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Special Issue – 3D Cell Biology

The third dimension: cell biology comes alive

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Within the confines of textbooks and journals, cells are by necessity depicted as simply as possible – in two dimensions, static, with specific components of interest highlighted. However, as cell biologists we understand that this portrayal is a somewhat pale imitation of the activity and complexity that govern the cell. Organelles and the cytoskeleton change shape frequently; signaling pathways are in constant flux and are often spatially constrained; many cells depend on their neighbors and external environment to function properly. In short, we know that biology is dynamically three-dimensional and, in recent years, much cell biological research has become so as well. In this special issue of *Trends in Cell Biology* we draw from diverse fields to showcase research that tackles fundamental questions of cell biology from a 3D viewpoint and asks how the inner architecture of the cell, and the external environment that surrounds it, impact upon cell function.

First, we offer two reviews of technologies that have revolutionized cell biology: microscopy and computational modeling. Clare Waterman and colleagues describe recent advances in 3D and 4D microscopy and discuss how different imaging techniques can be used to look further into the cell than ever before. David Odde and Alex Mogilner then describe computational modeling of cellular processes and discuss the types of questions that are best approached in 1D or 2D, versus those that require a 3D model.

Understanding the inner workings of a single cell is as ambitious a goal as ever, and the ability to track spatial and temporal subcellular dynamics adds yet further levels of complexity to this long-standing goal. In this vein, Jason Brickner and Lauren Meldi discuss how chromosomes are compartmentalized within the nucleus, and how the spatial organization of genetic material and nuclear proteins can influence gene expression. Gia Voeltz and Jonathan Friedman explain the 3D structure of the endoplasmic reticulum and discuss how the dynamic shape of this organelle allows it to perform its diverse functions. Keith Burridge and colleagues then describe the complex network of Rho GTPases, signaling components with such intricate spatial and temporal regulatory crosstalk that their effect on cellular functions such as migration and differentiation is probably best appreciated when considered at the network level.

In multicellular organisms, interactions between a cell and its surroundings are integral to proper function. During development, migrating cells must navigate 3D landscapes and, once at their destination, incorporate into a growing organ of a defined size and shape. Defects in these processes can impact upon the health of an organism. In their review, Ian Macara and colleagues examine the role of polarity proteins in epithelial organization and discuss how loss of polarity may be a key step in cancer progression. Katarina Wolf and Peter Friedl then describe the biophysics of cell migration and discuss how cells decide between using proteases to cut through the surrounding extracellular matrix or instead squeeze through available openings. Last, Don Ingber and colleagues offer a peek into the interdisciplinary marriage of engineering and cell biology with discussion of the past, present and future of 3D cell culture. Some researchers are now using microfabrication techniques to grow 'organs-on-chips', cell culture devices that approximate the spatial, mechanical and biochemical context of a living organ, and which offer new insight into how cells might act *in vivo*.

Although far from being an exhaustive list, we hope this collection offers insight into the breadth of questions being asked and the exciting advances being made in understanding the dimensional complexity of the cell. We thank the authors and reviewers for their contributions to this issue, and we thank you for reading! We always welcome feedback; please do contact us with your thoughts on this issue or any other. Look to future issues of *Trends in Cell Biology* for more articles on the ever-fascinating three-dimensional cell.

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