A New Way to Target Degradation of the Epidermal Growth Factor Receptor in Cancer Cells

Destabilization of the Epidermal Growth Factor Receptor (EGFR) by a Peptide That Inhibits EGFR Binding to Heat Shock Protein 90 and Receptor Dimerization

The epidermal growth factor receptor (EGFR) belongs to the ErbB family of transmembrane tyrosine kinases, which are involved in the regulation of cell proliferation, differentiation, and migration. The EGFR becomes active when it dimerizes with either itself or another protein in the presence of its ligand. The receptor’s abnormal activation is associated with a number of human cancers, which makes it attractive as an anticancer drug target. In this Paper of the Week, a team led by Mukesh K. Nyati at the University of Michigan Medical School demonstrated that a synthetic peptide containing the first six amino acids of the αC-β4 loop region of the EGFR inhibits the dimerization and activity of the receptor in the presence of its ligand. The short peptide sequence, which targets the receptor’s ATP-binding cleft and the dimerization face, also promotes EGFR interaction with Hsp90, a chaperone protein involved in EGFR degradation. The investigators say that this synthetic peptide, which they call Disruptin, “provides proof of concept for the development of a new class of anti-tumor drugs that specifically cause EGFR degradation.”

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