Targeting lipid signalling in disease
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Lipids are important mediators in cancer and inflammation, and in cardiovascular, degenerative and metabolic disease. A complex protein-lipid interaction network comprising phosphoinositides, sphingolipids, steroids and other lipid-derived mediators has been uncovered over the past few years. Many of the signalling lipids may directly interact with intracellular effector proteins to trigger multiple protein kinase cascades, nuclear receptors, stimulate guanine nucleotide exchange factors and small GTPases, while others act extra-cellularly on GPCRs. These signals therefore control metabolism, growth, proliferation and cell migration. Here, we provide an overview of this protein-lipid signalling network, and how it can be exploited to attenuate proliferative, inflammatory and metabolic disease.

Abbreviations

Key:
- key like domain
- PF domain
- pI/PR domain
- X-Y-Met
- Phospho
- SGF domain
- C1 domain
- C1 domain
- Phosphatase
- Activation or antagonist
- Inhibition

Adipocyte differentiation
- FAAH, fatty acid amide hydrolase
- Prostaglandin D2 receptor
- EP2 receptor
- EP4 receptor
- FP receptor
- LPA receptor
- Leukotrienes
- prostanoid; TSC, tuberous sclerosis; VEGF, vascular endothelial growth factor.
- sphingomyelin; Sph, sphingosine; SphK, sphingosine kinase; TG, triacylglycerol; TPK, tyrosine kinase;
- receptor; S1P, sphingosine 1-phosphate; SERM, selective oestrogen receptor modulator, hetero.
- hormon.
- lipase A2; DAG, diacylglycerol; DD, death domain; DP, prostaglandin D2 receptor.
- 5-LO, 5-lipoxygenase; ALX, lipoxin A4 receptor; C1/2 domain, conserved small signalling domain.

Metabolic disease
- Key:
- migration of macrophages to adipose tissue
- extracellular lipid-modifying enzymes
- inflammation
- key like domain
- PF domain
- pI/PR domain
- X-Y-Met
- Phospho