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# Prostaglandin production by the marine diatom with heterologous expression of cyclooxygenase

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## Abstract

Prostaglandins (PGs) are bioactive compounds, which are widely used as pharmaceuticals. They are biologically synthesized from C20 fatty acids through the action of cyclooxygenase (COX). Recently, heterologous expression of *cox* gene in photosynthetic organisms allows PGs biosynthesis. However, low C20 fatty acid content in host organisms remains a significant bottleneck for efficient PG production. In this study, we employed the marine diatom *Phaeodactylum tricornerutum*, which is rich in PG precursors; i.e. C20 fatty acids, for PG production.

A *cox* gene derived from the red alga, *Agarophyton vermiculophyllum* was introduced into *P. tricornerutum*. Then, a transformant with high expression of *cox* was selected. The COX-transformant produced both PGs derived from arachidonic acid and eicosapentaenoic acid. The total amount of PGs was 10.1  $\mu\text{g/g}$  of dry cell weight, which was the highest production of genetically engineered photosynthetic organisms.

On the other hand, the COX-transformant showed growth inhibition compared to wild type. That could be due to the cytotoxicity of PG. To avoid cytotoxicity of PG, *cox* gene expression was attempted using an expression-inducing promoter, the nitrate reductase (NR) promoter. The NR promoter can induce gene expression depending on nitrate concentration in the culture medium. By expressing COX under the control of the NR promoter, cell growth was not inhibited. These results indicate that induction of *cox* gene expression using the NR promoter in *P. tricornerutum* is a promising approach for efficient PG production.

**Keywords:** micro algae, marine diatom, *Phaeodactylum tricornerutum*, genetic engineering, cyclooxygenase, prostaglandin, C20 fatty acid, Nitrate reductase promoter

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