



Research Institute of Molecular Pathology

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Study suggests that successful blueprints are recycled by evolution

A study by researchers in Austria and the US finds evidence that the different cell types that make up organs have arisen only once during the course of evolution. The programs to develop these cells have been passed on ever since. The study which is published online by Nature Genetics has been supported by the GEN-AU Programme of the Austrian Ministry for Science and Research.

During the development of an embryo, a large number of different, specialised cell-types arise from the fertilised egg. The genetic information is identical in all cells of an organism. Different properties of cells arise because the activity of genes is controlled and regulated by so called transcription factors. By switching genes on or off, the body makes muscle cells, bone cells, liver cells and many more.

Scientists have been puzzling over the question whether the gene regulatory programs that control this development have been “invented” only once during evolution or whether they might have arisen anew in different species. Previous studies supported both theories to a certain extent.

A team of researchers in Austria and the United States has now looked at key regulatory proteins in six different species of the fruit fly *Drosophila*. They studied the development of the mesoderm, one of the three primary germ cell layers in the early embryo of all higher organisms. Mesodermal cells differentiate into muscle cells, heart cells, connecting tissue and bone, among others.

Evolution with a Twist

“Some of the fly species that we looked at are as closely related as humans are to other primates. Others are as distant as humans and birds”, explains Alexander Stark, a systems biologist at the Research Institute of Molecular Pathology (IMP) in Vienna and one of the authors of the study. The team focussed on the transcription factor Twist and looked at the binding sites for Twist on the DNA of the different species. It turned out that these binding sites are very similar in all the flies, suggesting that the program that regulates mesodermal development has been “recycled” rather than invented independently in these animals.

In addition to these results, the study also found that Twist interacts with partner transcription factors to specifically bind to DNA at the correct positions. A deeper understanding of these mechanisms will help understand how higher organisms such as humans develop and how flaws in the regulation of genes may lead to diseases such as cancer.

A network of collaborations

The study is the result of a fruitful cooperation between two former MIT-colleagues: Julia Zeitlinger, who is now at the Stowers Institute for Medical Research and the University of Kansas School of Medicine, identified the binding sites of transcription factors. Alexander Stark, who is now a Group Leader at the IMP and head of a sub-project of the Bioinformatics Integration Network III, was in charge of prediction and analysis of the data.

The Bioinformatics Integration Network (BIN), also sponsored under the Austrian GEN-AU Programme, develops bioinformatic solutions and offers them to other research groups. The network is led by Zlatko Trajanoski of the Medical University in Innsbruck.

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Other partners of BIN are the Institute for Genomics and Bioinformatics of the University of Technology in Graz, the Center of Integrative Bioinformatics at the Max F. Perutz Laboratories in Vienna, and the Research Institute of Molecular Pathology in Vienna.

Collaborations were also entered with the Institute for Theoretical Chemistry and the Department of Structural and Computational Biology, both at the University of Vienna, UMIT – the Health and Life Sciences University Hall/Tyrol, and CeMM, the Research Center for Molecular Medicine of the Austrian Academy of Sciences in Vienna.

The publication is the result of the sub-project „Cis-acting regulatory motifs“, led by Maria Novatchkova and Alexander Stark (both IMP), one of ten sub-projects of BIN. The Austrian Genome Research Programme has been initiated by the Austrian Federal Ministry for Science and Research in 2001.

The Paper “High conservation of transcription factor binding and evidence for combinatorial regulation across six Drosophila species” was published online in Nature Genetics on April 10, 2011:
<http://www.nature.com/ng/journal/vaop/ncurrent/full/ng.808.html>

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