EMBO Molecular Medicine

Cancer and neurodegeneration meet

What is molecular medicine? My view is that it is the scientific discipline that applies the tool-box of molecular biology to understand the pathogenesis of disease. Ideally such work translates into novel diagnostics and novel drug targets and treatments. It is clear that molecular medicine is not only borrowing knowledge and tools from other life sciences, but the field is itself also driving the development of novel technologies and the creation of new insights in biology. In fact, the nature of molecular medicine research, oriented towards pathophysiological processes, systems and models makes this field one of the spearheads of the rapid evolution in life sciences. Molecular genetics is exemplary in that regard; the massive investments made to sequence and annotate the human genome and to refine the analysis of genetic information were only possible because of the idea that medical benefits will emerge down the line. Obviously all life sciences profit from this boost.

> *» It was enriching to see how Cancer and Neurodegeneration researchers focusing on abnormal cell growth and cell loss, respectively, share so many questions, knowledge and tools. . . «*

Research into areas such as cancer, cardiovascular disease or neurology affects other disciplines and propels our knowledge with increasing velocity. EMBO Molecular Medicine aims to divulge this knowledge and promote a faster pace for its translation into the clinics. As our understanding of human pathophysiology increases so does our realization of the inevitable cross-talk between different molecular and cellular processes. A broad scope medical journal such as EMBO Molecular Medicine is a fruitful ground for such cross-fertilization. I recently experienced an interesting example of two, at first glance, very remote fields of research finding each other in similar molecular signalling pathways and experimental approaches. I am referring to a small meeting, 'Two faces of Evil: cancer and neurodegeneration', organized by the 'Fondation Ipsen' in Paris. While the title might appear ominous, scientifically it was a day full of good things. It was enriching to see how Cancer and Neurodegeneration researchers focusing on abnormal cell growth and cell loss, respectively, share so many questions, knowledge and tools to understand how normal physiological mechanisms go astray in both diseases.

There are striking examples of how studying cancer can unexpectedly lead to a better understanding of problems in neurodegeneration and *vice versa*. For instance, patients with lung or gynecological cancers sometimes develop auto-antibodies that cross the blood brain barrier and cause severe paraneoplastic neurological syndromes, including cerebellar neurodegeneration. These antibodies are part of the immunological response to the tumours, which can express brain proteins. Nova and other ribonucleic acid (RNA) binding proteins are examples of such proteins and their discovery prompted the in depth study of their messenger RNA (mRNA) targets and the identification of the proteins that were altered in these neurodegenerative processes. Further work resulted into novel insights in mRNA-protein regulatory networks and led to the development of novel technologies like high-throughput sequencing cross-linking and immunoprecipitation (HITS-CLIP) to study the interactions of microRNA and RNA targets in the brain (and other tissues). This is Molecular Medicine operating at its best: approaching medical relevant questions originating from observations in patients, followed by the progressive dissection of the molecular pathways underlying the observed events using existing knowledge from various life science disciplines, and finally pushing the borders when the limits of available knowledge are reached. By definition, the thinking is systemic and the approaches multidisciplinary. As for the ultimate goal: application of knowledge to develop treatments, cures or novel diagnostic markers.

Other examples came from the study of severe childhood brain cancers like medulloblastoma, which led to the identification of a Hedgehog signalling receptor, thought to play an important role in neurodevelopment and neuronal stem cell biology. Hedgehog antagonists displayed spectacular results in a mouse model for medulloblastoma and in (limited) trials in humans suffering from medulloblastoma or advanced basal cell carcinoma (transient) improvements in their health condition were observed.

The closer one gets to both topics the more examples one can find where studying proteins or processes in one field, results in new knowledge in the other. Proteins familiar to cancer biologists are equally recognizable by neurodegeneration researchers. For instance, the cyclin-dependant kinase member Cdk5, related to the well-known mammalian cell-cycle Cdks 1-4, is exported from the nucleus where it

suppresses cell division, to the cytoplasm where it appears to protect transiently against cell death, in neurons affected by Alzheimer's disease. Indeed, Alzheimer neurons appear to display an 'aborted cycling state' as demonstrated by their tetraploidy and staining for various cycling markers. Whether this is a protective phenomenon or on the contrary, drives neurons to cell death is unclear. Further work is certainly needed in this fascinating area of research that will hopefully drive both fields. Not surprisingly, also the p53 family members play essential roles in both cancer and degeneration illustrated for instance by how loss of p73 leads to neurodegeneration. This is not unlike the well-known p53 loss of function in many human cancers, although in Alzheimer's disease p53 seems to be up regulated.

» . . .the task of a journal like EMBO Molecular Medicine is timely and of utmost relevance. «

The interdisciplinary approach and mentality of researchers working at this interesting frontier and the knowledge and clinical potential that these studies carry tells me that the task of a journal like EMBO Molecular Medicine is timely and of utmost relevance. I hope that authors and readers will follow us in this endeavor: to create an international interdisciplinary forum, which highlights new findings, opens areas of research and provokes broad discussions and debate: '*Du choc des idées jaillit la lumière*'.

Bart de Strooper

Bart de Strooper is a Senior Editor of EMBO Molecular Medicine, Professor at the Katholieke Universiteit Leuven and Head of the VIB Department of Molecular and Developmental Genetics, K.U. Leuven.
VIB Department of Molecular and Developmental Genetics, K.U. Leuven, Leuven, Belgium
E-mail: Bart.DeStrooper@cme.vib-kuleuven.be
DOI 10.1002/emmm.201000078

