Laudatio for Dr. Benjamin Lehner

Centre de Regulació Genòmica, Barcelona, Spain

Winner of the Eppendorf Award for Young Investigators 2013

The laudatio was held by Prof. Reinhard Jahn (Director of the Max Planck Institute for Biophysical Chemistry, Göttingen, Germany) at the prize ceremony at the EMBL Advanced Training Centre in Heidelberg on 6 June 2013.

»Since the completion of the human genome project many of us have nourished the hope that we may soon be able to predict whether anyone of us will develop one of countless diseases or not. This hope was founded on the discovery that more and more diseases – common and rare ones – are associated with combinations of genetic variations. Thus, at some point in the future, sequencing of our genomes should allow for reasonably accurate predictions of future health problems, thus allowing for taking preventive measures as far as possible. I still remember how the first human genome sequence was hailed as a breakthrough, expected to transform personalized medicine to a new level.

Indeed, there are quite a few mutations in humans that lead with certainty to a defined disease (e.g. enzyme defects such as phenylketonuria). However, there are many more cases where some individuals carrying a given disease mutation do not develop the disease or only develop it much later in life than other individuals who carry the same mutation. One of the reasons is that the severity of the phenotype caused by given mutations is influenced by the interplay of countless other genetic variants that on their own do not display any aberrant phenotype, and by environmental factors. Every one using transgenic mouse models knows how important it is to ensure that there is no other variation when comparing transgenic with wildtype animals. Indeed, changing the genetic background of a mouse strain may completely abolish a phenotypic difference that we took great pains to establish in extensive experiments.

Although not entirely unexpected, this is rather frustrating. In fact, there is growing evidence that a given phenotype is determined by the often subtle interaction between hundreds of even thousands of genes. Tracing even a few of such genetic networks, particularly in complex metazoans such as humans – is a daunting task. To make matters worse, phenotypic diversity is observable even within populations with identical genetic makeup. For instance, identical twins show a surprising variability in diseases that are linked to genetic variations. Even in comparably simple model organisms such as the nematode C. *elegans* the phenotypic effect of a given mutation varies between individuals – the “penetrance” of the phenotype, as we say, is variable.

How can one solve these intricate riddles of nature? These are the type of questions that are being asked by Ben Lehner, the winner of this year’s Eppendorf Young Investigator Award, whom I would now like to introduce to you.

Ben Lehner is British. He did his entire academic education in Cambridge, UK. When he graduated from College in the year 2000, the sequencing of the human genome had just been announced as the breakthrough achievement of the decade. He has told me that this discovery made him wonder about the scientific topic he wanted to study. He then decided to work at a genomics institute and finally joined the Sanger Institute which is actually very close to Cambridge. While he was working on some large scale screens using the nematode C. *elegans*, he was puzzled by the phenotypic variability between individual worms of the same phenotype. Apparently, he was sidetracked by this observations and did a few experiments on his own. He told me that he was criticized for doing too many different things. Well, for the younger scientists in the audience I can only encourage you to ask such questions and preserve your curiosity – even though supervisors such as me want their postdocs to focus on the research project at hand. His "diversification" cannot have been too detrimental considering that he published 1st author papers in Nature and Nature Genetics during this period. At that time already he was focusing on genetic networks in C. *elegans*, a theme that he has continued to develop after establishing his own laboratory.

After completion of his postdoc, he moved to the Center for Genomic Regulation in Barcelona where he became a group leader at the EMBL-CRG Systems Biology Research Unit. How does a young British scientist from an "Ivy league institution" who never lived abroad before decide to work in Catalunya? Well, I have asked Ben this question, and he has told me the story that I would like to share with you. He was on vacations in Spain and happened to walk by the then construction site of the CRG. When checking what was being built at such a beautiful location directly at the Mediterranean beach, he thought "Wow, this is going to be a scientific institute!". Intrigued he checked out the place after return and learned that this is actually a very serious institute, with excellent people going there from places such as the UK or from Heidelberg, and he decided to apply. In fact this was the only application he sent for an independent position, and he

has been there ever since. He has been rising through the ranks, and evidently he had no reasons to regret his decision.

The research Ben has carried out in his lab is nothing short of groundbreaking. For his work, he is taking advantage of the full power of genome sequencing and the rapidly expanding data sets containing sequences from many individuals, from well characterized human cancers and from other sources. Ben uses a combination of experiments and bioinformatics to identify genetic networks, to understand why mutations are not randomly distributed, and why mutations associated with cancer are clustered in an unexpected and surprising manner. I do not want to steal his thunder – he is going to tell you about his work by himself – but his work is fundamental and has profound impact on our understanding of phenotypic variations including human disease.

Welcome the winner of the Eppendorf Young Investigator Award, Ben Lehner!«