Laudatio
for Madeline Lancaster, Ph.D.

Postdoctoral Fellow, Institute of Molecular Biotechnology
of the Austrian Academy of Sciences, Vienna, Austria
Winner of the Eppendorf Award for Young Investigators 2014

The laudatio was held by Prof. Reinhard Jahn (Director at the Max Planck Institute for Biophysical Chemistry, Göttingen, Germany) at the prize ceremony at the EMBL Advanced Training Centre in Heidelberg on 22 May 2014.

» The human brain is undoubtedly the most complex organ to exist in any living organism. The sheer dimensions of its complexity are beyond imagination: 1011 neurons (2 orders of magnitude more than the human genome has base pairs), connected by 1014 synapses. To put this number into perspective: this is about the sum in dollars of the gross national products of all countries worldwide. Complexity of the brain, however, is not limited to large numbers. Even with the most advanced imaging and reconstruction techniques it requires years and many hundreds of volunteers to reconstruct the connectivity of only a cubic millimeter of cortical tissue. Considering further that the brain is what distinguishes humans most from our closest evolutionary relatives there is no surprise that research on the human brain is one of the hottest topics in life sciences at present.

One of the most fascinating questions is how the enormous complexity of the brain with its refined regional differentiation, layered structure, multiple cell types, and exquisite connectivity can develop from a small set of pluripotent stem cells. In recent years, research

has provided key insights into the signaling cascades and into the ability to self-organize during development. For instance, the ontogenesis of neurons, of neuronal subtypes, and many steps of the differentiation and maturation of individual brain regions have been unraveled. Furthermore, we now know that the number of divisions of neuronal stem cells, giving rise to a neuronal progenitor cell and another stem cells (self-renewal) is critical for ultimately defining the size and complexity of a mammalian brain. Intriguingly, it has been remarkably tricky to reproduce even very early developmental steps of brain development under controlled laboratory conditions. It is common knowledge that pluripotent stem cells are the basis for all tissue and organ development and that these cells on their own should contain everything it takes to form a fully functional organ. Thus, major progress has been made in understanding the factors promoting differentiation of stem cells into particular cell types such as neurons, and journals like Nature gladly have published every transcription factor cocktail driving yet another lineage differentiation. However, it has been much more difficult to reach higher levels of complexity in the test tube and to understand the rules of the game. It is precisely this problem where Madeline Lancaster, the winner of this year's Eppendorf Young Investigator Award, has made truly remarkable progress.

Madeline Lancaster is US-American. She grew up in Utah, in Salt Lake City but decided to move to California for her academic education. Europeans usually get dreamy eyes when they think about California, with its wonderful beaches and palm trees, the spectacular national parks, the eternally warm temperatures, and the sunshine. However, California is also one of the world's centers of science and technology, being home not only to the famous Silicon Valley but also to some of the world's foremost academic institutions. Madeline attended the Occidental college in Los Angeles, a small liberal arts college as she told me, majoring in biochemistry. Her interests quickly focused on neuroscience. For her ongoing education, she was undecided whether to pursue her PhD at the CALTECH or at the University of California San Diego (UCSD). She selected UCSD because of the many rising stars she spotted at this place. In the end, she joined the lab of one of these rising stars, the lab of John Gleeson. John Gleeson is interested in the development of the mammalian brain. According to Madeline, she was at the right place at the right time because John was still in the early phases of developing his own laboratory. Thus he could spend lots of time in mentoring his graduate students, but he was already on a steep trajectory towards international leadership, publishing regularly in top journals, and becoming a HHMI investigator. During her time, Madeline worked on the role of the wnt signaling pathways in ciliopathies, human diseases related to cilia malfunction. It is only in

recent years that cilia that are present on virtually all cells were recognized to play a crucial role in signaling and tissue differentiation, affecting many organs including the kidney and the brain. The success of her work was quite spectacular, with two first author papers in Nature Medicine and one in Nature Cell Biology. In the 8 years I have been serving as dean of a large graduate school I cannot remember ever that a student finished his or her PhD with such a stellar record!

Being married to a European she decided to look for a postdoc position in Europe. She was attracted by Jürgen Knoblich in Vienna, whose work she found exciting and she also liked the discursive style and the freedom she would have in pursuing her ideas. The success of her work in Vienna was even more spectacular than that of her PhD work. As often in science, these projects are not planned meticulously from the onset – she did not go to Jürgen's laboratory to build a brain in a dish, but this is almost what she ended up doing. I do not want to take away anything from what Madeline is going to tell you by herself except of stating that her work has created quite a splash not only within her field but also in the general public, with quite bit of well-deserved media coverage. The work is of outstanding quality in all of its aspects and constitutes a breakthrough for future work on human brain development. It allows experimental access to problems such as the regulation of brain size and to developmental disorders affecting the brain that are difficult to study in mice, the standard mammalian model organism. Not surprisingly, the jury was unanimous in its decision to grant the Award to Madeline.

Let's welcome Madeline Lancaster, the Winner of the Eppendorf Young Investigator Award 2014! «