

## **Akt translocation under increasing insulin stimulation**

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Akt is a crucial signalling protein in mammalian cells. It plays a major role in cellular processes such as proliferation, cell survival, and metabolism and as such constitutes a vital cross-talk node between many signalling pathways in the cell. In particular, Akt is a key mediator of glucose transport in response to insulin, where it functions as a switch-like amplifier of the insulin signal. The dysregulation of Akt is associated with the development of diabetes, cancer and cardiovascular disease.

In unstimulated cells, Akt is found predominantly in the cytosol. Upon stimulation by insulin, cytosolic Akt translocates to the inner leaflet of the plasma membrane (PM) by a process that is largely unknown. After activation at the PM, the Akt may leave the PM in the still-activated state and phosphorylate its downstream substrates in turn.

The process of Akt translocation remains obscure. The arrival of Akt at the PM can be measured by total internal reflection fluorescence (TIRF) microscopy. Using the TIRF data as a guide, we have developed a compartmental model of Akt translocation in response to insulin. Although this is a good model for the initial application of insulin at physiological concentrations, it is possible to further stimulate the cell with repeated applications of insulin at increasing concentrations. Results of the analysis of the behaviour of the system under increasing doses of insulin can help identify the mechanisms acting in Akt translocation.