Overexpression of functional human oxidosqualene cyclase in Escherichia coli - DTU Orbit (23/01/2019)

Overexpression of functional human oxidosqualene cyclase in *Escherichia coli*

The generation of multicyclic scaffolds from linear oxidosqualene by enzymatic polycyclization catalysis constitutes a cornerstone in biology for the generation of bioactive compounds. Human oxidosqualene cyclase (hOSC) is a membrane-bound triterpene cyclase that catalyzes the formation of the tetracyclic steroidal backbone, a key step in cholesterol biosynthesis. Protein expression of hOSC and other eukaryotic oxidosqualene cyclases has traditionally been performed in yeast and insect cells, which has resulted in protein yields of 2.7 mg protein/g cells (hOSC in *Pichia pastoris*) after 48 h of expression. Herein we present, to the best of our knowledge, the first functional expression of hOSC in the model organism *Escherichia coli*. Using a codon-optimized gene and a membrane extraction procedure for which detergent is immediately added after cell lysis, a protein yield of 2.9 mg/g bacterial cells was achieved after four hours of expression. It is envisaged that the isolation of high amounts of active eukaryotic oxidosqualene cyclase in an easy to handle bacterial system will be beneficial in pharmacological, biochemical and biotechnological applications.

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