



# Small Molecule Inhibitor of Cholesterol Biosynthesis and Venous Angiogenesis

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## SUMMARY

UCLA researchers have identified a novel small molecule that inhibits the HMG-CoA reductase pathway, reducing cellular cholesterol and preventing vein-specific angiogenesis.

## BACKGROUND

Statins are a class of small molecule drugs used for lowering blood cholesterol levels and preventing cardiovascular disease. Atorvastatin, sold by Pfizer under the trade name Lipitor, is the best-selling drug in history, with sales exceeding \$11 billion in 2010. This figure is expected to drop dramatically with U.S. patent expiry and the availability of a generic version in November 2011. All statins, including atorvastatin, inhibit HMG-CoA reductase (HMGCR), an enzyme found in liver tissue that plays a key role in cholesterol production. Experimental evidence suggests that this key biochemical pathway also plays an important role in the oncogenic process, and statin administration *in vivo* has been shown to inhibit tumor growth. However, a number of rare but serious side effects have been attributed to statins, including muscle and liver damage. Researchers are working to identify the next generation of cholesterol-lowering small molecule drugs with greater efficacy and reduced side effects, and to understand and modulate the HMGCR pathway for cancer therapy.

## INNOVATION

Researchers at UCLA have identified a non-statin small molecule, aplexone, which reduces cellular cholesterol levels more effectively than atorvastatin (Lipitor). Like statins, aplexone inhibits the HMG-CoA reductase (HMGCR) pathway, but does not contain the same motif and thus likely inhibits the pathway through a different mechanism. Aplexone shows lower toxicity and a substantially lower molecular weight than atorvastatin. In addition to its role in inhibiting cholesterol biosynthesis, aplexone was found to repress angiogenesis and may inhibit tumor growth. This molecule can be further developed as both a cholesterol-lowering drug and a cancer chemotherapeutic.

## APPLICATIONS

- ▶ Reduction of cellular cholesterol.
- ▶ Inhibition of tumor growth through repression of angiogenesis.

## ADVANTAGES

- ▶ Inhibits the HMGCR pathway through a different mechanism than statins.
- ▶ Identifies probes specific to a phenotype of interest and thus does not require prior target identification and validation.

## STATE OF DEVELOPMENT

The cholesterol-lowering and antiangiogenic properties of aplexone have been tested *in vivo* in an embryonic zebrafish model.

## PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Published Application	<a href="#">20220009891</a>	01/13/2022	2011-417

## CONTACT

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## INVENTORS

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## OTHER INFORMATION

### KEYWORDS

Cholesterol, Cardiovascular, Oncology

### CATEGORIZED AS

- ▶ **Medical**
  - ▶ Disease: Cancer
  - ▶ Disease: Cardiovascular and Circulatory System
  - ▶ Therapeutics

### RELATED CASES

2011-417-0

- ▶ [Novel Non-Peptidomimetic Prenyltransferase Inhibitors](#)
- ▶ [Hydrodealkenylative C\(Sp3\)–C\(Sp2\) Bond Scission](#)
- ▶ [Small Molecule Agonists of VDAC2 to Treat Cardiac Arrhythmias and Heart Failure](#)
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