ABSTRACT

In 2022, Development launched its Pathway to Independence (PI) Programme, aimed at supporting postdocs as they transition to their first independent position. We selected eight talented researchers as the first cohort of PI Fellows. In this article, each of our Fellows provides their perspective on the future of their field. Together, they paint an exciting picture of the current state of and open questions in developmental biology.

Organ morphogenesis: tour de force

Priti Agarwal

How do organs attain their shape? This is one of the questions that has fascinated developmental biologists and tissue engineers for years. Organ morphogenesis, which generates intricate biological forms ranging from the loops of the gut to the branches of the lung, is the result of an interplay of signalling molecules and forces (Hamant and Saunders, 2020). The idea that physical forces and properties regulate development was introduced over a century ago by D’Arcy Thompson, a Scottish mathematician, who described the shape of living forms as the ‘diagram of forces’ (Thompson, 1917). However, following the rise of genetics and molecular biology in the mid-20th century, much less attention was paid to mechanics. With the advent of modern tools and technologies to perturb, analyze and model the forces generated and experienced by cells and tissues, D’Arcy Thompson’s notion of physical principles driving morphogenesis has not only been rejuvenated but is burgeoning by leaps and bounds in current times.

During morphogenesis, organs are exposed to cell-intrinsic as well as extrinsic mechanical signals (Vignes et al., 2022). Contractile forces generated within cells by cytoskeletal machineries drive cell shape change, cell migration, cell intercalation and cell multiplication. These processes can induce tissue-level alterations, such as tissue elongation and folding, to sculpt an organ with a distinct architecture and functionality (Heer and Martin, 2017; Lecuit and Le Goff, 2007).

Besides intrinsic forces, a growing organ also experiences extrinsic forces arising from adjoining developing tissues, the surrounding extracellular matrix (ECM) and shear stress from body fluids. Although the role of cell autonomous force regulators has been extensively studied, recent discoveries are unveiling the significance of cell-extrinsic mechanics in organ morphogenesis. A gradient of basement membrane stiffness along the anterior-posterior axis forms elongated oval-shaped Drosophila egg chambers (Crest et al., 2017); intertissue friction creates V-shaped skeletal muscles in zebrafish embryos (Tili et al., 2019); and osmotic pressure generated by swelling of hyaluronic acid transforms epithelial buds into tubes during zebrafish ear morphogenesis (Munjal et al., 2021). During my postdoctoral research, I revealed the collective roles of pressure from proliferating germ cells, localized ECM remodelling and spatiotemporally regulated cell–ECM adhesion in guiding the morphogenesis of the U-shaped Caenorhabditis elegans gonad (Agarwal et al., 2022).

These pieces of evidence reveal the instructive role of mechanical forces, like morphogens, in patterning different organ morphologies. However, it is unclear how these extrinsic forces translate into a specific organ shape. Extrinsic forces are sensed by several mechanosensors, including membrane-bound receptors, mechanosensitive ion channels, the actomyosin cytoskeleton, and others. These sensors eventually trigger the activation of downstream biochemical signals that modulate multiple cellular behaviours. This cascade of events is collectively referred to as mechanotransduction (Agarwal and Zaidel-Bar, 2021; Petridou et al., 2017). Owing to the complexity of in vivo systems, the mechanotransduction pathways responsible for defining precise 3D organ morphology remain largely elusive. Therefore, the future direction of research in this field will be to focus on identifying the key mechanosensors that sense external forces, understanding the signalling pathways they activate and determining how these pathways regulate the development of a reproducible organ shape.

Further, mechanical and biochemical signals are interdependent: mechanical stimuli affect the way cells respond to biochemical cues, and biochemical signals can also alter cell mechanics and force generation (Gilmour et al., 2017). How these signals feedback on each other to ensure robust organ morphogenesis remains an open question. I believe that a system-level approach that uses precision tools to map and perturb both physical forces and gene expression, live imaging combined with theoretical modelling and computational simulation, along with the use of in vitro models such as organoids, will shed light on these unaddressed issues. Insights into how biomechanics govern organogenesis would also pave the way for mechanotherapeutics: using mechanical cues to diagnose and heal diseases by modulating mechanotransduction pathways.

Calculating the energetic cost of building an embryo

Clotilde Cadart

Over the course of only hours or a couple of days, the fertilized egg transitions from one cell to millions of cells and an increasingly complex body plan emerges. Although the biochemical and
biomechanical regulation of tissue growth and morphogenesis during development have been extensively investigated over the past decades, the physical principles of how energy is supplied and used throughout embryogenesis remain poorly studied. Understanding such principles may reveal new regulators and constraints on development, as trade-offs between available energy and the energetic costs of tissue growth or maintenance are thought to exist in living organisms. In this brief Perspective, I highlight recent work from junior investigators that is shedding new light on this topic, and look to the future of the field.

Pioneering work from Jonathan Rodenfels and colleagues has shown that, during early zebrafish development, whole-embryo heat dissipation patterns, a metric for energy expenditure, are related to the energetic cost of cell cycle signalling pathways (Rodenfels, Neugebauer, and Howard, 2019). However, beyond the first hours of development, little is understood about how the energy expenditure of an organism is regulated and relates to its mass and body plan – partly owing to the technical challenges involved in measuring such variables. *Xenopus* embryos are an interesting model organism to tackle such questions as they are large enough to measure oxygen consumption rate, another metric for energy expenditure, at the single tadpole level. Leveraging this feature during my postdoctoral work in the Heald lab, I showed that about 50% of the energy spent by *Xenopus laevis* tadpoles is allocated to cellular maintenance costs, which vary with average cell size and ploidy in the embryo (Cadart et al., 2023).

One central variable to consider in understanding patterns of energy expenditure is therefore cell size. As a member of the cell size community since my PhD, I am convinced that understanding how cell size and cellular metabolism are connected will impact fields as diverse as aging (Lengfeld et al., 2021), development and evolution. From this perspective, I am particularly excited by the compelling work by Margarete Diaz-Cuadros and colleagues, who demonstrated that cell size-normalized changes in cellular metabolic rate explain the twofold discrepancy in developmental rate from mouse to human embryos (Diaz-Cuadros et al., 2023). From an evolutionary standpoint, cell size has been hypothesized to mediate correlations between genome size and organismal variables such as developmental rate, but experimental proof is scarce. Owing to their wide range of genome size, amphibians will be instrumental in unlocking such questions. Thanks to the work of Kelly Miller, who introduced the dodecaploid *X. longipes* species into the Heald lab, we have been able to show that metabolic rate across *Xenopus* embryo species scales with cell size, not genome size (Cadart et al., 2023).

As the largest cells, eggs must stock enough nutrients to supply energy to the embryo until it can feed. How egg resources are converted in the embryo to sustain its energy needs and how they constrain development remain poorly understood, although a recently established connection between glycan pools and tail regeneration capacity in *X. tropicalis* tadpoles suggests one potential route (Williams et al., 2021). Another approach may be to use concepts from thermodynamics to connect the transformation of energy stored in the egg into ATP with quantitative measurements of embryo energy expenditure (as reviewed by Ghosh et al., 2023).

Understanding how energy is supplied and used during embryo development is a very open question, which I am excited to explore, together with an emerging generation of scientists. I am convinced that a highly interdisciplinary approach will be needed, complementing developmental biology approaches with findings from the cell size community, metabolic studies, tools from thermodynamics and mathematics as well as incorporating evolutionary and ecology perspectives.

**Launching the stem cell field into a new era**

**Loic Fort**

‘Stem cell research can revolutionize medicine, more than anything since antibiotics.’ These words from Ron Reagan back in 2004 showed the excitement about stem cell technologies and opened new hopes for therapeutical opportunities. Not only were these words inspirational for an entire generation of scientists, but they also resonate today as a visionary statement: although the idea of stem cells as a cure for every disease and condition is still a fantasy, over 9000 clinical trials using stem cells are listed on the National Institutes of Health website (https://clinicaltrials.gov) to this day, and almost 20 FDA-approved stem cell therapies were reported in 2022 (https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/approved-cellular-and-gene-therapy-products). This frenzy has been facilitated following the introduction of induced pluripotent stem cells by the revolutionary work of Takahashi and Yamanaka (Takahashi and Yamanaka, 2006; Takahashi et al., 2007). Reprogramming technologies broke the dogma of mono-directionality of differentiation and allowed the community to access and study patient-derived stem-like models, opening a quasi-infinite source of questions and research.

The strict regulation over the use of mammalian (and particularly human) embryos has encouraged scientists to create innovative pluripotent stem cell-derived models aiming to mimic as precisely as possible the genetic, biochemical and mechanical processes occurring during development. The most recent and exciting advancement is the emergence of complex 3D structures modelling various aspects of development, from gastrulation (gastruloids) (Moris et al., 2020) to somitogenesis (somitoids) (Yamanaka et al., 2023; Miao et al., 2023) and organogenesis (Holloway et al., 2019; Kim et al., 2020), as well as relations between different tissues (assembloids) (Pasça, 2019). Perhaps most strikingly, recent models now allow the generation of whole embryo-like structures *in vitro* (Pedroza et al., 2023; Weatherbee et al., 2023; Oldak et al., 2023). To what extent these model systems are a true and robust replica of the natural embryos requires further investigation. However, these techniques offer an exciting opportunity for scientists to model human development and access a window to observe developmental phenomena that could otherwise be challenging to study. This toolkit puts the field of *in vitro* developmental biology at the leading edge of stem cell research and will allow scientists to investigate complex phenomena *in 3D*, such as intercellular interactions and early developmental decisions, and to probe crosstalk between healthy and unhealthy tissues. These new technologies facilitate my own research: I am fascinated to understand how cells sense and respond to their environment, with a particular interest in how physical forces are integrated and converted into a genetic information. Using gastruloids, I am able to probe for differential forces across multiple lineages, and ask questions about the relationship between mechanical force and cell identity.

Moreover, the advent of gene and base editing technologies such as CRISPR-Cas9 has opened up new possibilities for manipulating stem cells and their genomes. Researchers are exploring the potential of precise gene editing in stem cells to correct genetic disorders, combined with important efforts to improve the efficiency, safety and long-term viability of stem cell therapies.

Finally, with the rapid evolution of artificial intelligence and computational approaches, such as machine learning techniques, scientists are now able to analyze vast amounts of stem cell data and isolate specific patterns (Kamimoto et al., 2023). For example, AI algorithms can predict cell behaviour across development and identify new putative regulators (Kamimoto et al., 2023), making...
them a crucial in silico resource to generate hypotheses and better apprehend development.

With these new techniques, the old field of developmental biology is entering the 21st century and promises a bright and exciting future. It is important to note that the fate of stem cell research will also depend on ethical considerations, regulatory frameworks and ongoing public dialogue. As the field progresses, researchers will continue to navigate these complex issues to ensure responsible and beneficial advancements in stem cell research and its applications.

The evolutionary origins of animal development
James Gahan
A simple narrative has long prevailed about how animals evolved. In this story, life was single celled for billions of years before one lucky organism learned how to be multicellular and evolved all that developmental biologists hold dear: differentiation, morphogenesis, patterning etc. Although this narrative is not wholly incorrect, progress in recent years has radically changed our view of that single-celled ancestor and what it was capable of (Brunet and King, 2022). Much of this knowledge has come from studying the most closely related groups to animals, the unicellular holozoans. This has revealed unexpected complexity, causing us to rethink the nature of the ancestors of animals. On one level, genomics has played a huge part in this. When the first unicellular holozoan genomes were published there were numerous ‘animal-specific’ genes (Fairclough et al., 2013; King et al., 2008; Suga et al., 2013). With more sequencing, both genomes and transcriptomes, this list has become progressively shorter, and it is now clear there are few true animal innovations (and perhaps in the future there will be even fewer) (Richter et al., 2018). This means that the evolution of animals cannot be explained by an explosion of new genes with new functions, but rather that most genes were already present before animals and were co-opted into new functions. Combined with this has been an increased understanding of the complexity of life cycles in these non-animal groups, which show enormous diversity. Importantly many of these species have multicellular stages within their life cycles. In the choanoflagellates, the most closely related group to animals, colonies of the species Salpingoeca rosetta form from serial cell divisions (Dayel et al., 2011). In the ichthyosporeans you have the formation of multinucleated syncytia, which later cellularize (Suga and Ruiz-Trillo, 2013), while filastereans can form multicellular aggregates (Sebé-Pedrós et al., 2013). At a deeper level, the cell-biological mechanisms driving some of these multicellular transitions resemble those used during animal development, e.g. the formation of a polarized cell layer in ichthyosporeans (Dudin et al., 2019) and actomyosin-mediated apical contractility in choanoflagellates (Brunet et al., 2019).

So where does this leave that single-celled ancestor and what makes animals unique? Despite the massive progress there is still much we do not know. Genomics has provided a wealth of knowledge, but these groups are still under-sampled. Sequencing of more genomes across these clades will help to resolve the full repertoire of genes present in the ancestors of animals but, going beyond this, understanding how these genomes are regulated may be key to understanding the evolution of animals. The ability to regulate gene expression in a precise temporal and spatial manner is essential during animal development and relies on a complex set of mechanisms. When these mechanisms evolved is not clear as, except for a single pioneering study in the filasterean Capsaspora owczarzaki (Sebé-Pedrós et al., 2016), this is still an unexplored area. On the other hand, the field is on the cusp of a new revolution.

The pioneering efforts of several key groups has seen the development of functional approaches (transfection, CRISPR-Cas9) in a growing number of unicellular holozoan species, e.g. S. rosetta (Booth and King, 2020; Booth et al., 2018) and Capsaspora (Parra-Acero et al., 2018). This massive breakthrough releases the field from the ties of a purely descriptive framework and, in the coming years, will move researchers from describing the content of genomes and cell-biological processes to understanding gene function, allowing for a deeper level of comparison with animals. This will undoubtedly unleash a new understanding of the biology of these organisms and therefore the biology of our own ancestors, and may help in explaining the very origins of animal development.

Coordination is the key during wound repair and tissue regeneration
Leah Greenspan
How do we repair or rebuild a tissue after an injury? Whether one is studying whole body regeneration in planaria, heart regeneration in zebrafish, limb regeneration in axolotls or cutaneous wound repair in mice, the overarching goal is the same: to heal wounds and replace lost tissue faster and better with minimal residual negative consequences. Although a large body of work has revealed how various cell types, signalling pathways and metabolic and mechanical processes contribute to tissue regrowth and regeneration, it is still not well understood how all these factors coordinate together to restore tissue function. Zebrafish are a particularly amenable model organism for the study of this coordination because of their optical clarity, high regenerative capacity and the plethora of tools available to visualize different aspects of wound healing and tissue regrowth live. These assets, as well as recent advances in high-resolution microscopy, will make it possible for future tissue regenerative and reparative studies in zebrafish to tackle complex wound healing questions.

Among the tools available in zebrafish are a growing number of transgenic lines that label various cell types, allowing for the direct observation of different cell–cell interactions during injury repair and tissue regeneration, such as the association of macrophages with growing vessel tips during wound angiogenesis (Gurevich et al., 2018). In addition, new fluorescent molecular reporters have been developed that permit signalling dynamics during tissue regrowth to be captured in real time. This has led to fascinating discoveries such as the propagation of Erk signalling waves during zebrafish scale regeneration (De Simone et al., 2021), showing that signals can occur in more than just an on/off pattern and that signalling dynamics play an important role in tissue regeneration. Beyond cell types and signals, fluorescent metabolic sensors have helped decipher the role that glycolysis and other metabolic pathways play in wound healing. For example, work from Enrique Amaya’s lab has used a FRET-based sensor for lactate levels to show that these increase transiently after larval zebrafish fin fold amputation, with lactate inhibition leading to an impairment in wound contraction (Scott et al., 2022). Other FRET-based sensors that can measure changes in tension have also been generated in zebrafish (Lagendijk et al., 2017), but these tools have yet to be used under regenerative or reparative conditions. As mechanical forces play a major role in wound repair it will be important to use these tension sensors to monitor tensile changes during the healing process and understand their contribution. Each of these tools alone can be used to study interesting aspects of tissue repair, but using them together will reveal more than just the sum of their parts.

My current research takes advantage of the many transgenic lines available in zebrafish to monitor the regrowth and recruitment of
keratinocytes, neutrophils, macrophages, and blood and lymphatic vessels in real time during cutaneous wound healing (Greenspan et al., 2022 preprint). In the future, I plan to combine the available fluorescently labelled cell lines, molecular reporters, and metabolic and mechanical sensors to better understand how these different components act in concert to rebuild or repair a tissue after injury. ‘Seeing is believing’, and it is my expectation that visualizing the coordination of many aspects of wound healing and tissue regeneration in living animals will yield innumerable new discoveries and lead to previously unappreciated new avenues for regenerative therapies.

How biological fluid flows shape organ morphogenesis
Thomas Juan

Although William Harvey first proposed the concept of blood circulation in 1628, it is only much more recently that we have begun to understand the influence of biological fluid flow on development and physiology (Ribatti, 2009). Fluid flow plays a crucial role in embryonic morphogenesis by exerting mechanical forces on tissues and initiating intricate signalling pathways that guide organ formation. This brief Perspective examines the importance of biological fluid flow during embryonic development and discusses the future directions of this exciting field of research.

Biological fluid flow occurs in various developmental processes, involving tissues such as the left/right organizer (LRO) in vertebrates, the circulatory system and the central nervous system (Daems et al., 2020). These flows are generated through the coordinated action of motile cilia, arterial pulsations, muscle contractions and respiratory movements. Fluid flow can be classified as either laminar or turbulent, depending on the physical properties of their propelling structures and the organs they traverse (Freund et al., 2012). When fluid flows through lumens, it exerts mechanical forces on surrounding tissues, including wall shear stress and wall stretching. Specialized mechanosensory proteins, such as ion channels, integrins, junctional complexes and G protein-coupled receptors, perceive these mechanical cues and translate them into intracellular signalling cascades (Duchemin et al., 2019). Notably, the primary cilium, acting as a cellular antenna perpendicular to the flow within lumens, is a well-studied organelle involved in flow mechanosensation. During my PhD (in which I identified a role for the conserved regulator of laterality, Myo1D, in cilia orientation within the zebrafish LRO; Juan et al., 2018), the field was engaged in a stimulating debate: does fluid flow trigger signalling cascades solely through its mechanical properties, or does it also carry signalling molecules? Studies in zebrafish and mouse LRO strongly support the former hypothesis, showing that mechanical stimulation of cilia using optical tweezers can induce localized calcium-mediated signalling (Djenoune et al., 2023; Katoh et al., 2023), but we cannot exclude that the two systems act in concert to promote local signalling.

Another flow-responsive organ exhibiting remarkable similarities with the LRO is the heart, in which flow-induced calcium elevations are observed in the valves. My postdoc work has been focused on the essential role of multiple mechanosensors belonging to the Pkd and Piezo families in cardiac valve development (Juan et al., 2023). Although disruption of these genes recapitulated conditions associated with disturbed blood flow, it is also known that the adenosine triphosphate (ATP)-dependent purinergic receptor pathway is crucial for blood flow mechanosensation in valves, independently of the Piezo proteins (Fukui et al., 2021). Thus, it is clear that multiple independent flow mechanosensation systems can be active in the same tissue – whether and how these are integrated remains an open question.

In the coming years, I suggest that studying organ-specific mechanosensory proteins will likely be a key focus of future investigations, as different organs may employ distinct sets of mechanosensors to sense and respond to fluid flow. Integrating multidisciplinary approaches, including novel ex vivo or 3D in vitro models, structural biology, and live imaging of mechanical stimuli using sensors (Yaganoglu et al., 2023), will contribute to unravelling how proteins can change conformation to sense fluid flows and their associated signalling pathways, and how these changes are interpreted by the cell to effect developmental outputs.

Human stem cell-based organoids to answer questions in paediatric cancer research
by Polina Kameneva

During development, the diversity of cells is formed through intricate cell differentiation processes – the gradual change of the transcriptional programmes and cellular states from early developmental programmes to a terminally differentiated state. The disruption of these processes can lead to cells being stalled in development, and there is a hypothesis that this may be one of the causes of paediatric cancer (Jessa et al., 2019). Therefore, the areas of paediatric cancer research and developmental biology are highly interconnected and fuel mutual insights. For example, recent single-cell omics-driven approaches have resulted in the alignment of neuroblastoma single-cell transcriptomic profiles with healthy human foetal tissue counterparts – adrenal glands – revealing possible cell-of-origins or onco-foetal transformations (Kameneva et al., 2021; Janský et al., 2021; Kildsiute et al., 2021; Bedoya-Reina et al., 2021). Identification of the cell-of-origin is crucially important for paediatric cancers as it provides insight into which developmental programmes have gone awry and helps to shape strategies to push differentiation in the right direction. From the mechanistic point of view, novel computational tools can predict transitions between cellular states in healthy and disease scenarios, infer the underlying gene regulatory networks (Aibar et al., 2017; Faure et al., 2023) and therefore reveal possible therapeutic targets.

Despite this progress, one key remaining question is how we choose which of the newly identified targets can be actually useful for patients. For this, high-throughput screening platforms, amendable for genetic manipulation for testing the validity of newly identified targets, become indispensable. Human stem cell-based differentiation protocols and organoids combined with multi-omic readouts can serve as high-throughput platforms for the initial screens of the validity of cancer vulnerabilities. As an example, the generation of different brain region organoids from genetically engineered human stem cells, recapitulating the genetic lesions associated with glioblastoma, has resulted in models resembling specific tumour subtypes, providing mechanistic insight into the effects of particular genetic lesions and serving as a screening platform for efficient treatments (Bian et al., 2018).

Further advancement in our abilities to generate human-equivalent organoids and recapitulate different tissues fully depends on a deep understanding of the natural developmental process and the ability to imitate this in the laboratory setting. A crucial advantage of organoid technology is the opportunity to genetically manipulate cultured human stem cells and, for example, to control the occurrence of genetic lesions during organoid formation, therefore modelling human paediatric cancer initiation – the process that is currently impossible to observe. Such new models will help to answer long-standing questions, for example, of the
existence of drug-resistant cells before treatment, which may eventually lead to the relapse of the drug-resistant tumours. Another mystery of cancer initiation is that not all cells that carry the genetic perturbations will transform into cancer cells. What are the mechanisms which allow some cells to resist cancer transformation? Such approaches, along with systemic unbiased multi-omics readouts, have a high potential to reveal crucial principles of developmental stability during cell fate differentiation. I am looking forward to taking an active part in the development of such new tools and advancing our understanding of the very early events of development, tumorigenesis, and the susceptibility of different cellular states to genetic and non-genetic drivers of paediatric tumours.

**Seeing human development with stem cells**

Yuchuan Miao

Like many in the developmental biology field, I am obsessed with the utter beauty of embryo development. It appears magical that millions of cells organize themselves into a constellation of patterns and shapes. These elegant dynamics and amazing robustness have inspired generations of scientists to illuminate their mechanisms from diverse angles. As a cell biologist by training, I couldn’t agree more that seeing is believing, and that visualizing the detailed dynamics is one of the best ways to reveal mechanisms. I want to watch embryo development in real time – I want to see how cells adopt different fates, how they divide and move around, how they die and how these intriguing cell behaviours are precisely orchestrated into our body plan. I am especially interested in understanding the development of our own species, which would have significant impacts on treating congenital diseases and advancing regenerative medicine.

Clearly, however, we have restricted access to human embryos and limited techniques to label or perturb them. Much of our knowledge of their development comes indirectly from studies using model animals such as mice and chicken. Although we have gained much understanding through the lens of genetics, in-depth comprehension on the cell level is impeded by the need for laborious dissection and advanced microscopy setups, as well as limited manipulating techniques. Moreover, the enormous complexity of embryo development makes it extremely hard to disentangle causal relationships during mechanistic inquiries.

Stem cell-derived embryo models might provide an important step forward. Human pluripotent stem cells can be used to model various processes of human development in the petri dish (Arias et al., 2022; Fu et al., 2020; Rosado-Olivieri and Brivanlou, 2021; Shahbazi and Zernicka-Goetz, 2018; Shao and Fu, 2022). Also, 3D models can recapitulate key features of patterning and morphogenesis in addition to cell fate specifications. These allow us to peek into previously inaccessible stages of human development such as gastrulation. Excitingly, high-resolution live imaging becomes much easier as the cells can be genetically labelled with numerous biosensors reporting a variety of cell behaviours. In combination with a range of sophisticated perturbation tools, in vitrō models provide unlimited materials for quantitative investigations. With these models, human-specific traits and aetiology of congenital diseases can be investigated in simplified contexts. These trade-offs make it manageable to decode the system. During my postdoc, I have built a simplified model of somitogenesis that does not display polarized tissue elongation or sequential somite formation as the embryo does. Rather, it spreads symmetrically as a flat disc and generates somite-like structures all at once (Miao et al., 2023). In this simplified scenario, entirely anterior- or posterior-fated somites are formed. This intriguing feature led to the identification of a cell sorting mechanism underlying somite polarity patterning, which was missed by almost all previous studies. Thus, in vitrō models challenge the embryonic system in a new context to reveal what it can do, which helps us see what might be masked by the tremendous complexity.

To be clear, stem cell-derived models can never replace embryos. The biggest disadvantage is that they are not embryos. Insights gained through in vitrō studies must be thoroughly validated in real embryos before overreaching conclusions can be made. Still, for a cell biologist fascinated by the incredible dynamics of cells and aiming to advance a cell-centred view of development, stem cell-derived models are the perfect tools. With so many wonderful in vitrō models around, this is truly the best time to study developmental biology.

References


