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Therapeutics, Cardiovascular Disease, cholesterol repression

Links:
Inventor Website

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Background
Cardiovascular diseases are the leading cause of death in the United States. A major risk factor is the level of circulating cholesterol and LDL. Statins have become the first line of treatment to lower cholesterol synthesis in the liver and is one of the most prescribed classes of drugs. However, statins can exhibit adverse side effects and do not exhibit efficacy in every patient.

Invention Description
A team of Penn State researchers have developed several indazole derivatives that are capable of repressing the expression of genes that facilitate de novo cholesterol synthesis. These composition-of-matters mediate this action by acting as a selective Ah receptor modulator, which has been previously shown to repress cholesterol synthesis. However, the invention's compounds do not exhibit xenobiotic metabolism, which has occurred in other cardiovascular disease therapeutic candidates. Research results indicate that these compounds can largely block the increase expression of cholesterol synthesis genes upon statin treatment. These compounds also exhibit anti-inflammatory activity in the liver.

Status of the Invention
Experimental data on primary human hepatocytes has shown that the compounds are capable of limiting statin induced expression of cholesterol synthesis genes. These compounds also lower the expression of cholesterol synthesis genes in mouse liver.

Commercial Applications
The subject invention represents a possible new class of drugs that can either work alone or as an adjuvant with statins. The compounds have been shown to be well tolerated in mouse treatment studies and do not exhibit any overt toxicity.