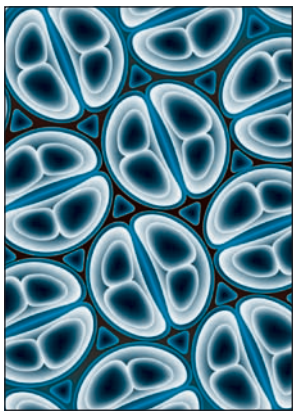
EuroDYNA starts to unlock Pandora's Box of genome function



Understanding how the genome functions is one of the major challenges in biology. No small feat one might say but the implications are manifold. Detailed knowledge of the principles and mechanisms underlying the control of gene expression is vital for understanding the cause of many diseases, and for developing rational procedures for genomic engineering, including gene therapy and stem cell engineering, and for many biotechnology applications.

"People cannot expect medical applications like cures but they can expect us to describe biological pathways in more detail. This will provide us with much better tools to monitor disease, disease remission and disease progression. Essentially EuroDYNA has made a significant contribution to getting hold of molecular markers for certain conditions, one of them being cancer but this also includes ageing," said Colin Logie, Chair of the EuroDYNA Scientific Committee.

The EUROCORES Programme EuroDYNA has approached the challenge of understanding the genome by bringing together researchers from across Europe.

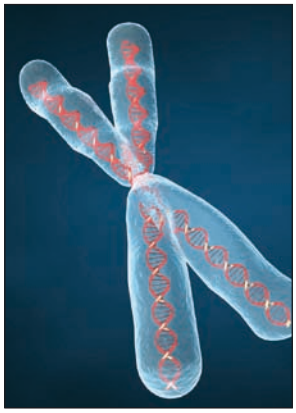
"EuroDYNA has exposed me to new and different approaches to biological problems and that has made a difference. It's made a difference to my research," said David Shore, University of Geneva and the Project Leader of "Environmental stress-induced dynamic modulation of chromatin structure, gene expression and nuclear architecture in yeast".

The Programme has gathered and combined expertise in many different fields of research. At a meeting in Dresden in September 2007, members of the EuroDYNA community as well as invited speakers from the US and Canada came together for a EuroDYNA-organised session. On this occasion talks focused on the subject "Chromatin and the cell cycle" and the speakers covered everything from plant cells, via Drosophila cells to mammalian cells.

Chromatin and the Cell Cycle
The EuroDYNA Session at ELSO, Dresden, 1 September 2007
Organisers: Colin Logie and David Shore

Invited speakers:

- Mary Ann Osley (Albuquerque) - a pioneer in chromatin.
  Histone metabolism, transcription and the cell cycle
- Rainer Renkawitz (Giessen), selected talk
  The Drosophila insulator protein dCTCF binds to different genomic sites than Suppressor of Hairy wing, shares cofactor CP190 and is required for the function of the homeotic Bithorax complex
- Mieke van Lijsebettens (Ghent) who presented findings on cell cycle control during A. thaliani development. *The plant BRE1 H2B ubiquitylase has a function in cell cycle regulation during early leaf and root growth*
- Alain Verreault (Montreal), who talked about *Histone H3-Lys56 acetylation: a new twist in the chromosome cycle*
- Francis Stewart (Dresden) - an Australian recombineering pioneer.
  Global analysis of histone modifications by mass spectrometry



Alain Verreault, University of Montreal and speaker at the EuroDYNA session at ELSO, focuses his research on how chemicals in the environment affect DNA. Verreault's research has many implications for the treatment of cancer using chemotherapy. He has found that a process called acetylation, when an acetyl group is added to a protein, globally affects the proteins that package DNA (known as histones) during DNA replication. Both the acetylation of histones and its timely removal are important for efficient DNA repair and cell survival in response to DNA damage. For instance, when the genes HST3 and HST4 were removed from yeast cells, acetylation could no longer be removed from histone proteins, which resulted in increased DNA damage, both spontaneous and in response to chemotherapeutic agents that damage DNA. This research could prove tremendously important to cancer treatment, but Verreault also emphasised "I suspect that other acetylation sites play a role in higher eukaryotes and more research is needed".

However, medicine is not the only area where the EuroDYNA research has implications. The regulation of plant growth is a topic of both scientific and economic importance. Understanding the molecular mechanisms behind leaf size, shape and number could result in tools to improve food and bioenergy production.

Plant leaves start to grow as a result of the activation of transcription factors, proteins that bind to DNA and initiate the transcription of DNA to RNA. In other words, transcription factors are the triggers initiating the information from DNA to be translated into proteins and peptides, which determine cell type and function in all organisms. Some of the triggers that control leaf growth have already been identified but the question many cell biologists ask is; what are the mechanisms that regulate the transcription factors? This is what Mieke Van Lijsebettens and her group "Chromatin and growth control" at the Department of Plant Systems Biology at VIB/ Ghent University, Belgium are looking into.

"The leaf has been developed as an experimental system to identify upstream regulatory genes for growth by analyzing Arabidopsis mutants with altered leaf size and shape," said Van Lijsebettens during her talk in Dresden. She reported that her group had found a putative upstream regulatory gene called HISTONE MONOUBIQUITINATION 1 (HUB1) that mediates gene activation and cell cycle regulation by chromatin modification leading to the coordination of growth in multiple organ types.

For more information see the EuroDYNA website at www.esf.org/eurodyna

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Colin Logie

A moment with Colin Logie

In a recent interview, Colin Logie, Chair of the EuroDYNA Scientific Committee, talks about organising the EuroDYNA session at ELSO and about future challenges for the cell biology field and for EuroDYNA.

Why did you choose the topic "Chromatin and the cell cycle" for the EuroDYNA session at ELSO?
Although we know a lot about the cell, DNA and chromatin, we still lack insight into how it functions. To understand how things function you have to put them into context. One thing about life is that it is cell based and one thing about cells is that they are always the product of the cell division of a previous cell. So, to really understand chromosomes we really have to understand how the chromosomes behave in the cell cycle. I think during the session we saw an example of very disparate talks ending up with conclusions about chromosomes which fitted together because they fit the context of the cell cycle as the common denominator.

What, in your opinion, are the challenges in your field?
One of the frontiers of this field is to really see what happens inside living cells. We have done many beautiful experiments in the recent past (by we, I mean the Scientific Community) but what we really need is multi-molecular assembly dynamics data. These things are very difficult to see at the moment and we really need to be able to see them to find out which factors are playing roles of messengers and which ones are playing more structural roles. Essentially it boils down to physically describing the isomerisations that take place in the cell, the DNA and also in the membranes. We also need to find ways of estimating the energetic code of each transaction and of integrating these types of data over multiple length scales from the nanometer to the micrometer. From this we should be able to formulate a mathematical description of biological systems.

What's also a big challenge is our ability to monitor things at the right timescale. We know that molecules function on the level of millions as well as thousands of a second and this spans six maybe even seven orders of magnitude. Right now we don't have good modelling systems to integrate all the data at those different time and length scales and I think that's a major challenge. It's not so complicated to address this. We need durable funding of scientific research; we need to maintain and sometimes also improve career opportunities, support institutes where innovation and originality are encouraged and promote communication amongst scientists. The latter is very important and something that ESF has been doing very well. We need communication between disciplines but also within disciplines.

What can the Scientific Community expect from EuroDYNA as a collaboration?
One field which is moving forward at the moment is nanoscience. By looking in great detail using biophysical methods on single molecules we are actually studying nanomotors which are driven by ATP. The exciting application for this is that maybe one day such motors can be harvested to produce DNA-based machines. EuroDYNA's contribution in this field involves what we are doing in defining the forces that are deployed by these motors. At the moment the physical description of biology is lagging behind but we are getting there now by finding forces, distances and time.

The full podcast with Colin Logie can be found on the EuroDYNA website at www.esf.org/eurodyna