Synopsis of Original Research Paper

Overproduction of essential and new fatty acids through microbial metabolic engineering

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Polyunsaturated fatty acids (PUFAs) play important roles as structural components of membrane phospholipids, and as precursors of the eicosanoids of signaling molecules including prostaglandins, thromboxanes and leukotrienes. The principal PUFAs are dihomo-g-linolenic acid (n-6 PUFA; Δ8, Δ11, Δ14-20:3), arachidonic acid (n-6 PUFA; Δ5, Δ8, Δ11, Δ14-20:4), and eicosapentaenoic acid (n-3 PUFA; Δ5, Δ8, Δ11, Δ14, Δ17-20:5). All mammals synthesize eicosanoids which are involved in the inflammatory response, reproductive function and so on. Therefore, studies on PUFAs are important in both the medical and pharmaceutical fields. We have studied the fatty acid metabolism in the filamentous fungus, Mortierella, which produces some C-20 PUFAs (e.g., dihomo-γ-linolenic acid, arachidonic acid and eicosapentaenoic acid). In this study, at the gene level, we investigated desaturase and elongase involved in PUFA metabolism of this strain. We cloned Δ9-desaturase b gene from the gene library of this Mortierella strain. The predicted amino acid sequence showed similarity to those of other Δ9-desaturases including stearoyl-CoA desaturase from several living organisms including yeast, rat and so on. This sequence also contained a cytochrome b5-like domain at the C-terminus, being different from the Mortierella Δ6-desaturase which has the corresponding domain at the N-terminus. This finding suggests that this domain in the desaturase would play the role of a unique electron transport system, binding a heme group. We also cloned a part of the elongase gene from the *Mortierella* strain for the first time. Further works would lead to the overproduction of various PUFA through gene manupulation in the *Mortierella* strain.