

S08-2 Atherosclerosis and lysophospholipid receptors

○Fumikazu OKAJIMA¹

¹Gunma Univ., Inst. Mol. Cell. Reg.

Lysophospholipids, such as sphingosine 1-phosphate (S1P) and lysophosphatidic acid (LPA), play important roles in basic biological activities, including proliferation, motility, morphological change, and apoptosis. Five S1P receptors (S1P1-5) and five LPA receptors (LPA1-5) have been identified so far. Recent studies have shown that there are more candidates of LPA receptors. Lysophospholipids are carried by high-molecular weight substances, such as lipoproteins, in blood circulation. It is well known that the change in the plasma lipoprotein profiles is related to the risk of cardiovascular diseases, including atherosclerosis, probably due to the differential roles of lipoprotein species on cholesterol metabolism; low-density lipoprotein (LDL) supplies cholesterol into the cells and high-density lipoprotein (HDL) removes excess cholesterol from the cells. Recent studies, however, suggested that lipoproteins exert cholesterol metabolism-independent actions on the cardiovascular system through lipoprotein-associated lysophospholipids. For example, S1P is accumulated in HDL and mediates anti-atherogenic actions, including stimulation of survival, stimulation of migration, and inhibition of adhesion molecule expression in endothelial cells and, in contrast, LPA is present in LDL and oxidized LDL, and mediates pro-atherogenic actions, including stimulation of migration and proliferation of smooth muscle cells. The lysophospholipid receptors are widely expressed in various types of cells and organs in addition to the cardiovascular system. Lysophospholipids and their receptors, therefore, are potential molecular targets for not only cardiovascular diseases but also various types of diseases, including cancer.