INTRODUCTION

Metabolism Is Not Boring

SO INVESTIGATOR STEVEN MCKNIGHT ADMONISHED HIS AUDIENCE LAST SPRING after a presentation at a conference (on metabolism and cancer, no less). He may have been "preaching to the choir" in this case, but what led him to issue such a blunt reminder? It seems that for a generation of biological scientists, metabolism was an area of biochemistry to be mastered and then put aside. Metabolism was always there in the background, providing the cell with the energy and resources to do what was required, but was rarely recognized to determinedly influence, and be influenced by, the physiological state of the cell.

This special issue of *Science* celebrates a resurgence of interest in metabolism and an appreciation of its central role in disparate areas of cell biology, physiology, medicine, and synthetic biology (www.sciencemag.org/special/metabolism/). McKnight's Perspective (p. 1338) takes a broad look at the field and justifies his excitement that recognizing the reciprocal regulation of metabolism and other cellular processes promises to advance our understanding of complex physiology.

There is renewed interest in the metabolism of cancer cells and its potential as a therapeutic target. Levine and Puzio-Kuter (p. 1340) review metabolic changes in cancer cells, as well as the recent suggestion that alterations in a metabolic enzyme can lead to the production of an "oncometabolite" that supports cancer cell growth. When energy sources are limited, cells use a process known as autophagy for breaking down cellular components to provide substrates for metabolism. Rabinowitz and White's Review (p. 1344) discusses roles of autophagy in metabolism, its regulation, and its implications for cancer and degenerative diseases.

Of course not all fields have neglected metabolism over the years, and an enormous literature describes the role of insulin and related hormones in controlling cellular metabolism. In a Focus Issue of *Science Signaling*, a Research Article and Perspective describe an unexpected signal from the insulin receptor that confers sensitivity to cell death when insulin is not present. Also highlighted are a role for lipids as cellular sensors of glucose metabolism and a mechanism by which cells can survive oxidative stress by shifting the activity of the cell's protein degradation complex, the proteasome.

In *Science Translational Medicine*, Vallerie and Hotamisligil review how in a strategy to combat obesity and insulin resistance, a therapeutic inhibitor of cell signaling pathways must have coordinated actions in multiple cell types. Back in *Science*, Bass and Takahashi (p. 1349) review new insights into the interaction of metabolism with circadian clocks. Displacement of eating and periods of activity away from the normal light-dark cycle, as experienced in jet lag or shift work, have marked effects on metabolic diseases.

Cellular metabolic pathways, particularly in yeast or bacteria, can be exploited to synthesize compounds that are difficult or expensive to produce by other means. Keasling (p. 1355) reviews advances in metabolic engineering and looks forward to a future in which customized microbes made by computer-aided design can efficiently produce desired chemicals, ranging from fuels to pharmaceuticals.

See? It's not boring at all!

– L. BRYAN RAY

Metabolism

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See also Science Translational Medicine *and* Science Signaling *at www.sciencemag.org/special/metabolism/.*

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