

Superfamily	Family	Most studied family members	Molecular target(s)	Biosynthetic enzymes	Inactivating Enzyme	CNS cellular targets	Refs
Anandamide and its analogues	<i>N</i> -acyl-ethanolamines (anandamide and its congeners)	<i>N</i> -arachidonoyl-ethanolamine (anandamide)	↑CB ₁ , CB ₂ ↑TRPV1 ↓TRPM8 ↓Ca _v 3.3 ↑PPAR _γ	1) NAPE-PLD 2) ABHD4 +GDE1 (sequentially)	FAAH	Neurons Astrocytes Microglia Endothelium Neural stem cells	1-12
		<i>N</i> -oleoyl-ethanolamine	↑PPAR _α		FAAH, FAAH-2	Neurons	
		<i>N</i> -palmitoyl-ethanolamine	↑TRPV1 ↑GPR119 ↑GPR55		FAAH, NAAA	Neurons Microglia	
Other long chain fatty acid amides	Primary amides	Oleamide	↑5-HT _{2A,2C} ↓5-HT ₇ ↑GABA _A ↓Gap junctions	GLYAT + PAM (sequentially)	FAAH, FAAH-2	Neurons Astrocytes Microglia Endothelium	13-14
	Lipoaminoacids	<i>N</i> -arachidonoyl-glycine	↑GPR18 ↓Ca _v 3.2	GLYAT-L2	FAAH	Neurons Microglia	15-19
		<i>N</i> -arachidonoyl-serine	↓Ca _v 3.2 ↑GPR55?	?	?	Neural stem cells	
		<i>N</i> -arachidonoyl-taurine	↑TRPV1 ↑TRPV4 ↓Ca _v 3.2	?	FAAH	Neurons	
	Lipo-neurotransmitters	<i>N</i> -arachidonoyl-dopamine	↑TRPV1 ↓Ca _v 3.3 ↑CB ₁ ↓TRPM8 ↑PPAR _γ	FAAH	COMT	Neurons Astrocytes Endothelium	8, 15 20-22
		<i>N</i> -oleoyl-dopamine	↑TRPV1 ↓Ca _v 3.3 ↑GPR119			Neurons Endothelium	
		<i>N</i> -arachidonoyl-serotonin	↓Ca _v 3.3 ↓TRPV1 ↓FAAH	?	Cytochrome P4502U1	Neurons Astrocytes	
		<i>N</i> -oleoylserotonin	↑GPR119			?	
		<i>N</i> -arachidonoyl-GABA	↓Ca _v 3.3	?	?	Neurons	
	2-AG and its analogues	2-acyl-glycerols (2-AG and its congeners)	2-AG	↑CB ₁ =CB ₂ ↑GABA _A ↑TRPV1	PLCβ + DAGLα or DAGLβ (sequentially)	MAGL ABHD6 FAAH ABHD12	Neurons Astrocytes Microglia Endothelium Neural stem cells
2-linoleoyl-glycerol			↑GPR119			?	
2-acyl-glycerol ethers		2-arachidonoyl-glycerol ether (Noladin ether)	↑CB ₁ >>CB ₂	?	Esterification into phospholipids by unknown transacylases	Neurons	28
	<i>O</i> -acyl-glycerol esters	<i>O</i> -arachidonoyl-glycerol ester (Virodhamine)	↑↓CB ₂ >>CB ₁	Non enzymatically, from 2-AG?	FAAH?	?	29
Anandamide metabolites	COX-2-derived (Prostamides)	Prostamide F2α	Heterodimer between FP and its Alt4 splicing variant	COX-2 + prostaglandin F synthases	?	Dorsal horn neurons	30-32
	lipoxygenase-derived	15-hydroxy-anandamide	TRPV1	15-lipoxygenase + reductase	?	Dorsal horn neurons	33
2-AG metabolites	MAGL-derived	Prostaglandins (E ₂ , F _{2α})	EP1, EP2, EP3, EP4, FP	MAGL + COX-2 + prostaglandin synthases (sequentially)	15-Hydroxy-prostaglandin dehydrogenase; 15-keto-prostaglandin-Δ(13)-reductase	Neurons Astrocytes Microglia Endothelium	35-37
	COX-2-derived	Prostaglandin- E2 glycerol ester-	Unknown G _{q/11} -coupled receptor	COX-2 + prostaglandin E synthases	?	Striatal neurons Astrocytes?	30 31 34

Supplementary Table 1

The “endocannabinoidome”. Endocannabinoids, endocannabinoid-related mediators and their metabolic enzymes and receptors. Only molecular targets activated (\uparrow) or inhibited (\downarrow) at low μM concentrations (or lower) *in vitro* are shown. Abbreviations are defined in the main text, except for: COMT, catechol-O-methyl-transferase; FAAH-2; fatty acid amide hydrolase type-2; GLYAT, glycine

N-acyl-transferase; GLYATL2, GLYAT-like 2; GPR, orphan G-protein coupled receptor; NAAA, N-acylethanolamine acid amidase; PAM, peptidylglycine alpha-amidating monooxygenase; PPAR, peroxisome proliferator-activated nuclear receptor; TRPM8, transient receptor potential of melastatin type-8; TRPV4, transient receptor potential of vanilloid type-4.

References for Supplementary Table 1

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