Statin-like drugs as a new treatment for cancers expressing mutant p53

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Technology description

Problem or Unmet Need:
Over 50 percent of human tumors contain mutations in the gene encoding p53, a protein thought to play a role in early carcinogenesis. Currently, it is viewed as a tumor suppressor that enables oncogenesis through a loss of function. However, mutant p53 has recently been shown to exhibit carcinogenic gain-of-function properties as well. One such function appeared to result from an upregulation of the sterol biosynthesis pathway. Inhibition of this pathway could thus pave the way for entirely new treatments against mutant p53 expressing cancers.

To examine the newly discovered gain-of-function properties of mutant p53, a 3D culture model was used. In this model, mammary epithelial cells were cultured in a laminin-rich extracellular matrix and form structures highly reminiscent of acinar structures found in vivo. A genome-wide expression analysis then identified the sterol biosynthesis pathway as being upregulated by oncogenic mutant p53. HMG-CoA Reductase is the rate-limiting enzyme in the sterol biosynthesis pathway and inhibitors of this enzyme (the statin family of drugs) have been well studied. Two different statins were tried on two separate breast cancer cell lines, and it was found that these drugs dramatically reduced the growth and invasiveness of the cancer cells in 3D culture and in some cases lead to dramatic tumor cell death. Accordingly, statins or other HMG-CoA Reductase inhibitors may offer a novel therapeutic option to cancer patients whose tumors express mutated p53.

Application area

The research indicates a role of the sterol biosynthesis pathway early in carcinogenesis.
The technology could enable development of broad-spectrum treatments of cancers that display p53 mutations.
If downstream carcinogenic effects of sterol biosynthesis upregulation are found, further therapeutic targets may be identified.

Advantages

Statins are FDA approved and widely used, thus limiting potential cytotoxic side effects of therapy.

In combination with p53 genotyping, the technology could enable increased cancer treatment efficacy.

Institution

Columbia University