Mevalonate pathway

The Mevalonate pathway, also known as the Isoprenoid pathway or HMG-CoA reductase pathway is an essential metabolic pathway present in eukaryotes, archaea, and some bacteria.

The pathway produces two five-carbon building blocks called isopentenyl pyrophosphate (IPP) and dimethylallyl pyrophosphate (DMAPP), which are used to make isoprenoids, a diverse class of over 30,000 biomolecules such as cholesterol, heme, vitamin K, coenzyme Q10, and all steroid hormones.

The mevalonate pathway begins with acetyl-CoA and ends with the production of IPP and DMAPP.

It is best known as the target of statins, a class of cholesterol lowering drugs. The drug Lipitor (Atorvastatin) inhibits HMG-CoA reductase within the mevalonate pathway. As of 2015, Lipitor remains the world's best selling drug of all time with $125 Billion USD in sales.

Lovastatin is a 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitor that impacts the mevalonate pathway. The inhibition of intermediates in the mevalonate pathway affects signaling cascades and oncogenes associated with brain tumor stem cells (BTSC). In a review, Amadasu et al. showed the possible mechanisms where lovastatin can target BTSC for different varieties of malignant brain tumors [1].

1)
Amadasu E, Kang R, Usmani A, Borlongan CV. Effects of Lovastatin on Brain Cancer Cells. Cell Transplant. 2022 Jan-Dec;31:9636897221102903. doi: 10.1177/09636897221102903. PMID: 35670207.