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EDITORIAL

Human development: a Special Issue

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In September 2014, *Development* organised a four-day workshop titled 'From Stem Cells to Human Development'. In planning this meeting, we sought to fill what we saw as a gap in the meeting calendar – a way of bringing together a diverse cross-section of researchers with a common interest in using the rapidly developing tools of stem cell biology, genetic engineering and genomic analysis to understand human development (for a review of the meeting, see Medvinsky and Livesey, 2015). The enthusiasm with which this workshop was met, from invited speakers and registered participants alike, confirmed our view that we are now in a period in which significant inroads into understanding human development will be made. With our ever-improving ability to model tissue development *in vitro* and to manipulate the human genome (and epigenome), we are now in a position to analyse human organogenesis and to understand how it differs from that in other model organisms – and hence to start to probe the developmental biology underlying the evolution of our species.

As we wrote in an editorial in January, "The human development field represents an essential growth area for the developmental biology community, and *Development* is keen to play an active role in supporting and inspiring it" (Pourquié et al., 2015). This Special Issue celebrates that aim – bringing together a collection of Reviews and Research Articles that directly address a broad range of topics in human developmental biology: from the earliest stages of human development to cellular ageing and degeneration, and from basic questions of how an organ is formed to ways in which we might translate this knowledge in the clinic. We are also supporting this initiative with a second 'From Stem Cells to Human Development' meeting, to be held in September 2016. More details on what should be a fantastic follow-up event can be found at http://workshops.biologists.com/from-stem-cells-to-human-development-2/.

Studying human development is obviously a challenging endeavour, given the practical and ethical difficulties in working with human material. However, as discussed by Dianne Gerrelli and colleagues (2015), there is a growing set of resources for researchers, including the Human Developmental Biology Resource (with which the authors are affiliated), which provides embryonic and foetal material and a range of valuable services. Maintaining and developing such resources will be essential as research on human development progresses.

Complementing work using human tissue, much of the research into human development relies on the generation and manipulation of human pluripotent stem cells (hPSCs) – either embryonic (hESCs) or induced (hiPSCs). There has, however, been much debate surrounding the pluripotent status of such hPSCs, particularly when compared with their mouse equivalents, as well as their *in vivo* counterparts. In their Review, Martin Pera and colleagues (Davidson et al., 2015) discuss these controversies in the light of recent attempts to generate truly naïve hESCs. Kathy Niakan and co-workers are also interested in pluripotent states and human-mouse comparisons. In their Research Article (Blakeley et al., 2015), they report single-cell RNA sequencing analyses of human and mouse preimplantation epiblasts, identifying important differences in the transcriptomes – and presumably therefore the development – of the early human and mouse embryo. One challenge in the field has been that functional assays for pluripotency of human cells are limited. To address this, Hiromitsu Nakauchi and colleagues (Masaki et al., 2015) investigate whether generating inter-specific chimeras (using mouse epiblasts and PSCs from various species) might provide an alternative assay system. Also using mouse embryology to probe human development are Felipe Vilella and colleagues, who describe a microRNA secreted in human endometrial fluid that can promote mouse embryo adhesion during implantation (Vilella et al., 2015), potentially identifying a novel route by which the efficiency of implantation can be modulated.

In another research paper investigating the role of microRNAs in human development (Jönsson et al., 2015), Malin Parmar and co-workers analyse the microRNAs expressed in the human foetal brain and in PSC-derived neural progenitor cells, identifying region-specific microRNAs that probably influence neural cell fate. Generating a functional nervous system requires not only that cell fate is correctly defined, but also that appropriate connectivity is established and that neurons are properly supported by glia. Frederick Livesey and colleagues address the former problem in cortical neuron cultures (Kirwan et al., 2015), while Motoharu Sakaue and Maya Sieber-Blum describe a protocol for generating supporting Schwann-like cells from human epidermal neural crest stem cells (Sakaue and Sieber-Blum, 2015). Meanwhile, Ikuo Suzuki and Pierre Vanderhaeghen (2015) review various aspects of studying neural development using hPSCs and discuss how these approaches should allow us to gain insights into the evolution of the human brain.

Katie Pollard and Lucia Franchini's interests also lie in understanding human evolution, but from a genomic perspective. Their Review (Franchini and Pollard, 2015) discusses how we can combine sequencing information with functional genomics and stem cell biology to identify and characterise changes in the human genome that might have led to human-specific developmental traits. They highlight the importance of appropriate experimental systems – not only model organisms but also through human stem cells and organoids – in which to test the function of human-specific genomic features. The ability to model not only cellular differentiation but also tissue formation in a dish constitutes a major breakthrough in the field over the past decade. Meritxell Huch and Bon-Kyoung Koo review the latest advances in generating endodermal organoids from both embryonic and adult stem cells (Huch and Koo, 2015) and provide a perspective on where this field is heading. The Review by Neil Hanley and colleagues (Jennings et al., 2015), while also focussing on endoderm development – in this case, pancreas – provides a complementary viewpoint, discussing what is known

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about human pancreas development *in vivo* and how these insights translate into our ability to generate β-cells *in vitro*.

Turning to other organs, Christine Mummery and Charles Murry and their colleagues both focus on heart development. Mummery's work (van den Berg et al., 2015) characterises the transcriptome of the human foetal heart and compares it with the RNA profile of PSC-derived cardiomyocytes. Meanwhile, Murry's study (Palpant et al., 2015) provides insights into how cardiomyocytes are specified in a hESC system. The final Research Article of this issue returns to the topic of organoid formation, this time the mammary gland. Christina Scheel and co-workers (Linnemann et al., 2015) present an organoid system that allows the regenerative potential and morphogenetic dynamics of mammary epithelial cells to be studied.

Although understanding human development is an important goal in itself, the translational potential of this field is clear: if we can grow human tissues *in vitro*, we can use these to model disease, to test potential drugs and to develop cell therapies. Two Spotlights in this issue discuss these aspects of the field. Scott Thies and Charles Murry (2015) present some of the most promising preclinical data and clinical trials of stem cell therapies, while Elsa Vera and Lorenz Studer (2015) highlight a potential problem with using stem cell-derived models in disease research: both hESCs and hiPSCs are 'young' cells, whereas many diseases – particularly neurodegenerative disorders – afflict the old. Although these articles stray from the classic scope of a developmental biology journal, we hope that they illustrate the continuum of both the field, from basic understanding of developmental processes to their applications in regenerative therapy, and of development itself – from embryogenesis through post-embryonic maturation to ageing and decline.

We have a limited number of print copies of this Special Issue to give away to interested readers. If you would like one, please send an email to dev@biologists.com with your mailing address. Whether in print or online, we hope you enjoy this Special Issue on Human Development. We see an exciting future for this field, and we want *Development* to be at the heart of it. We therefore encourage those of you working in this area to consider *Development* as a potential venue for the publication of your best work and we look forward to many more exciting human development papers finding their way into the pages of our journal.

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