A recent IRCM breakthrough impacts cancer research

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A team of scientists at the Institut de recherches cliniques de Montréal (IRCM) led by Dr. Jean-François Côté, Director of the Cytoskeletal Organization and Cell Migration research unit, identified a novel molecular mechanism in the control of cell motility. Their findings were published online today in *Current Biology*, a journal from the Cell Press group. This scientific breakthrough could eventually lead to the development of new cancer-treating drugs that could block the spread of tumours (metastasis).

"As many as 90% of cancer patient deaths are attributable to metastasis, which explains the importance of understanding the molecular mechanisms at the basis of this harmful process," says Dr. Côté. "This is why, over the past few years, we have focused our research on DOCK180, a protein involved in intracellular signalling networks, and more particularly on the DOCK180/Rac1 signalling pathway, which is suspected to be a key mediator of tumour metastasis."

Unlike normal cells that migrate throughout embryonic and adult life to perform their specialized functions, cancer cells metastasize in order to lethally spread throughout the body. At a molecular level, DOCK180 specifically activates the small Rac1 protein, which, in turn, modifies a cell's shape and promotes cell motility and invasion. Dr. Côté's team had previously demonstrated in detail how DOCK180, with the help of its binding partner ELMO, acts on Rac1 to promote robust cell migration.

"We knew that this signalling pathway had to be regulated to prevent

uncontrolled cell migration in normal conditions, but until now, the mechanisms involved had been eluding us and other scientists," explains Manishha Patel, a PhD student in Dr. Côté's laboratory and co-author of the study. "With our recent findings, we demonstrated that the ELMO protein closes in on itself to enter a repressed state, thus preventing the activation of the DOCK180/Rac pathway."

"Our team identified three regions in ELMO that allow it to toggle between a closed/inactive and open/active shape," adds Dr. Yoran Margaron, a postdoctoral fellow in the same research unit and one of the article's co-authors. "We showed that if we disrupt ELMO's regulatory feature and maintain the protein in an open state, we can fully activate the DOCK180/Rac pathway and significantly increase the migration potential of cells."

The researchers' next step is to investigate the regulation of ELMO in cancer cells. Based on their latest findings, they will attempt to maintain ELMO in a repressed state within cancer cells to prevent metastasis, which could have a major impact on the development of potential cancer treatments.

More information: For more information, please refer to the online article published by *Current Biology*. The print publication will be available on November 23, 2010.

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