Synopsis of Original Research Paper

Genetic engineering for synthesis of human ceramides in yeast

Kouichi Funato

Graduate School of Biosphere Science, Hiroshima University

Yeast has been widely and successfully used to produce polypeptides, enzymes, vitamins, and lipid components of high commercial interest. Here we describe progress using the yeast Saccharomyces cerevisiae as an industrial organism for production of human-type ceramides. The yeast cells do not synthesize sphingolipids desaturated at the Δ4-position of the dihydrosphingosine, which are found in many eukaryotic organisms including humans. Instead, they produce sphingolipids hydroxylated at the C-4 position. Therefore in order to 'humanize' ceramide biosynthesis in the yeast, it is necessary to eliminate endogenous yeast ceramide biosynthetic pathway and introduce a heterologous DES1 gene encoding a sphingolipid Δ4-desaturase. Indeed, the resultant yeast strain was capable of synthesizing Δ4-desatulated sphingolipids. Furthermore, we observed that the engineered yeast can produce a human-type ceramide, ceramide NS. Since ceramides play a critical role in maintaining the permeability barrier function of the skin, the yeast-derived human-type ceramide could be used for clinical applications to improve the impaired barrier function seen in several skin diseases including atopic dermatitis.