

Discovery of a mechanism that controls the expression of a protein involved in numerous cancers

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(PhysOrg.com) -- Researchers at the Institute for Research in Immunology and Cancer (IRIC) of the Université de Montréal have identified a new mechanism controlling the transmission of an abnormal signal at the origin of several cancers. In an article published in the journal Cell, Marc Therrien's team explains the recent discovery of a protein complex that controls the RAS/MAPK signalling pathway, responsible for some of the deadliest cancers, including pancreatic, colon and lung cancers, and melanomas. This regulating mechanism could prove to be a promising therapeutic target for the treatment of these diseases. The study conducted on the drosophila model organism is to be verified in humans in a forthcoming step.

Marc Therrien and his team focus their research on the RAS/MAPK signalling pathway, which is deregulated in several tumours. To send a message to the cell, the information must be relayed by proteins contained in this signalling pathway. In the case of the RAS/MAPK pathway, the message is given by RAS and the last protein in the pathway, MAPK, transmits the message to the cell's control centre, the nucleus. However, the RAS/MAPK pathway sometimes transmits erroneous messages which cause the cell to proliferate non-stop. "Our study shows that a protein complex, EJC, controls production of the MAPK protein, which acts directly on the cell. When this complex is deficient, the signalling pathway is inhibited which restricts the chaotic proliferation of the cell at the origin of many cancers," Marc Therrien



explains. "If we target EJC and the factors that regulate its activity, we could potentially prevent the transmission of abnormal signals that trigger several cancers."

In addition to serving as a promising therapeutic target for treating <u>cancer</u>, the regulating mechanism discovered for MAPK could also apply to several other genes. "Our research could serve to explain the production of other proteins with a behaviour similar to MAPK. This mechanism could help us to understand gene expression in general," Marc Therrien concludes.

The breakthrough was made possible by the SOLiDTM Next Generation Sequencing System manufactured by Life Technologies, which enabled the researchers to view the overall consequences of the elimination of EJC on the expression of all of the cell's genes. "IRIC has adopted a cutting-edge technological infrastructure, without which this kind of work would be impossible," explains Dr. Guy Sauvageau, Chief Executive Officer and Scientific Director of the IRIC. "The Life Technologies sequencing equipment allows us to perform cutting-edge research by quickly obtaining accurate and complete results."

More information: Ashton-Beaucage D, Udell CM, Lavoie H, Baril C, Lefrançois M, Chagnon P, Gendron P, Caron-Lizotte O, Bonneil E, Thibault P, Therrien M. (2010) The exon junction complex controls the splicing of MAPK and other long intron-containing transcripts in Drosophila. *Cell* 143 :251-262

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