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Editorial overview: Developmental neuroscience 2017 Paola Arlotta and Pierre Vanderhaeghen



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Paola Arlotta is a Professor of Stem Cell and Regenerative Biology at Harvard University and an associate member of the Stanley Center for Psychiatric Research at the Broad Institute of Harvard and M.I.T. Her laboratory studies the molecular underpinnings governing the birth, differentiation, and assembly of clinically relevant cortical neuron types into the cerebral cortex. Her laboratory integrates developmental and evolutionary knowledge to inform novel strategies for circuit repair in the cortex and for modeling of neurodevelopmental disease in the dish.

Pierre Vanderhaeghen



Université Libre de Bruxelles (ULB), Institute for Interdisciplinary Research (IRIBHM), ULB Institute of Neuroscience (UNI), WELBIO, Université Libre de Bruxelles, 808 Route de Lennik, B-1070 Brussels, Belgium e-mail: pvdhaegh@ulb.ac.be Whoever contemplates the last 25 years of tremendous progress in developmental neurobiology would be right to describe it as a golden age, and may therefore be tempted to ask the same question raised by the artists of the Renaissance: "What can we do beyond what was already accomplished in the Ancient golden age?". Could it be that all fundamental mechanisms of neural development have been identified and exposed, leaving to the younger generations the painstaking dissection of whatever tiny details were left incompletely uncovered? Well, of course not, as surely as there has been plenty to create and admire beyond the Parthenon, Milo's Venus, or the Odyssey.

Yes, we may indeed have entered an era of post-classical neural development, which gives us access to an unprecedented world of possibilities to challenge the now-established views, and shed light on the many remaining obscure corners of brain development. Because there are many mysteries left to solve in the developing brain, indeed, as the reviews presented in this Issue will demonstrate. And they will also show that, to keep in line with the art metaphor, today's developmental neurobiology does seem to share many features of modern art, in particular the ability to mix and match old and new models and concepts, to reveal complexity through variations on seemingly invariant themes, and to combine unrelated reductionist approaches to reach holistic views.

Neural development is classically thought to involve discrete steps, such as neural induction, regional patterning, cell differentiation and specification, morphogenesis, and finally neural circuit formation and refinement. But while this textbook view makes it easier to represent these complex processes, to teach and learn and think about them, in real life neural development is not a fixed ladder-like structure, but rather emerges from a time-driven continuous flow of events, within which most of the so-called steps are in fact highly intermingled. This will be exemplified by many of the reviews that address multiple mechanisms or steps of development, once separated and now highly integrated.

Another feature that emerges is that most of the authors discuss concepts drawn from several model systems. This comparative approach leads to a more holistic view of development, tightly linked to evolution. It enables the identification of universal mechanisms that can be found across species or brain regions, for instance, or, on the opposite hand, highlight divergent strategies. One can start to grasp how it is that neural circuits share many features across regions, systems or species, but yet display specific, sometimes unique characteristics that allow them to make us what we are, as individuals and as a species. Pierre Vanderhaeghen is currently professor and WELBIO investigator at Université Libre de Bruxelles, Belgium. His laboratory studies the mechanisms that control the development of the cerebral cortex, with special emphasis on neurogenesis and circuit formation, in links with human brain evolution and diseases. Moreover, while there is general acceptance that neural development does stop at some arguable point in time, beyond which the brain starts to function as a mature organ, when exactly this occurs is much less clear, and the answer quite variable depending on the model, substructure, or species considered. Several reviews will examine this point, focusing on how brain structure and function can change beyond the ontogeny of its circuit blueprint, through refinement, plasticity, or regeneration.

Studying neural development as a continuum of intermingled processes has been challenging, yet a new era is starting when revolutionary technology, including single-cell analysis, is primed to make ground-breaking advances in our understanding of not only the diverse cellular composition of the nervous system, but also of the mechanisms that shape and wire this cell diversity, with unprecedented temporal and spatial resolution.

A first set of reviews deal with emerging views on how stem/progenitor cells balance self-renewal and differentiation, through cues that are sometimes already well known and at other times quite surprising. Guillemot and Hassan start with a most classical theme, proneural factors highly conserved throughout the animal kingdom, and discuss recent discoveries of unexpected ways in which these proteins are regulated, in particular novel mechanisms of post-transcriptional control, and of novel roles, such as promoting not only neural differentiation but also the proliferation of stem cells. They also discuss how these factors have become powerful tools for lineage reprogramming from non-neuronal to neuronal cells. Focusing on the cerebral cortex, Delaunay et al. explore how a basic feature of the cell, mitosis, can affect neurogenesis in highly diverse vet specific ways. The shape, polarity, and degree of symmetry of the neural stem/progenitor cell as it divides can profoundly influence the identity of its progeny, although, at the same time, cell division can be surprisingly uncoupled from fate specification. The impact of specific properties of stem cell division is best exemplified by the outer radial glial cells: Ostrem et al. review the latest molecular and cellular findings on this fascinating progenitor cell population of the cortex, with emphasis on their characteristic pattern of mitotic somal translocation, in relation with human brain evolution and disease.

Like cell division, metabolism is a fundamental aspect of cell biology, yet it has been generally considered at best a mere permissive developmental cue. Knobloch and Jessberger discuss recent findings that directly link various metabolic flows, from glycolysis to lipogenesis, to neural stem cell biology and neurogenesis. These new data are likely only the tip of the iceberg for the emerging view of metabolism as a critical hub that integrates developmental cues and neural cell fate decisions.

Time has always been a fundamental coordinate in biology, but how it is encoded and used in neural development has remained quite mysterious compared with our depth of knowledge on space and its role in patterning distinct brain regions. Rossi et al. provide a comprehensive comparative overview throughout species and systems, from fly retina to human cortex, of how time is encoded into lineages to generate ordered cellular diversity. They delineate the elements that appear to be evolutionarily conserved, but also point out that in vertebrates temporal patterning seems to be less deterministic, leaving open the question of whether complementary mechanisms are involved.

Applying a holistic approach to the daunting question of the origin of one of the most diverse neuronal cell types of the brain, the cortical inhibitory Download English Version:

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