The endocannabinoids anandamide and 2-AG are synthesized and released on demand in a paracrine fashion. NAPE needs arachidonic acid as a precursor and is cleaved by a phospholipase D (NAPE-PLD) into anandamide. The key enzyme in synthesizing 2-AG from diacylglycerol is diacylglycerol lipase. Anandamide and 2-AG primarily activate cannabinoid receptors (CB₁, CB₂), but anandamide could also act as a ligand for TRPV1 and GPR55. The existence of an endocannabinoid membrane transporter (EMT) is still controversial. The main enzyme in degrading anandamide is FAAH, whereas 2-AG is degraded by MAGL. EMT, GPR55 and TRPV1 are considered part of the endocannabinoid system. Abbreviations: 2-AG, 2-arachidonoylglycerol; CB, cannabinoid receptor; EMT, endocannabinoid membrane transporter; FAAH, fatty acid amide hydrolase; GPR55, G-protein coupled receptor 55; MAGL, monoacylglycerol lipase; NAPE, N-arachidonoyl phosphatidylethanolamine; NAPE-PLD, N-arachidonoyl phosphatidylethanolamine phospholipase D; TRPV1, transient receptor potential cation channel subfamily V member 1.


Figure 1 Scheme of the endocannabinoid system