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PRODUCTION OF A BLOCKBUSTER DRUG USING BIOCATALYSIS

Simvastatin (Zocor) is a blockbuster drug used towards the treatment of hypercholesterolemia. Simvastatin exhibits potent inhibitory activity towards hydroxymethylglutaryl coenzyme A reductase (HMGR), the rate-limiting step of cholesterol biosynthesis. We have developed an *Escherichia coli*-based, whole-cell biocatalytic process that can convert a precursor molecule Monacolin J (MJ) to simvastatin in one-step, utilizing a readily available dimethylbutyryl thioester substrate. The enzyme that catalyzes the conversion is the acyltransferase LovD from *Aspergillus terreus*. In this presentation, we will present recent metabolic engineering and protein engineering work that have resulted in significant enhancement in the efficiency and throughput of the whole cell system. The biocatalytic process has been scaled to 30,000L fermentations in the production of genetic simvastatin drugs.

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