

Neuroscience Center of Excellence

Chancellor's Award Lecture
in Neuroscience



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Wolfson Institute
for Biomedical Research,
University College London,
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8th Floor

Neuroscience Center
of Excellence
Conference Room

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**Discovery of the
Mechanism that Enables
the Provision of Nutrients
to Proliferating Cells**

Cell proliferation is accompanied by an increase in the utilization of glucose and glutamine. The proliferative response is dependent on a decrease in the activity of the ubiquitin ligase anaphase-promoting complex/cyclosome (APC/C)-Cdh1 which controls G1-to-S-phase transition by targeting degradation motifs, including the KEN box. This occurs not only in cell cycle proteins but also in the glycolysis-promoting enzyme 6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase isoform 3 (PFKFB3), as we have recently discovered in cells in culture as well as in proliferating human T lymphocytes. Moreover, we have found that glutaminase 1 is a substrate for this ubiquitin ligase and appears at the same time as PFKFB3 in proliferating cells. Glutaminase 1 is the first enzyme in glutaminolysis, which converts glutamine to lactate, yielding intermediates for cell proliferation. Thus APC/C-Cdh1 is responsible for the provision not only of glucose but also of glutamine and, as such, accounts for the critical step that links the cell cycle with the metabolic substrates essential for its progression.