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Contemporary morphogenesis

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Introduction

Developmental biology tackles the fundamental question of how a complex functional multicellular organism is produced from a single cell, uncovering the principles of how cells multiply themselves, determine their fates, and organise into tissues and organs. Due to the sheer breadth of biological processes that such studies provide insights into, developmental biology impacts almost every other biological discipline. Accordingly, findings in the field of developmental biology can have extremely wide-reaching social implications with major impacts on both health and sustainability. In the biomedical arena, developmental studies have identified key pathways underlying tumour progression and metastasis in humans, which have enabled novel prognostic and therapeutic methods for treating cancers (1). Understanding developmental processes inspires tissue engineers to direct the self-assembly of tissues for regenerative medicine (2). Understanding plant morphogenesis, meanwhile, can help provide improved strategies for crop and plant cultivation, impacting on food security (3). Indeed, prominent developmental biologists have recently stated their support for the recognition of developmental biology as the foundation underpinning many biological disciplines (4,5).

The ’80s and ’90s were an exciting time in developmental biology, with large-scale genetic screens in flies and fish leading to the discovery of key signalling pathways later found to be central to mammalian development and disease (4). However, studies of these pathways were restricted to genetic techniques and phenotypic analysis, with limited ability to perform in-depth mechanistic analyses at the cellular level, or probe these processes in the context of tissue or organ development. More recent technological advances have revolutionised the field of

developmental biology. Phenotypic analyses have been transformed from simple qualitative observations to quantitative characterisations, enabling the extraction of parameters with which to model complex processes and facilitating an unprecedented understanding of diverse aspects of morphogenesis. The field has benefited enormously from the continual advancement of genetic and imaging techniques, including super-resolution live cell imaging, *in silico* modeling, sophisticated image analysis pipelines, genome editing and genome-wide analysis.

Recent, high-profile applications of such state-of-the-art techniques include: *in toto* imaging of post-implantation mouse development, allowing reconstruction of cell fates, movements and divisions to compile a reference atlas of development (6); biophysical analysis of mouse blastocysts linking luminal pressure to force-dependent junctional remodelling promoting early embryo growth (7); scRNA-seq analysis of embryonic heart development to define lineage specification and segregation dynamics, and understand how dysregulation of cardiogenic pathways leads to specific morphological heart defects (8); and use of morphometric analysis and force microscopy to reveal links between tissue/matrix stiffness, junctional remodeling and tissue morphogenesis (9). These multidisciplinary approaches to developmental questions represent excellent examples of developmental biology as a fast-moving contemporary research field.

Structure and overview of contributions

The Royal Society Hooke Scientific Discussion Meeting “Contemporary Morphogenesis” was held in October 2019 with the aim to bring together scientists who, while sharing a central interest in developmental biology, represent a large range of complementary disciplines, from biophysics and applied mathematics to genomics and molecular biology. This theme issue presents the key topics that emerged from that meeting. It comprises original research and review articles, broadly organised into four interlinked research areas, with the roles of dynamic cytoskeletal architecture, cell-cell and cell-ECM interactions, and integration of extracellular signalling emerging as common themes.

At the cellular level, this theme issue includes insights into how cell adhesion is regulated to promote cell and tissue shape (14), novel image analysis platforms for extracting and linking

protein localisation, cell geometry and tissue architecture (15), and an overview of how microtubules regulates cell behaviours to promote tissue morphogenesis (16).

Expanding on the tight links between cell shape and behaviour and tissue morphogenesis during development, we feature review articles into the roles of cytoskeleton-mediated forces (17), junction formation (18) and cell intercalation (19). The extracellular matrix is a highly specialised mediator of multiple developmental processes, signalling to cells through modulating tissue stiffness or mediating bioavailability of secreted signalling molecules. Examples of how cell-matrix interactions promote morphogenesis include an overview of egg development in *Drosophila* (20), and insights into the spatiotemporal correlation of a matrix-remodelling MMP with migratory cell populations in the *Xenopus laevis* embryo (21).

We conclude by considering how embryonic patterning and morphogenesis interact in specific developmental contexts. Integration and interpretation of morphogen signals patterns many developing organs, with single morphogens acting upon a variety of systems - exemplified here by discussions around how retinoic acid mediates patterning at the organ level (22), and how mathematical modelling has enhanced our understanding the roles Shh plays in patterning and morphogenesis (23). Symmetry breaking is another key step in axis establishment, and the development of inherently asymmetric organs. Mechanistic links between symmetry breaking and morphogenesis are explored in a number of contexts, including how actin flows drive polarity formation in the *C. elegans* zygote (24), asymmetric patterning in lineage segregation during early mouse development (25), and how mechanical asymmetries promote tissue folding (26). Finally, we review how changes in cell states from epithelial to mesenchymal (and vice versa) are controlled and coordinated to facilitate tissue morphogenesis (27).

These contributions exemplify how the combination of classical developmental biology approaches with mathematical modelling, biophysics, whole-genome and single-cell approaches, and state-of-art image analysis now facilitates the use of model organisms to investigate biological processes across scales, from subcellular to whole organism. Thus, in addition to improved mechanistic insights into embryonic development, it is anticipated that these multidisciplinary approaches will reinforce the position of developmental biology alongside organoid technology in underpinning biomedical research, including regenerative medicine. Although the breadth of represented topics might seem overwhelming, they all share a unified theme: as such, a key focus of this theme issue is on *in vivo* studies since they uncover how

cells behave in a natural environment in an organism which is often different to cell behaviour in a culture dish. Nowadays, it is more important than ever to study developmental processes in intact organisms, and extract quantitative information and create models. Additionally, pushing forward exciting technical advances in developmental biology will ensure that these fields continue to be supported by the best mechanistic fundamental research.

We hope that this theme issue helps to facilitate the exchange of novel techniques, methods of analysis, and modelling approaches within the wider community and thus drive the innovation which is vital to ensure that contemporary approaches to developmental biology continue moving from strength to strength.

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