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Metabolic engineering for the microbial production of isoprenoids: Carotenoids and isoprenoid-based biofuels

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ABSTRACT

Isoprenoids are the most abundant and highly diverse group of natural products. Many isoprenoids have been used for pharmaceuticals, nutraceuticals, flavors, cosmetics, food additives and biofuels. Carotenoids and isoprenoid-based biofuels are two classes of important isoprenoids. These isoprenoids have been produced microbially through metabolic engineering and synthetic biology efforts. Herein, we briefly review the engineered biosynthetic pathways in well-characterized microbial systems for the production of carotenoids and several isoprenoid-based biofuels.

Contents

1. Introduction

Isoprenoids, also called terpenoids or terpenes, are the most abundant and highly diverse (structurally and functionally) group of natural products synthesized in almost all living organisms. Many isoprenoids have been used for pharmaceuticals, nutraceuticals, flavors, cosmetics, food additives and biofuels. Isoprenoids are usually classified into groups according the number of carbons: hemiterpenes (C5), monoterpenes (C10), sesquiterpenes (C15), diterpenes (C20), triterpenes (C30) and tetraterpenes (carotenoids, C40).

All isoprenoids derive from isopentenyl diphosphate (IPP) and

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its isomer dimethylallyl diphosphate (DMAPP) (Fig. 1). They can be produced by two metabolic pathways, the mevalonate pathway (MVA or MEV) [1] and the 1-deoxy-D-xylulose-5-phosphate (DXP) pathway (also called the 2-C-methyl-D-erythritol 4-phosphate pathway, MEP pathway) [2]. The MVA pathway is mainly present in archaea, fungi, plant cytoplasm and other eukaryotes. The DXP pathway is mostly found in bacteria and plant plastids. The MVA pathway initiates with the condensation of two acetyl-CoAs by thiolase to produce acetoacetyl-CoA. Subsequently, another acetyl-CoA is condensed with acetoacetyl-CoA to synthesize 3-hydroxy-3-

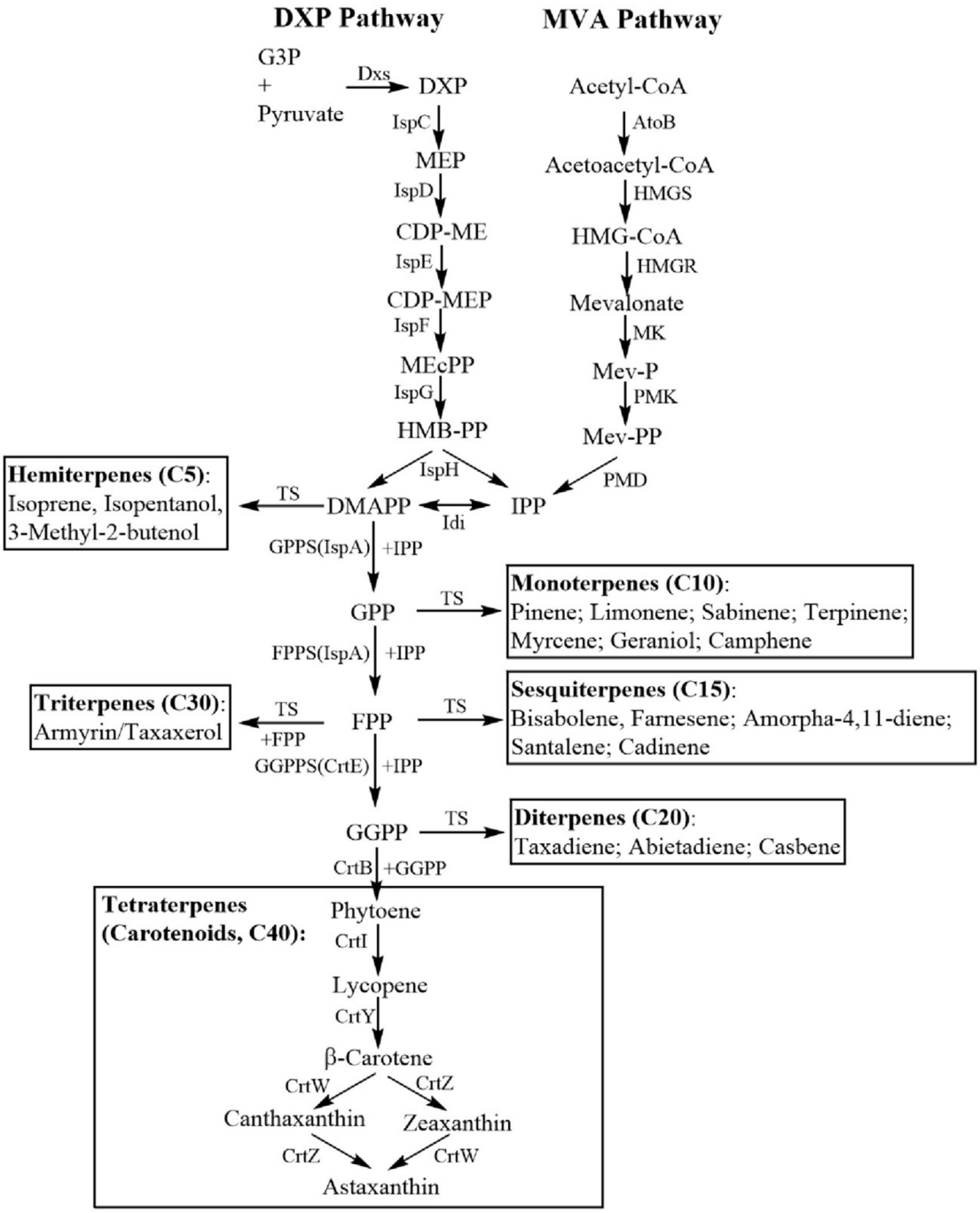

Fig. 1. Isoprenoid biosynthetic pathway. G3P: Glyceraldehyde 3-phosphate; DXP: 1-deoxy-D-xylulose-5-phosphate; MEP: 2-C-methyl-D-erythritol-4-phosphate; CDP-ME: 4-diphosphocytidyl-2-C-methyl-D-erythritol; CDP-MEP: 4-diphosphocytidyl-2-C-methyl-D-erythritol-2-phosphate; MEcPP: 2-C-methyl-D-erythritol-2,4-cyclodiphosphate; HMB-PP: 4-hydroxy-3-mehtyl-butenyl 1-diphosphate; HMG-CoA: 3-hydroxy-3-methyl-glutaryl-CoA; Mev-P: Mevalonate 5-phosphate; Mev-PP: Mevalonate diphosphate; IPP: Isopentenyl diphosphate; DMAPP: Dimethylallyl diphosphate; GPP: Geranyl diphosphate; FPP: Farnesyl diphosphate; GGPP: Geranylgeranyl diphosphate; Dxs: 1-deoxy-D-xylulose-5-phosphate synthase; IspC: 1-D-deoxy-D-xylulose 5-phosphate reductoisomerase; IspD: 2-C-methyl-D-erythritol-4-phosphate cytidylyltransferase; IspE: 4-diphosphocytidyl-2-C-methyl-D-erythritol kinase; IspF: 2-C-methyl-D-erythritol-2,4-cyclodiphosphate synthase; IspG: 1-hydroxy-2-methyl-2-(E)-butenyl-4-diphosphate synthase; IspH: 4-hydroxy-3-methyl-2-(E)-butenyl-4-diphosphate reductase; Idi: Isopentenyl diphosphate isomerase; AtoB: Acetoacetyl-CoA synthase; HMGS: Hydroxymethylglutaryl-CoA synthase; HMGR: Hydroxymethylglutaryl-CoA reductase; MK: Mevalonate kinase; PMK: Phosphomevalonate kinase; PMD: Mevalonate diphosphate decarboxylase; GPPS: GPP synthase; FPPS: FPP synthase; GGPPS: GGPP synthase; TS: terpene synthase.

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