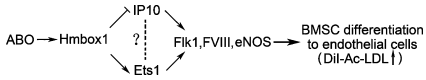
In this ISSUE

A Box for Endothelial Differentiation

Bone marrow stromal cells (BMSCs) are capable of differentiating into numerous cell types, including those that make up our blood vessels, bones, fat tissue, cartilage, and even our brain. The multipotent nature of BMSCs makes them compelling therapeutic tools for tissue repair and growth. For example, differentiation of BMSCs into vascular endothelial cells (VECs) is known to be important for angiogenesis and in repairing damaged blood vessels. How this differentiation process is regulated, however, is not well understood. Now, Su *et al.* (DOI: 10.1021/cb100153r) report the identification of a small molecule, referred to as ABO, that promotes differentiation of BMSCs to VECs.

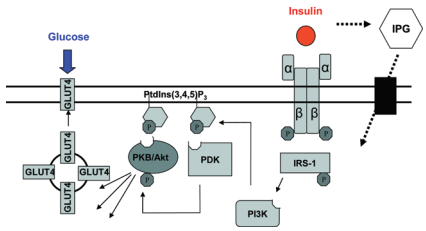
A capillary-like tube formation assay and immunofluorescence experiments demonstrated that ABO induces differentiation of BMSCs into VECs, and microarray analysis revealed that treatment with ABO resulted in increased expression of a gene called Hmbox1 and decreased expression of six other genes. Additional biochemical and RNA knockdown studies offered insights into the specific roles of these genes in BMSC differentiation, illustrating the utility of using small molecules to elucidate genes and pathways involved in cellular differentiation processes.



Mimicking Insulin, Or Not

The peptide hormone insulin is a key regulator of numerous important metabolic processes, including glucose homeostasis. Indeed, insufficient production of or impaired response to insulin is the basis for types I and II diabetes, respectively. For over two decades, it has been proposed that endogenous small molecules derived from second messenger compounds called inositol phosphoglycans (IPGs) can act as insulin mimetics, but the mechanisms underlying these effects have remained elusive. Using an impressive suite of techniques including organic synthesis and *in vitro*, *ex vivo*, and *in vivo* assays, Hecht *et al.* (DOI: 10.1021/cb1002152) explore the presumed insulin mimetic activity of synthetic IPGs.

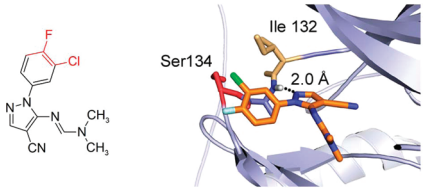
Based on specific structures implicated in the literature as insulin mimetics, five IPGs were synthesized. Extensive analysis into their insulin-like activity, including their ability to induce the phosphorylation of protein kinase B, stimulate glucose uptake and promote lipogenesis in fat cells, as well as to decrease blood glucose levels in mice, was conducted. In each case, compelling data was presented suggesting that IPGs do not in fact possess insulin mimetic activity.



A Star Inhibitor for Aurora B Kinase

Aurora kinases are key regulators of various aspects of cell division, and their overexpression in numerous cancers has also implicated them as potential cancer drug targets. Aurora B kinase is involved in cytokinesis, when the cytoplasm is divided between two daughter cells, but the inherent difficulty in finding selective kinase inhibitors has hampered determination of the precise role of the enzyme. Now, Smurnyy *et al.* (DOI: 10.1021/cb1001685) report that the small molecule Binucleine 2 is a highly selective Aurora B kinase inhibitor, and demonstrate the power of using this compound to explore Aurora B function.

Comparison of the phenotypes observed upon treatment of *Drosophila* cells with Binucleine 2 and RNAi of Aurora B hinted that Binucleine 2 might function as an inhibitor of Aurora B. Indeed, it was demonstrated that Binucleine 2 is an ATP-competitive inhibitor highly selective for *Drosophila* Aurora B kinase over other Aurora kinases. Sequence alignment comparisons, molecular modeling studies, and structure–activity analysis pointed to the molecular basis for this selectivity, and imaging experiments suggested some unexpected roles for Aurora B during the cell division process.



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