Protein inhibits cancer cell growth

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(PhysOrg.com) -- Researchers at the University of Toronto and Goethe University in Germany have discovered a protein that can inhibit the growth of cancer cells, providing crucial clues for the future development of new drugs to treat the disease.

The protein, called HDAC6, controls the stability of the epidermal growth factor receptor (EGFR), a key player in cancer.

"Our teams discovered that HDAC6 acts as a molecular brake to shut down the expression of the human EGFR," said Professor Igor Stagljar of biochemistry and molecular genetics, one of the lead authors of a study published in the Dec. 22 issue of the journal *Science Signaling*. Professor Ivan Dikic at Goethe University was co-lead on the study.

"Since EGFR is overactive in breast, lung, colon and pancreatic cancers, this discovery can open new avenues for cancer treatment," said Stagljar, a principal investigator at U of T's Terrence Donnelly Centre for Cellular and Biomolecular Research.

EGFR is nestled into the cell membrane on the surface of human cells where, after it gets activated by molecules called ligands, causes cells to divide. In several cancer cell types, the activity of this receptor is dramatically increased, which stimulates cells to grow rapidly and out of control. Because of its key role in driving the proliferation of cells, EGFR is a target of several cancer drugs currently in development, as well as several approved therapies.

To study the cellular role of EGFR in human cells, Stagljar's lab first developed a technology called MYTH, a unique test that can monitor interactions between membrane proteins. This technology can reveal proteins that tightly associate with EGFR on the cell surface. Using MYTH, the researchers identified more than 80 proteins that interact, and presumably communicate, with the human EGFR. Among them was a cytosolic protein, HDAC6, which they showed helps in stabilizing EGFR in human cells.

"These findings offer fresh insight into how HDAC6 regulates EGFR degradation and provides clues for the design of improved cancer therapies," Stagljar said. Specifically, a carefully planned combinatorial chemotherapy that inhibits both the EGFR receptor and its newly identified "brake" (HDAC6) could have a beneficial effect for treating breast, lung, colon, and pancreatic cancers.

In the next phase of their research, Stagljar and his colleagues plan to extend the MYTH technology to interrogate all human receptors that regulate cell proliferation and are therefore implicated in the onset of cancer. Such a global analysis of proteins that associate with human cell surface receptors may provide novel avenues for the treatment of different types of cancers.

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