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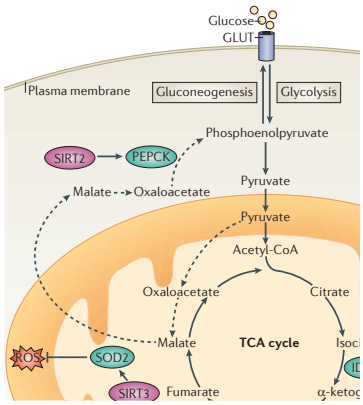

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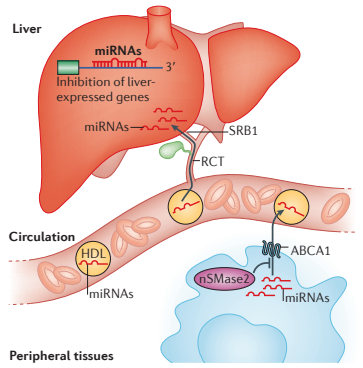

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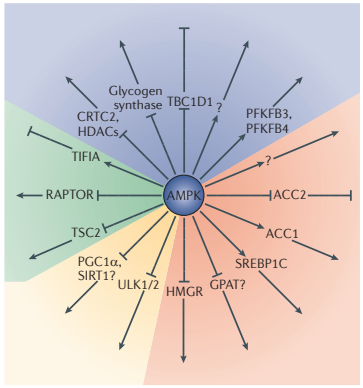

A hub for energy balance p251

The metabolic pathways of cells, for many years relegated to the backbenches of biochemistry lecture halls, have now been firmly reinstated as a central driving force throughout cell biology. The ability of cells to rapidly adapt to changes in nutrient availability, and to integrate information about their metabolic state to drive cell behaviour seems intuitive in retrospect, particularly now that we appreciate the extent to which proteins can be modified and regulated by small molecules. In this issue, we present a set of specially commissioned articles that highlight how metabolic pathways interface with cell biological processes.

Technical advances have facilitated this conceptual shift. As outlined in the Innovation article by Gary Siuzdak and colleagues on page 263, our ability to 'read out' the metabolic state of cells has been enabled in part by advances in mass spectrometry that now allow unbiased analysis of global metabolite profiles. The increasing use of metabolomics is providing unexpected links between shifts in metabolic pathways and cellular phenotypes.

The influence of signal transduction on metabolic pathways has been appreciated for some time, but the extent to which this regulation is reciprocal is only now becoming clear. In addition to intracellular energy sensors such as AMP-activated protein kinase (AMPK) and sirtuins — the topics of the Reviews on page 251 and 225, and of the Journal Club on page 207 — there is now increasing evidence that metabolites themselves, such as acetyl-CoA, can alter signal transduction by regulating metabolite-sensitive protein modifications such as acetylation. As Craig Thompson and Kathryn Wellen discuss (page 270), such modifications reveal the ways in which the metabolic state of the cell directly interfaces with signal transduction.

On page 213, Peter Tontonoz and Anna Calkin review how metabolites can also directly mediate changes in gene expression, by associating with nuclear receptors such as liver X receptors, which themselves orchestrate different metabolic pathways. Such changes in metabolism-associated gene expression can also be fine-tuned by microRNAs, as discussed by Anders Näär and Veerle Rottiers on page 239.

Together, these articles highlight the increasing appreciation of how cells balance their energy intake, use and storage to meet their changing needs, and how the metabolic state of the cell directly influences its behaviour. A better understanding of this crosstalk at both a cellular and organismal level is crucial, given the increasing prevalence of metabolic disorders, including type 2 diabetes and obesity.