

## **In silico methods to explain the molecular activity of the Ras oncogen in signal transduction**

Alfonso Valencia and Gloria Fuentes, scientists working in the Structural Biology and Biocomputing Programme of the Spanish National Cancer Research Centre (CNIO), have proposed new models to explain the molecular details of the interaction between the oncogene Ras and its most important effectors. The results of this study are described in an article which was recently published in the journal *Trends in Biochemical Sciences*. They could be basis for the design of small molecules, peptides or mutagenesis analyses, aimed at selectively modulating the interactions of Ras with Raf kinase, phosphoinositol-3 kinase (PI3K) and RaIGDS, thus controlling the pathways that these proteins are involved in.

The proteins of the Ras superfamily are molecular switches involved in diverse signalling pathways that transmit information through interactions between proteins. The malfunction of this protein was initially characterized by the group of Mariano Barbacid, who in the 1980s discovered the first mutation that activates the cancer-causing potential of Ras.

Due to the biological importance and its implications in cancer, this system has been extensively studied. However, the characterization of the structural details of the association of Ras with its effectors is difficult via experimental methods such as crystallography and NMR spectroscopy. The authors have employed an alternative approach using computational docking algorithms that combine physical properties and biochemical data extracted from the literature to generate structural models of Ras and its effectors. The models thus derived can provide an atomistic understanding of important biological issues, such as how Ras discriminates between its various effectors.

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