

# Selective Retinol Biosynthesis in *S. cerevisiae*

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## Editorial

Retinol, a component of vitamin A, is becoming a more popular cosmetic ingredient. A combination of retinoids was created in prior attempts at microbial production of vitamin A. To efficiently produce retinol with high purity, the precursor and NADPH supply were first improved to improve retinoids accumulation in the *S. cerevisiae* strain constructed from a -carotene producer by introducing  $\beta$ -carotene 15, 15-dioxygenase, followed by retinal reduction screening of heterologous and endogenous oxidoreductases. Env9 was discovered to be an endogenous retinal reductase with in vitro activity. When the antioxidant butylated hydroxytoluene was added to prevent retinoids degradation, 443.43 mg/L of retinol was produced at 98.76 percent purity in bi-phasic shake-flask culture by co-expressing Env9 with the *E. coli* ybbO. In fed-batch fermentation, the retinol titer reached 2479.34 mg/L. The success of selective retinol biosynthesis would pave the way for its biotechnological manufacture [1].

Vitamin A (retinoids), an essential vitamin for the human body, is involved in maintaining vision, controlling cell differentiation and apoptosis, stabilising epithelial cell morphology and function, the generation of B and T helper lymphocytes, and other physiological functions. The market for vitamin A, which includes retinol and its active derivatives retinal and retinoic acid, is currently expanding. Since it was shown to have similar anti-wrinkle properties as retinoic acid but with less side effects, retinol has been employed as a key anti-aging ingredient in cosmeceuticals. Furthermore, because of its anti-infective, anticancer, and antioxidant properties, retinol has been used in the production of food, pharmaceuticals, nutraceuticals, and animal feed additives. Vitamin A is a breakdown product of carotenoids called provitamin-A in nature. These carotenoids are produced naturally in photosynthetic organisms and have the ability to release at least one molecule of retinal when catalysed by a carotenoid cleavage dioxygenase. The core double bond cleavage event mediated by -carotene 15,15-mono (di) oxygenases, in particular, might create two molecules of retinal from a single molecule of -carotene. Bio-reduction and oxidation mechanisms can then convert retinal to retinol and retinoic acid, respectively [2].

When the BLH gene expressing -carotene dioxygenase from the archaeon *Halobacterium* sp. NPC-1 was introduced into a -carotene-producing *E. coli*, it resulted in the generation of 136 mg/L retinoids, which were a mixture of retinol, retinal, and retinyl acetate. Retinoids were synthesised with a retinal/retinol ratio of 1.67 from xylose using an engineered *S. cerevisiae* strain, according to a recent study. Despite the absence of retinal reductase/oxidase in these tests, a combination of retinoids was generated. When overexpressed in *E. coli*, the aldehyde reductase ybbO was found to raise the retinol fraction in retinoids from 38 to 53 percent. However, the enzyme(s) responsible for retinol production during *S. cerevisiae* vitamin A biosynthesis have yet to be

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discovered. The mining and overexpression of endogenous and exogenous enzymes with retinal reductase activity is expected to increase the retinol fraction in yeast-produced vitamin A, perhaps leading to selective retinol biosynthesis with a greater commercial value [3, 4].

Currently, retinol is manufactured commercially using chemical synthesis. Alternative methods of microbial retinol production have been investigated, but they are limited to a mixture of retinoids such as retinol, retinal, and retinoic acid. For the selective generation of retinol utilising xylose, we introduced heterologous retinol dehydrogenase into retinoids mixture-producing *Saccharomyces cerevisiae*. Although the expression of human RDH10 and *Escherichia coli* ybbO increased retinol synthesis, retinal remained the most important product. *S. cerevisiae* with human RDH12, on the other hand, synthesised retinol selectively while producing very little retinal [5].

Only retinol was generated by the resultant strain (SR8A-RDH12). However, because to an internal redox imbalance, more glycerol was accumulated. To correct the redox imbalance, *Lactococcus lactis* noxE, which codes for H<sub>2</sub>O-forming NADH oxidase, was also added. The resultant strain had a 30 percent greater yield and produced 52 percent less glycerol and 52 percent more retinol than the original strain. Because the retinol produced was not stable, we looked at culture and storage variables such as temperature, light, and antioxidants to find the best circumstances for retinol production. Finally, by introducing human RDH12 and NADH oxidase into *S. cerevisiae*, we were able to efficiently produce retinol from xylose.

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## Conflict of Interest

The author shows no conflict of interest towards this manuscript.

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