'MaMTH' advance: New technology sheds light on protein interactions

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Scientists have a better way to study human proteins—large molecules that are part of every cell in the body—thanks to a new technology developed by University of Toronto researchers. The technology tracks a class of proteins called membrane proteins as they interact with other proteins to either maintain health or contribute to disease.

Membrane proteins make up about one third of all proteins in the human body, and their malfunction is associated with more than 500 diseases. But they've been hard to study because understanding their role depends on observing their interactions with other proteins.

"This technology gives us a new tool to examine membrane proteins in their natural environment of the human cell," said Igor Stagljar, a Professor in the Donnelly Centre for Cellular and Biomolecular Research. "As well, it's sensitive enough to detect minor changes upon introduction of drugs, so it should prove useful in the development of therapeutics, particularly for cancer and neurological diseases."

The journal *Nature Methods* published the research online today.

Stagljar and his colleagues also applied the new technology, which they dubbed MaMTH (for Mammalian-Membrane Two-Hybrid assay), to identify a protein that plays a role in the most common form of lung cancer called non-small cell lung cancer.

That protein, CRKII, interacts with another protein called an epidermal

growth factor receptor. Mutation of this receptor—which is already the target of several cancer drugs either approved or in development—causes a proliferation of cancer cells.

"CRKII most likely regulates the stability of mutated epidermal growth factor receptors and drives cancer growth by promoting signaling, or communication, within cancer cells," said Julia Petschnigg, lead author on the paper and a postdoctoral fellow at U of T. "We found that a combinatorial chemotherapy that inhibits those mutated receptors and CRKII could be beneficial in treating lung cancer."

The research was highly collaborative, involving cancer clinicians, bioinformaticians and researchers in five labs around Toronto and Boston. Stagljar and his lab spent four years developing the MaMTH technology, which they adapted from a similar technology that captures protein-protein interactions in yeast.

Next, the group will apply their technology to study some of the 500 proteins that are mutated in other human diseases.

"You simply cannot publish meaningful research in proteomics without collaborating," said Stagljar, who is also a Professor in the Departments of Biochemistry and Molecular Genetics. "Fortunately, we have access to great cross-disciplinary expertise and infrastructure in the Donnelly Centre. Science is alive and well in Toronto."

More information: The Mammalian-Membrane-Two-Hybrid (MaMTH) assay for probing membrane protein interactions in human cells, DOI: 10.1038/nmeth.2895

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