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

Lead Inventor: Carol Prives, Ph.D., William Allen Freed-Pastor, Arnold Levine, Ph.D., Scott Lowe, Ph.D.

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Over 50 percent of human tumors contain mutations in the gene encoding p53, a protein thought to play a role in early carcinogenesis. Classically, this gene is thought to be a tumor suppressor that causes cancer through a loss of function. However, mutant p53 has recently been shown to exhibit gain-of-function properties as well, causing cancer formation by enabling normally suppressed pathways. One such oncogenic pathway activated by this mutation is the sterol biosynthesis pathway. Inhibition of this pathway using HMG-CoA Reductase inhibitors, commonly known as statins, could thus 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. Using a 3D culture model, breast tissue cells were cultured with an inducible p53 mutation. 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 this pathway and inhibitors of this enzyme (the statin family of drugs) have been well studied. However, no statin is currently indicated for treatment of cancer. Two different statins were tested 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, HMG-CoA Reductase inhibitors such as statins may offer a novel therapeutic option to cancer patients whose tumors express mutated p53.

### Applications:

* The research indicates a role of the sterol biosynthesis pathway early in carcinogenesis.
* This technology suggests a new indication for statins in cancer therapy.
* 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 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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Further Information: Columbia | Technology Ventures
Jullian G. Jones, Ph.D., J.D.; Tel: (212) 851-0258
Email: TechTransfer@columbia.edu