LAR, a phosphatase that seems to act as by adding phosphates rather than removing them

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Platelet derived growth factor receptor (PDGFR) is a protein on the cell surface that interacts with other proteins. It plays a role in increasing the growth, dividing and movement of cells upon contacting the growth factor, a type of extracellular signalling molecule produced by human body. When the growth factor bind to PDGFR, phosphate groups (PO_4) are added on to the receptor through intracellular chemical reactions, which leads to its activation.

This process of phosphate addition is called “phosphorylation”. As phosphorylation can occur on the amino acid tyrosine in the protein, the protein that performs phosphorylation is called “protein tyrosine kinase”. Importantly, the phosphorylation process can be reversed by another type of protein called “protein tyrosine phosphatase” that removes the phosphate group added by kinase and converts the protein back to its original state. Many enzymes and receptors are switched on and off by phosphorylation and dephosphorylation. Reversible phosphorylation results in structural changes in many enzymes and receptors and causes them to become activated or inactivated.

The phosphorylation of the PDGF receptor leads to the phosphorylation and activation of other proteins through a series of kinase and phosphatase activity, and finally affects the expression of the information contained in the genes and therefore changes the behaviour of the cell.

The LAR-RPTP (leukocyte common antigen-related subfamily of receptor protein tyrosine phosphatase) is a type of tyrosine phosphatase. The fact that LAR regulates the phosphorylation and activation of proteins that themselves are activated by the tyrosine kinase growth factor receptors suggests that LAR could also have effects on the phosphorylation of PDGFR and its downstream signal transduction.

Interestingly, in this study, results suggested that LAR phosphatase increased the phosphorylation of the PDGF receptor and other intracellular molecules affected by it. This suggests thats LAR has the function of a protein kinase rather than a phosphatase. The phosphorylation of PDGF receptor and its signalling effectors were clearly decreased in the cell with LAR phosphatase deleted compared to the normal cells. As a phosphatase, LAR could only exert this positive regulatory action indirectly. One of the possible mechanisms of this is through the Src kinase (Sarcoma kinase), which can be activated by LAR when dephosphorylated. When Src kinase ids activated by LAR it phosphorylates the PDGF receptor and signalling effectors that are affected by PDGFR. This hypothesis is partly supported by the finding that the activity of Src is decreased in cells lacking LAR. However, further studies need to be carried out to for definite conclusions.

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