DOI:
10.1038/nrm1957

In the news

A NEW DRUG TARGET?

The function of the ubiquitously expressed class IA phosphatidylinositol 3-kinase (PI3K) p110α catalytic subunit, which is frequently mutated in human cancers, has been delineated by a team of researchers led by Bart Vanhaesebroeck at the Ludwig Institute for Cancer Research, London, UK, and Dominic Withers at the University College London Centre for Diabetes and Endocrinology, UK. PI3Ks are a family of lipid kinases that are involved in signal transduction; the roles of most PI3K isoforms in both normal physiology and disease have remained elusive — until now.

In the study, published in *Nature*, the team used a knock-in mouse gene-targeting strategy to abrogate p110α-kinase activity without removing the protein, and this resulted in a 50% loss of function. Their findings show that p110α has a key role in cell growth and metabolism by controlling the signalling of insulin, insulin-like growth factor-1 and leptin.

Interestingly, although these knock-in mice had increased insulin levels and showed glucose intolerance, they did not develop diabetes. Bart Vanhaesebroeck commented that "The finding that these mice, despite having dampened insulin signalling, showed no signs of developing diabetes, is welcome news, as this suggests that drugs that block p110α function in cancer cells may not have the severe metabolic disturbances first expected." (Ludwig Institute for Cancer Research, 12 April 2006).

The authors' findings could have immediate implications for the development of small-molecule inhibitors of p110α as anti-cancer agents. "Accurate information" says Vanhaesebroeck "on the specific role of p110α is needed urgently by the pharmaceutical industry, which is preparing to initiate clinical trials based on PI3K inihibition, not only in cancer but also in inflammation, allergy and auto-immunity." (Ludwig Institute for Cancer Research, 12 April 2006).

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