Statin drugs as a treatment for cancers expressing the mutant p53 gene

Technology #m11-022

Over 50 percent of human tumors contain mutations in the gene encoding p53, a protein thought to play a role in early development of cancer. Classically, this gene is believed to suppress carcinogenic tumors by inducing a loss of function. Mutant p53, however, has recently been shown to exhibit gain-of-function properties, causing cancer formation by proliferating normally suppressed pathways. A genome-wide expression analysis identified the sterol biosynthesis pathway (e.g. mevalonate pathway) as being up-regulated by oncogenic mutant p53. This technology describes a method for treating mutant-p53-related cancers using HMG-CoA reductase inhibitors, commonly known as statins. HMG-CoA reductase is the rate-limiting enzyme in the sterol biosynthesis pathway. As such, inhibition of this pathway using statins could pave the way for entirely new treatments against mutant-p53-expressing cancers.

In vitro studies demonstrate HMG-CoA Reductase inhibitors (statins) can reduce cancer cell growth and invasiveness

Unlike the conventional focus on p53-mediated oncogenesis as a loss-of-function phenomenon, this technology targets the recently observed gain-of-function noted in the sterol biosynthesis pathway. Accordingly, the technology utilizes statins, a well-studied and well-tolerated class of HMG-CoA reductase inhibitors commonly used for the treatment of high cholesterol, to inhibit the increased sterol biosynthesis found in mutant-p53-expressing cancers. In vitro, the technology was able to dramatically reduce the growth and invasiveness of breast cancer cells in 3D culture. In some cases, administration of the technology led to dramatic tumor cell death. The technology has been tested and verified on two separate breast cancer cell lines using two different types of statins.

Lead Inventor:

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Applications:

• Research tool to study the role of the sterol biosynthesis pathway in early carcinogenesis.
• The use of statins as a cancer therapeutic.
• 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 among the most carefully studied class of drugs in use and are well tolerated with an excellent safety profile.
• Statins are already FDA approved and widely used for other indications.
• In combination with p53 genotyping, this technology could enable increased cancer treatment efficacy.

Patent information:

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Related Publications:


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