EuroDYNA conference magnifies small components for big issues: finding the answer to human disease

At a recent EuroDYNA conference in Brno, Czech Republic, 60 scientists from nine European countries came together to present their research in the field of genetics and cell nucleus architecture - often referred to as the body's building blocks. It is hoped that this could lead to a better way of combating human diseases.

The conference demonstrated that there is still much to learn about the body's small components but that scientific synergy and pan-European collaboration could help to achieve this goal.

Following in the footsteps of Nobel Prize winners

The conference touched on the issue of RNA interference (RNAi). RNAi was a hot topic in recent years as the field of gene therapy has expanded to encompass the area of RNA interference. RNA interference occurs in plants, animals, and humans and it is of great importance for the regulation of gene expression, participating in defense against viral infections, and keeping jumping genes under control. RNAi is already being widely used in basic science as a method to study the function of genes and it may lead to novel therapies in the future.

The field has garnered a Nobel Prize in medicine this year through scientists Andrew Fire, Stanford University School of Medicine, US and Craig Mello, University of Massachusetts Medical School, US for their research on RNA interference – gene silencing by double stranded RNA.

One of the conference delegates, Leonie Kamminga, Hubrecht Laboratory, Utrecht, described her work looking at proteins involved in RNAi. In her talk Kamminga concentrated on the Piwi proteins which are involved in stem cell maintenance. Recently, a new class of small RNAs was discovered that interact with Piwi. These are called piRNAs and they are present in the testes of mice, rats and humans, but not in the ovaries. In the zebrafish, which Kamminga studies, there are two Piwi proteins: Ziwi and Zili.

"Ziwi is only expressed in the primordial germ cells of the zebrafish embryo. These are the precursors of the adult germ cells. Loss of ziwi results in an absence of germ cells, probably due to cell death," said Kamminga.
"Unlike in other vertebrates, we found piRNAs in both the ovaries and testes of zebrafish" she added.

Investigating the glue of life

Other issues that attracted the attention of the conference goers included the different stages and mechanisms of cell division.

Kim Nasmyth, University of Oxford, is trying to answer how chromatids (the two arms of the chromosome) are held together and also, how they are separated during cell division.

"Cohesin is what holds sister chromatids together", explained Nasmyth.

The cohesin is made up of two strands of proteins called SMC, proteins which are present in animals and bacteria. These are linked by a hinge and bound together at the head. By looking at circular DNA running trapped between the cohesin protein arms, Nasmyth and his team have found that the cohesin hinge has to be opened in order for DNA to enter the cohesin structure. Nasmyth believes that the most likely mechanism for the entry of DNA into the structure is through an opening of the hinge.

For cell division to occur, the restructuring of chromatin, the material which makes up the chromosomes, into morphologically distinct chromosomes is essential. Currently the molecular mechanisms underlying this process are poorly understood.

Jan Ellenberg, EMBL, Heidelberg presented data that indicate that maximum compaction of chromatin occurs in late anaphase instead of the metaphase (two different parts of the cell cycle).

He noted that the process which compacts the chromatid prior to cell division does not require condensin complexes, another complex whose function rather seems to be to make already compacted chromosomes sufficiently rigid to withstand the forces of the mitotic spindle, a cell structure which functions to segregate the chromosomes during cell division.

In addition Ellenberg found that cohesin complexes establish sufficiently long lived interactions with chromatin during replication to remain bound to chromosomes until mitosis.

As cell division is essential for growth and replenishment of tissues and organs, understanding these mechanisms has significant implications for understanding normal physiology and disease. This is especially important as no cellular process is 100% efficient and cell division failure is deleterious and can lead to tumours.

Scaffolding provides nuclear structure

The structural organization of the cell nucleus and chromosomes is a great challenge of biological research, something which was also highlighted.

Ulrich Laemmli, University of Geneva, found that the structure of the nucleus is not random and it is largely determined by functional interactions related to gene expression.

Laemmli and his team have found that in the areas of the nucleus called nucleopores, a promoter is required to interact with the nucleopore basket in order for genes to be expressed. This interaction also serves as a boundary element (BE), separating gene expression. When the promoter-basket interaction was disrupted, the team found that the nuclei became fragile, indicating that this interaction is involved in providing nuclear structure.

EuroDYNA has only been an active programme since 2005 but already it is clear that research advances will come from this unique collaboration. Like the community effect described by John Gordon, University of Cambridge “when cells are close together, the effect will be amplified”, the take home message from this conference is that scientific

synergy leads to better research results and understanding the small processes will ultimately lead to a greater understanding of the body as a whole.

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