Botany

PG-SEM-II Paper – BOT-203

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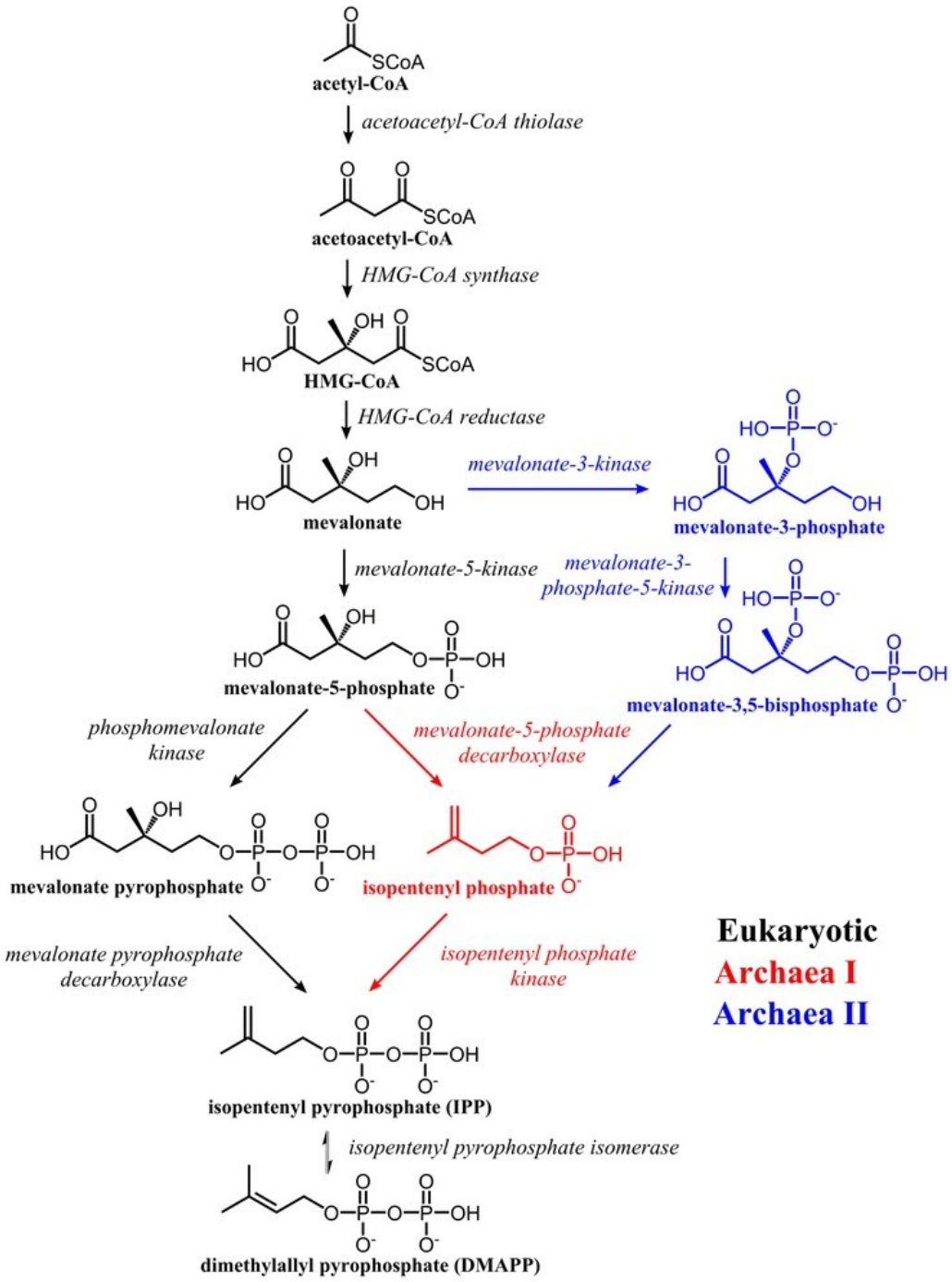
Mevalonate Pathway

Introduction

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, vitamin K, coenzyme Q10, and all steroid hormones.

The mevalonate pathway begins with acetyl-CoA and ends with the production of IPP and DMAPP.[3] It is best known as the target of statins, a class of cholesterol lowering drugs. Statins inhibit HMG-CoA reductase within the mevalonate pathway.

Mevalonate Pathway



Upper mevalonate pathway

The mevalonate pathway of eukaryotes, archaea, and eubacteria all begin the same way. The sole carbon feed stock of the pathway is acetyl-CoA. The first step condenses two acetyl-CoA molecules to yield acetoacetyl-CoA. This is followed by a second condensation to form HMG-CoA (3-hydroxy-3- methyl-glutaryl-CoA). Reduction of HMG-CoA yields (R)-mevalonate. These first 3 enzymatic steps are called the upper mevalonate pathway.

Lower mevalonate pathway

The lower mevalonate pathway which converts (R)-mevalonate into IPP and DMAPP has 3 variants. In eukaryotes, mevalonate is phosphorylated twice in the 5-OH position, then decarboxylated to yield IPP. In some archaea such as *Haloferax volcanii*, mevalonate is phosphorylated once in the 5-OH position, decarboxylated to yield isopentenyl phosphate (IP), and finally phosphorylated again to yield IPP (Archaeal Mevalonate Pathway I). A third mevalonate pathway variant found in *Thermoplasma acidophilum*, phosphorylates mevalonate at the 3-OH position followed by phosphorylation at the 5-OH position. The resulting metabolite, mevalonate-3,5-bisphosphate, is decarboxylated to IP, and finally phosphorylated to yield IPP (Archaeal Mevalonate Pathway II).