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Review

Stem cell regulation by lysophospholipids

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Abstract

Lysophosphatidic acid (LPA) and sphingosine 1-phosphate (S1P) regulate a diverse range of mammalian cell processes, largely through engaging multiple G protein-coupled receptors specific for these lysophospholipids. LPA and S1P have been clearly identified to have widespread physiological and pathophysiological actions, controlling events within the reproductive, gastrointestinal, vascular, nervous and immune systems, and also having a prominent role in cancer. Here we review the recent literature showing the additional emerging role for LPA and S1P in the regulation of stem cells and their progenitors. We discuss the role of these lysophospholipids in regulating the proliferation, survival, differentiation and migration of a range of adult and embryonic stem cells and progenitors, and thus are likely to play a substantial role in the maintenance, generation, mobilisation and homing of stem cell and progenitor populations in the body.

Keywords: Lysophosphatidic acid; Sphingosine 1-phosphate; Lysophospholipid; Stem cells; Progenitor cells; G protein-coupled receptors

Contents

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1. Introduction

Lysophospholipids are simple phospholipids that are not only metabolites of membrane phospholipid synthesis, but often also bioactive signalling molecules. The most widely studied signalling lysophospholipids are lysophosphatidic acid (LPA) and sphingosine 1-phosphate (S1P), which both influence a diverse range of cellular processes, including proliferation, survival, adhesion, migration, morphogenesis and differentiation. As outlined in recent reviews, it has now been established that LPA and S1P play important roles in the immune [1–4], cardiovascular [5–9], nervous [7,10–12], reproductive [7,13–15], and respiratory [8,15–17] systems, as well as in cancer [18–22]. Here we add further support to the notion that the physiological and pathophysiological actions of lysophospholipids are yet to be fully realised, and highlight their emerging role in the stem cell/progenitor system.

2. Lysophospholipid metabolism and signalling

2.1. LPA metabolism

Several mechanisms exist for the formation and degradation of LPA (Fig. 1A). These pathways have been extensively reviewed previously [23,24], and thus will only be briefly described here.

Extracellular LPA can be derived from the action of secreted phospholipase A_1 and A_2 (PLA_1 and PLA_2) in deacylation of phosphatidic acid. The main source of extracellular LPA in serum and plasma, however, appears to be from the cleavage of lysophospholipids like lysophosphatidylcholine by lysophospholipase D (lysoPLD, also called

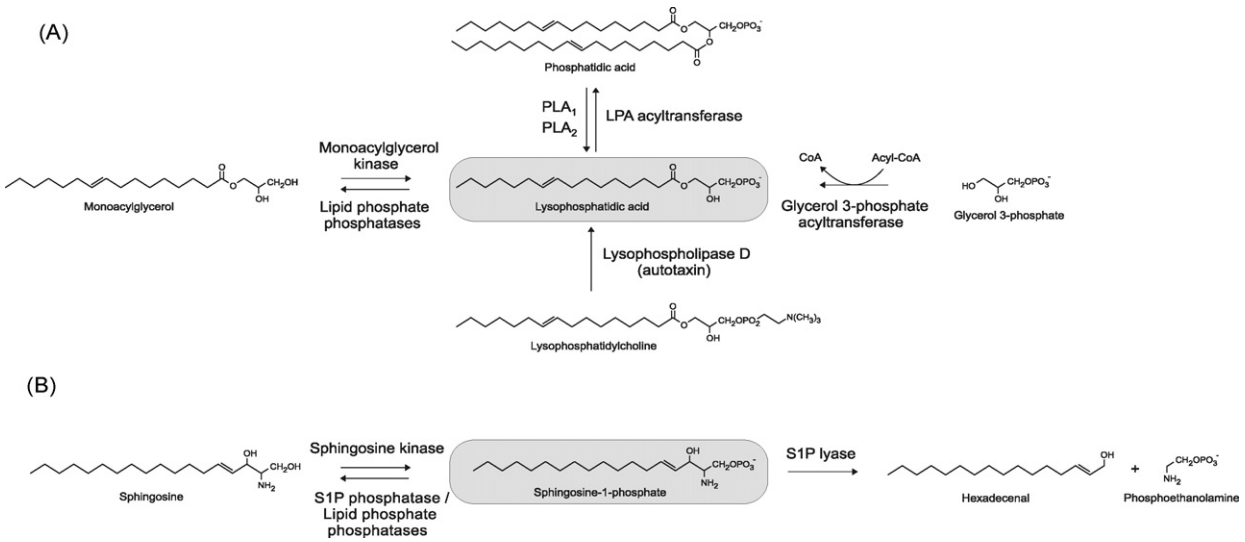

Fig. 1. Pathways of lysophosphatidic acid and sphingosine 1-phosphate metabolism. Key enzymes for the formation and degradation of LPA (A) and S1P (B) are shown.