regulatory functions of these complexes. The project is funded by a European Commission Seventh Framework Programme (FP7) grant of almost 12 million Euros and brings together scientists from eight academic institutes, three biotech companies, and a large pharmaceutical company. The project will play a key role in training future scientists in multidisciplinary science, both within and outside the consortium, and will recruit and involve additional young investigators.

Although it has been known for over a decade that these complexes play a fundamental role in determining stem cell fate, how these complexes work remains very unclear. Recent studies have shown that the NuRD and PRC complexes are not static entities, but rather that their compositions and structures are dynamic. A key goal will be to understand this complexity and determine how their activity is modulated at a system-wide level. Initially, the project will elucidate the composition, genome-wide localization, and structures of these complexes. The next step is to understand how the activities of the complexes are regulated. The project will use high-throughput genomics, epigenomics, and quantitative mass spectrometry, and will develop novel methods for studying the localization of proteins at a single-molecule level. The aim is to integrate the data into a multi-scale model of gene regulation by the NuRD and PRC complexes during self-renewal and stem cell differentiation.

"A major goal of the project is to translate the understanding of the roles of these complexes in stem cells into future molecular therapies. In particular, the project will look at the epigenetic processes that deregulate gene expression in cancer, specifically during the onset, development or progression of leukaemia," said *Luciano Di Croce*, Research Professor at the Centre for Genomic Regulation, Barcelona, and Scientific Coordinator of the 4DCellFate project. *Ernest Laue*, Professor at the University of Cambridge, remarked: "We believe that elucidating the details of how the PRC and NuRD complexes regulate stem cell differentiation will have significant potential for studying disease progression, and for the development of drugs for personalised molecular therapies."



Nucleosome Remodeling and Deacetylase (NuRD) complex, one of the proteins involved in regulating differentiation in embryonic stem cells