



Science Signaling front cover image: 3D structure of DAPK (green and yellow) when bound to calmodulin (violet and blue), obtained by X-ray crystallography.

Communications system hacked

Cells rely on a range of signalling systems to communicate with each other and to control their own internal workings. Scientists from the European Molecular Biology Laboratory in Hamburg (Germany), have now found a way to hack into a vital communications system, raising the possibility of developing new drugs to tackle disorders like neurodegeneration, cancer and cardiovascular disease. Using the ESRF beamlines BM14 and ID29, as well as others at DESY, they have pieced together the first snapshot of what two of the system's components look like while interacting.

One way that these signalling systems work is by triggering a flood of calcium ions inside the cell. These get picked up by a receiver, a protein called calmodulin, which turns this calcium signal into action by switching various parts of the cell's machinery on or off. Calmodulin regulates a set of proteins called kinases, each controls the activity of specific parts of the cell, consequently altering the cell's behaviour.

The results revealed the molecular structure of one of these kinases, a protein called death-associated protein kinase (DAPK), when bound to calmodulin. The structure showed how calmodulin binds to a particular section of DAPK, switching the kinase on so that it can go and change the function of its targets. The team then worked out which of DAPK's building blocks, or amino acids, were crucial for calmodulin to bind.

Reference

I De Diego *et al.* 2010 *Science Signaling* **3(106)**.