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EDITORIAL

Human development: recent progress and future prospects

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As readers of Development are no doubt aware, one of my [O.P.'s] main aims as Editor-in-Chief has been to publish high-quality stem cell papers, and to increase the profile of the journal in that field. Back in 2012, we put together a strategic plan to help us achieve that aim, one of the strands of which was to organise a meeting – as a prominent signal of interest in the stem cell arena. As we looked at the already-crowded meeting calendar to identify a focus for a potential meeting, we quickly realised that, while there are myriad meetings covering stem cell biology, there were none that concentrated on what we saw as a prime niche for the journal: the use of stem cells to understand human development. Thus, the first of what has turned into a series of meetings entitled 'From stem cells to human development' was born, and was held at Wotton House in Surrey, UK, in 2014.

In the wake of that meeting, we immediately decided that we should plan a repeat event, and we also organised a Special Issue on human development, which was published in September 2015. Now, 4 years on, we are about to hold the third 'From stem cells to human development' meeting (returning again to Wotton House in late September) and, to coincide with this, are publishing our second Special Issue on human development – for which this editorial serves as introduction. As we commented previously (Pourquié et al., 2015), 'those of us present [at the first meeting] had the impression of witnessing at first hand the emergence of this new field of human developmental biology'. So how has the field come on in the past 4 years? Certainly, we have made huge progress in our ability to differentiate human pluripotent stem cells (hPSCs) along diverse lineage trajectories and to improve the maturation state of those differentiated cells. We are also improving our tools and resources to study the human embryo with, for example, a new high-resolution atlas and database (de Bakker et al., 2016), and improved imaging techniques to visualise cells and tissues *in situ* (Belle et al., 2017). CRISPR technologies facilitate manipulation of the human genome and transcriptome in ways scarcely imaginable a decade ago, and single-cell 'omic approaches allow us to analyse cell types and lineages in unprecedented detail (Camp and Treutlein, 2017). And, following on from the tremendous advances of the past 5-10 years using organoids to study organogenesis *in vitro*, we are beginning to use equivalent approaches to study the very early embryo – published reports thus far have generally used mouse stem cells (e.g. Rivron et al., 2018; Sozen et al., 2018; van den Brink et al., 2014) but these methodologies are now being extended to human stem cell systems. It is safe to say that the field has moved on a long way since we planned our first meeting, and Development is excited to be in a position to support and nurture the field as it progresses further.

This Special Issue reflects several of the themes mentioned above. Three papers report protocols for differentiation of hPSCs, down the spinal cord (Verrier et al., 2018; Ogura et al., 2018) and somite (Nakajima et al., 2018) lineages. It is notable that the two manuscripts looking at spinal cord differentiation use different methodologies and aim at distinct end points – neuromesodermal progenitors in the former case, and differentiated neurons in the latter. As a community, we still have much to understand about how different protocols impact on the final cell state that can be generated. But although our methods still need improving in many cases, we are already at a point where the cell types produced can be used to address developmental questions and to model disease, as shown by Nakajima et al., focussing on a rare endochondral ossification disorder.

Two of the contributions to this Special Issue use single-cell profiling to characterise differentiation trajectories and cell-type identities in developing human organs – the fetal pancreas (Ramond et al., 2018) and kidney (Menon et al., 2018). As shown by Ramond et al., these datasets provide a benchmark against which *in vitro* data can be compared to assess the validity and robustness of experimentally accessible cell culture or organoid models. The gene expression signatures of progenitor and intermediate cell types identified by such sequencing approaches also provide valuable insights into lineage trajectories during organogenesis. Three further papers in this issue make use of human tissue samples to examine developmental mechanisms: Jan et al. (2018) characterise meiotic defects during spermatogenesis (providing insights into the mechanisms underlying sub- or infertility in men), Lee et al. (2018) focus on the trophoblast progenitor cell niche in the early human placenta, and García-León et al. (2018) analyse the role of Notch signalling during thymic development.

In addition to these research papers, our Special Issue contains a number of Review and Spotlight articles that we hope will prove of interest to our readers. Rawlins and colleagues (Nikolić et al., 2018) review our current state of knowledge on human lung development from both *in vivo* and *in vitro* studies, while Kobayashi and Surani (2018) provide a brief overview of what we do – and don't – understand about the human germline. Taking *in vitro* organogenesis one step further from more conventional 2D and 3D cultures, Ingber (2018) discusses the latest 'organ-on-a-chip' technologies (pioneered by his lab), and how they can contribute to our understanding of development as well as serve as valuable tools for modelling disease and drug development.

Finally, it is crucial to remember that this research does not take place in a vacuum. Although we can manipulate the human genome, or grow an embryo in the lab for a couple of weeks, should we? Rossant (2018) discusses some of the ethical concerns associated with human gene editing in the light of a recent report from the National Academy of Sciences (National Academies of Sciences, Engineering, and Medicine, 2017). Such issues will continue to be a matter of public debate, and we hope that the Development community will find this piece – and other articles we have recently published on such ethical matters – useful in framing the key arguments in this arena.

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All that remains is for me to thank our authors, referees and editors for their work in pulling together this Special Issue, and to invite you to browse through the articles contained in it. Development is committed to continuing to publish some of the best papers from the human development field and we hope you will consider sending your next manuscript our way!

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