

Cell biology: At the center of modern biomedicine

Priya Prakash Budde,¹ Elizabeth H. Williams,² and Tom Misteli³

¹Reviews Editor, ²Executive Editor, and ³Editor-in-Chief, *The Journal of Cell Biology*

How does basic cell biology contribute to biomedicine? A new series of Features in *JCB* provides a cross section of compelling examples of how basic cell biology findings can lead to therapeutics. These articles highlight the fruitful, essential, and increasingly prominent bridge that exists between cell biology and the clinic.

The discipline of cell biology began as a mostly academic endeavor, driven by the curiosity of biologists to understand what cells look like and how they work. But many basic cell biological insights have turned out to have real-world implications and applications. One of the most notable examples is the seminal work of Mike Brown and Joe Goldstein, who in the 1970s deciphered the fundamental mechanisms of cholesterol receptor trafficking and its relevance to heart disease, thanks in part to studies on cells from patients with familial hypercholesterolemia (Brown and Goldstein, 1986). For decades, their collaborative work has served as a shining example of the power of basic cell biology in a highly relevant disease setting.

Today, cell biology is a major driver of all aspects of biomedicine. The diagnosis of a disease increasingly relies on genetic, molecular, and cellular markers, and drug discovery has shifted from blind screening to targeted molecular design informed by our genetic, molecular, and cellular understanding of a disease. Technological advances in areas such as genome sequencing and high-throughput screening have made it possible to go from a basic discovery in the laboratory to a clinical trial at an unprecedented

pace. As a result, the application of basic research to the clinic can easily happen during the career of a researcher and is a much more attainable goal than in decades past.

To highlight the importance of basic cell biology to biomedicine, *JCB* is publishing a series of Feature articles, each of which represents a story, often a personal account by a key researcher, to give both historical and practical insight into how basic cell biological observations have contributed to therapeutic advances. These articles will be freely available online from the time of publication and distributed as a collection in *JCB*'s Special Issue 2013 at the American Society for Cell Biology annual meeting later this year.

We begin the series with three articles in this issue of *JCB*. The first, from Francis Collins and colleagues (Gordon et al., 2012), shows how a chance encounter at a social event led to the surprising discovery that the premature aging syndrome progeria is caused by a mutation in lamin A and then led to clinical trials in record time. The second (Davis and Schlessinger, 2012) describes the culmination of decades of focused, methodical work studying signaling pathways and oncogenic mutations that led Yossi Schlessinger and colleagues to develop a drug to target the B-Raf kinase in melanoma. In the third, Frank Bennett and colleagues (Rigo et al., 2012) illustrate how merging the strengths of industry and academia is leading to the development of tools that fix the pre-mRNA splicing defect in spinal muscular atrophy.

In upcoming articles, Larry Steinman will describe how the development of the potent multiple sclerosis drug Natalizumab arose from studies on receptors involved in immune cell migration.

Gergely Lukacs and colleagues will show how analyzing the cell biology of disease mutations in the cystic fibrosis transduction channel (CFTR) is informing the development of specific reagents to correct channel dysfunction. Christine Seidman and colleagues will present insights into cardiac cell biology that have emerged from studying animal models of heart disease. Other articles from Larry Goldstein, Johan Auwerx, and Sakari Kauppinen will touch upon a few of the hottest fields in current translational research—stem cells, metabolism, and microRNAs—to provide an update on progress in these areas.

Not all of the articles are simple success stories; some highlight the difficulties in the path from basic cell biology to the clinic. Oliver Hantschel and Giulio Superti-Furga will present some of the stumbling blocks inherent to the current way that drugs are developed and provide some suggestions for ways to streamline the process. Fred Goldberg will chart the development of the proteasome inhibitor Bortezomib, a successful treatment for multiple myeloma that faced major obstacles on the road to the clinic. Tony Oro will discuss drug resistance in basal cell carcinoma and efforts to understand and overcome this growing problem. This piece, like several others, makes the important point that studying the cell biology of disease is not a one-way street; disease cells are extraordinarily powerful, naturally occurring experimental tools that provide novel insight into basic cell biology.

© 2012 Budde et al. This article is distributed under the terms of an Attribution-Noncommercial-Share Alike-No Mirror Sites license for the first six months after the publication date [see <http://www.rupress.org/terms>]. After six months it is available under a Creative Commons License [Attribution-Noncommercial-Share Alike 3.0 Unported license, as described at <http://creativecommons.org/licenses/by-nc-sa/3.0/>].

Correspondence to Priya Prakash Budde: pbudde@rockefeller.edu

Therapeutic discoveries can arise both from the study of an apparently inconspicuous cell biological pathway that suddenly is found to be at the center of a disease and from the use of disease mutations and animal models of disease to support and inform a basic cell biology research program. Either way, cell biologists are well situated to contribute to understanding the basis of disease and to developing therapeutics. This is a win-win situation for researchers, clinicians, and not least of all the people whose lives are improved by our efforts. We hope that the examples assembled in this series will inspire cell biologists to embrace both the basic research and therapeutic challenges that lie ahead.

References

- Brown, M.S., and J.L. Goldstein. 1986. A receptor-mediated pathway for cholesterol homeostasis. *Science*. 232:34–47. <http://dx.doi.org/10.1126/science.3513311>
- Davis, M.J., and J. Schlessinger. 2012. The genesis of Zelboraf: Targeting mutant B-Raf in melanoma. *J. Cell Biol.* 199:15–19.
- Gordon, L.B., K. Cao, and F.S. Collins. 2012. Progeria: Translational insights from cell biology. *J. Cell Biol.* 199:9–13.
- Rigo, F., Y. Hua, A.R. Krainer, and C.F. Bennett. 2012. Antisense-based therapy for the treatment of spinal muscular atrophy. *J. Cell Biol.* 199:21–25.