EDITORIAL

nature cell biology

A decade of *Nature Cell Biology*

On the occasion of the ten year anniversary of the journal, we reflect on how cell biology has evolved.

Nature Cell Biology was launched ten years ago to provide a forum to "foster the exchange of ideas between all areas of cell biology". Our first editorial noted that cell biology is a "broad discipline" that includes membrane traffic, cytoskeletal dynamics, adhesion, apoptosis, cell division, nuclear organization and signal transduction. Ten years later, these areas remain at the heart of the journal's scope. As cell and developmental biologists have moved to dissect biological processes at the molecular and cellular level, so too have molecular biologists increasingly investigated 'where' and 'when' molecular processes occur in the cell. *Nature Cell Biology* has vigorously kept apace with these fundamental shifts in the field. In the past decade, the rate of discovery in cell biology has been driven by technological breakthroughs on various fronts — imaging and high-throughput genomic and proteomic approaches, to name a few — and these changes too are reflected in our pages.

To mark this anniversary, we have assembled a collection of papers published over the past decade, spanning the diverse subject areas covered in this journal (www.nature.com/ncb/webfocus/10th-anniversary).

Technology as a driving force

Advances in light microscopy coupled with novel approaches to fluorescently label proteins and the development of more sensitive cameras has facilitated the study of protein dynamics with unprecedented subcellular resolution. It is now possible to observe single motors moving on a cytoskeletal filament, follow RNAs during transcription and to visualize cell division *in vivo*. "It is now possible to make live movies that reveal many fascinating things about cell behaviour that were essentially invisible ten years ago", says David Morgan (University of California, San Francisco). These advances permit a quantitative dissection of events *in vivo*. "Ten years ago, no one would expect an experimentalist to be able to measure the rates or extents of reactions in live cells or to include a mathematical model and simulation of a process in their paper. These things are not required at the present time but are gradually becoming standard in the field", says Tom Pollard (Yale University).

Since the publication of the human and mouse draft genomes, advances in array technology, high-throughput sequencing analysis and mass spectrometry have paved the way for global analysis of gene and protein expression and posttranslational modifications. Robert Weinberg (Massachusetts Institute of Technology) notes that "This has allowed the definition of phenotypic states of cells in a fashion that is totally different from our conceptions of a phenotype 20 and 30 years ago". Analysis of protein function has been revolutionized by the ability to manipulate protein levels *in vivo* and *in vitro* in different systems, for example, through small-interfering RNAs and the use of conditional knockouts in mammals.

Shifting concepts

New technology has spurred new insights into cell biological processes. It is now clear that cells use numerous ways, including cytonemes and exosomes, to explore their environment and communicate with one another. Signalling pathways are non-linear and cannot be considered in isolation; similarly there is extensive coupling between regulatory processes previously considered as distinct, such as transcription and mRNA export. Communication between subcellular structures — including different cytoskeletal filaments, various cell junction types, the nucleus and the cytoplasm, and distinct organelles — is far more intimate than previously assumed, making it increasingly challenging to manipulate specific processes in isolation. In addition, says Tom Misteli (National Institutes of Health), there is "the realization that every cellular process is dynamic, involves dynamic equilibria of interactions of previously thought of static components. As a consequence it has become clear that all cellular events must be explored and understood as dynamic processes."

During this time, some fields have matured whereas others have been revived. While the core machinery in cell-cycle research has been to a large extent identified, the focus has now turned to how the cell cycle responds to environmental cues and assaults, and the molecular details of how cell-cycle transitions are executed. Similarly, key components of the cell migration apparatus have been characterized in detail, but much remains to be learnt about their interaction, and how migrating cells navigate a physiological setting and switch between alternative modes of migration. By contrast, our understanding of autophagy — first discovered in the 1950s — and of its importance in development and disease has rapidly progressed since the discovery of the first gene shown to regulate autophagy in the late nineties. "Autophagy is the only mechanism available to the cell for the degradation of entire organelles including mitochondria. This has important implications with regard to mitochondria-associated diseases and apoptosis. Thus, the shift is in appreciating the widespread involvement of autophagy in cellular physiology", says Daniel Klionsky (University of Michigan).

Developmental biologists have increasingly focused on mechanical forces, for example, tension driving events such as cell rearrangments or shape changes during morphogenesis. "Mathematical modeling is critical to verify these physics-based models. Accordingly, collaborations between cell/developmental biologists and mathematical scientists or physics are becoming increasingly important. To facilitate these collaborations, quantitative treatments of data are more critical than before", comments Masatoshi Takeichi (The Institute of Physical and Chemical Research, RIKEN).

A major conceptual breakthrough has been the discovery of a new mode of gene expression control — through small RNAs. Since the finding that double-stranded RNA induces gene silencing in worms, rapid progress has been made in understanding the biogenesis and biological function of endogenous small RNAs. "This has truly been a watershed event for cell biology of the last decade. However, with the passage of time, miRNAs will soon be relegated to the status of additional components of the intracellular signal-processing circuitry, having a status equivalent to that of signal-transducing proteins and small second messenger molecules." predicts Robert Weinberg.

Identification and characterization of tissue-specific stem cells and their niches, and the discovery that differentiated mouse and human somatic cells can be reprogrammed into a pluripotent state represents another significant milestone from the past decade. As Sean Morrison (University of Michigan Life Sciences Institute) notes, a pivotal event was the finding that "tissue homeostasis and stem cell maintenance are regulated by same networks of proto-oncogenes and tumour suppressors that were originally discovered to regulate cancer cell proliferation."

The road ahead

Despite the progress of the past decade — clearly as much, if not more, probably remains to be discovered (Box 1). We are far from a comprehensive understanding of the cell as an integrated system. Although there is an increased appreciation of the complexity of signalling pathways, predicting cellular phenotypes remains challenging. Thus, the promise of systems biology remains as yet unfulfilled. Achieving this will require a more comprehensive 'parts list' and quantitative data. Advances in imaging now allow cell and developmental biologists to study how cells behave in a physiological setting *in vivo*. In particular, light-gated control of cellular events with high precision in time and space using regulatory proteins with fluorescent tags promises to move the field forward.

Evolving means to communicate biology

The world has now embraced the web as a major means of communication. Google has emerged to dominate search, Wikipedia has graduated to a high quality comprehensive encyclopedia and blogging has become widespread. The world of research and scientific publishing is, by no means, immune to these profound shifts in sharing and accessing information. Online publishing now makes it possible for journals to present 'raw' data and metadata. Comments by readers on manuscripts post-publication also has the potential to engage the wider community in the assessment of a study. Cell biologists today are faced with ever more choices for where to publish their best work. As we enter our second decade, *Nature Cell Biology* commits itself to meeting the diverse needs of our readership as we continue to publish the best that cell biology has to offer.

A change of chief

This anniversary issue also coincides with the departure of our Chief Editor Bernd Pulverer and the appointment of Sowmya Swaminathan as his successor. Bernd joined the journal in 2002 and guided the team through its formative years. Bernd has also had a strong role in establishing new online resources at Nature Publishing Group, including the Signalling Gateway, and has been a driving force in improving data presentation across the Nature journals. Known among many things for his distinctive writing style, his ability to push a deadline to its tipping point and his apparent inability to be offended, Bernd will be sorely missed by the team and we wish him and his family much happiness in their move to Heidelberg.

BOX 1 Reflections on cell biology

"I believe that there is an ongoing revolution in organogenesis and morphogenesis. The ability to identify and image live mammalian stem cells in their correct tissue context will be a big breakthrough. Mapping lineages, will finally provide a detailed picture of how organs develop — knowledge that will be essential to a deep understanding of cancer and other diseases involving defects in cell fate specification. […] I expect that classical physiology and metabolism will return to the forefront as we begin to figure out at a molecular and cellular level how various tissues talk to one another and co-ordinate their behaviors." **Ian Macara** (University of Virginia).

"Will we actually be able to use stem cells to develop new therapies for diseases that are currently incurable? Will we be able to improve the treatment of certain cancers by targeting cancer stem cells? Will many cancers be hierarchically organized as per the cancer stem cell model, or only a few? To what extent do cancer cells and stem cells have different metabolic regulation than other somatic cells, and to what extent are key cellular decisions, like survival, proliferation, and differentiation ultimately metabolically regulated based on their energy and nutrition status?" **Sean Morrison** (University of Michigan Life Sciences Institute).

"Does the accuracy or noise in nuclear processes such as RNA processing have an impact on disease and development?" **Pamela Silver** (Harvard Medical School).

"The challenge now is to understand how fundamental cell biology relates to physiological and pathological events. How does the basic cell biology machinery contribute to physiological process such as differentiation and aging and to understand disease mechanisms at the cellular level in the context of cells in tissues and organisms." **Tom Misteli** (National Institutes of Health).

"Digital communication has also changed how experiments are planned, executed and published. In the long term this may be the most significant technology driving change in cell biology and other sciences", **Phillip Sharp** (Massachusetts Institute of Technology).

"An important dimension to the current thinking about the mechanisms of genome maintenance has been the spatio-temporal insight into how repair and signalling proteins communicate with damaged chromosomes and indeed with other cellular compartments", **Jiri Lukas** (University of Copenhagen).