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Human Mdm2: A new molecular link to late-stage metastatic breast cancer

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A large proportion of late-stage breast cancers that have spread to other parts of the body (metastatic breast cancers) are characterized by overexpression of the protein Mdm2.

Lindsey Mayo and colleagues, at Indiana University School of Medicine, Indianapolis, have now determined what drives this increased Mdm2 expression and found that Mdm2 helps promote cancer cells take on more aggressive characteristics, making it a potential target for drugs to treat late-stage metastatic breast cancer.

In the study, a signaling pathway triggered by the molecule TGF-beta-1 was found to increase Mdm2 expression in human cancer cell lines. Expression of activated molecules involved in this pathway correlated with Mdm2 expression in many late-stage breast cancer samples analyzed.

The increased level of Mdm2 in the human cancer cell lines led to decreased expression of the key tumor suppressor p53. More importantly, it enabled the cells to gain the ability to move freely in vitro after exposure to TGF-beta-1 (a key feature of cells that cause metastatic tumors). As an antagonist of the effects of Mdm2 on p53 prevented TGF-beta-1 from enabling cells to move freely in culture, the authors suggest that targeting Mdm2 might help prevent progression of late-stage breast cancer.

More information: TGF-β1-induced expression of human Mdm2

correlates with late-stage metastatic breast cancer. View this article at: www.jci.org/articles/view/3919 … EC7lQbgq0ivAliJkn5z3

Source: Journal of Clinical Investigation