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Cancer: Defective Cell Surface 'Glue' Is Key to Tumor Invasion

A remarkable discovery into how tumour cells invade normal tissue should lead to vital diagnostic tools and help develop strategies to stop the spread of cancer cells. A new study by scientists at the Montreal Neurological Institute and Hospital of McGill University reveals that the surface of aggressive tumour cells lack the strong molecular 'glue' responsible for binding normal cells together. This allows tumour cells to break away, detach from their neighbors, and spread to other regions of the body.

Certain proteins, called cadherins, are located on the surface of cells and play a vital role in cell adhesion or 'gluing' cells together, ensuring the proper organization of tissue. What happens to the cells and the 'glue' that binds them in tumour growth and metastases is poorly understood. "We were concerned that previous research showed that N-cadherin, an adhesive molecule, was important for both normal tissue organization, as well as tumour metastasis," says Dr. David Colman, Director of The Neuro and corresponding author of the study. "We therefore decided to further investigate this apparent paradox."

The team studied the levels of N-cadherin on tumour cell surfaces. "Our study shows that a non-adhesive form of N-cadherin, termed proNcad is present in a much higher proportion on the surfaces of the most invasive melanoma, brain tumour cells, breast cancer and prostate tumour cells, compared to less invasive tumour cells," says Dr. Deborah Maret, Research Associate and Lead Author. This non-adhesive form of N-cadherin never reaches the cell surface in normal tissues.

"It appears that although total N-cadherin levels remain constant, the higher levels of the non-adhesive proNcad promote detachment, tumor cell migration and invasion," adds Dr. Maret. "This supports an overall conclusion that non-adhesive (proNcad) and adhesive (Ncad) forms of cadherins co-exist on tumour cell surfaces, but it is the ratio between these functionally opposite molecules that directly dictates the invasion potential of tumour cells." Because the differences between the two forms of cadherin are so small, previous studies have missed detecting the non-adhesive proNcad form on tumour cell

surfaces. Hence it was assumed that all Ncad on the tumour cell surface was of the adhesive type. "We were astounded that this was not the case at all," says Dr. Colman.

"As a brain tumour surgeon, I know that stopping cancer cells from migrating is critical for patient survival," says Dr. Rolando Del Maestro, Director of The Brain Tumour Research Centre and a co-author on the study. "We are determined to improve treatment options for patients. We have already introduced new neurosurgical methods and technologies that are unique in North America and are spearheading multidisciplinary initiatives to advance brain tumour research."

Determining the ratios of Ncad and proNcad on the cell surface may serve as a tremendously valuable tool for the staging and progression of malignant tumors. The findings may also shed light on new treatment strategies to arrest the metastatic spread of invasive tumor cells.

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Deborah Maret, Eugenia Gruzglin, Mohamad Seyed Sadr, Vincent Siu, Weisong Shan, Alexander W Koch, Nabil G Seidah, Rolando F Del Maestro and David Colman. *Surface expression of precursor N-cadherin promotes tumor cell invasion. Neoplasia, 2010; 12 (12): 1066-1080 DOI: 10.1593/neo.10954*