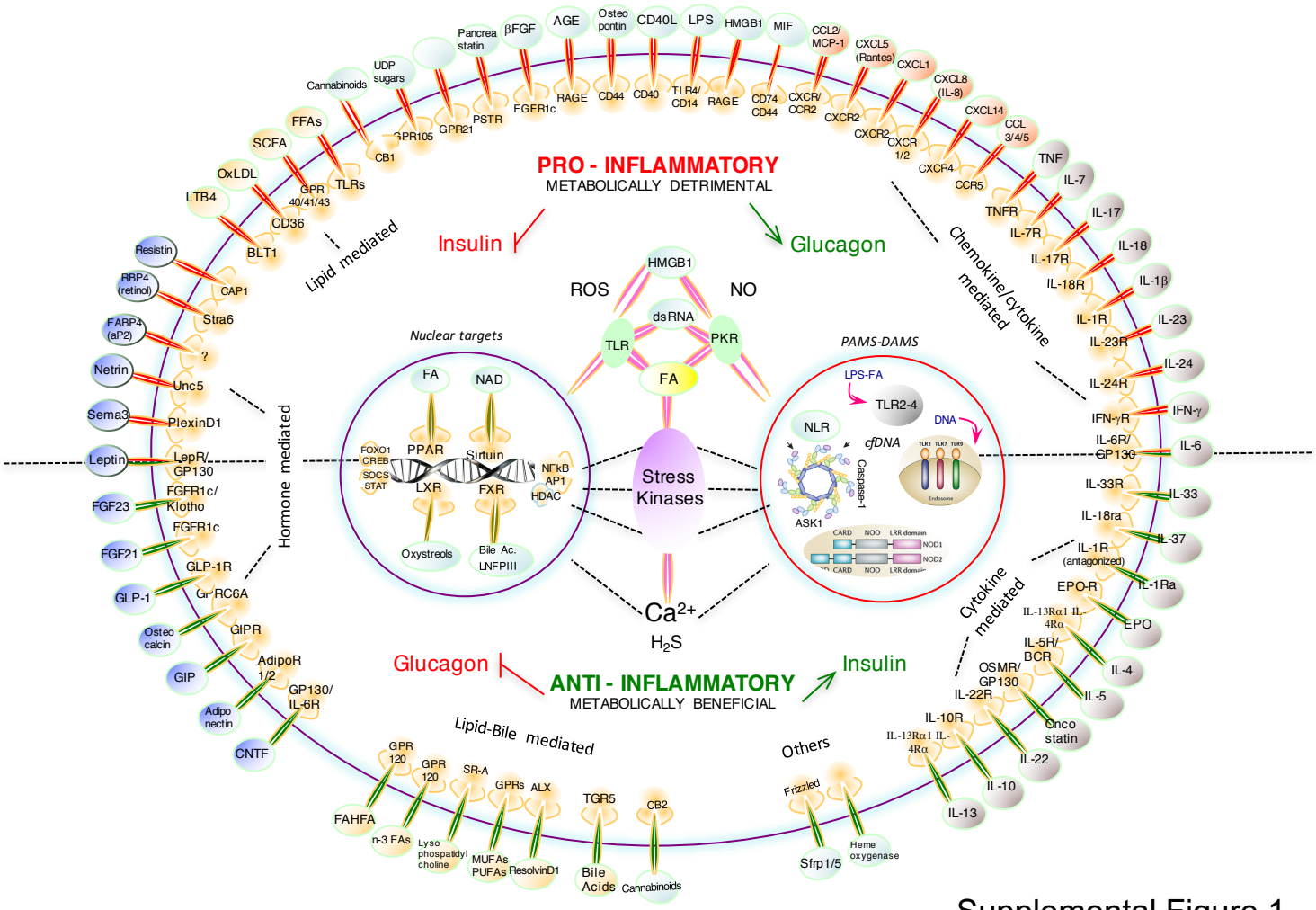

Supplemental Figure 1

Supplemental Figure 1. Immune signals and their receptors with described effects on metabolism. Many signals and receptor pairs have been implicated in metabolic inflammation, by activating stress kinase signaling, altering transcriptional programs, or conferring post-translational protein modifications. In general, pro-inflammatory signals block insulin signaling and promote glucagon action, whereas the anti-inflammatory signals result in the opposite. This scheme is provided only as a framework to explore the mediators of immunometabolic integration and it is well established that many other metabolic hormones and signaling pathways are also influenced by immune response. Intracellularly, all of these diverse signals converge on multiple stress kinases and involve signaling intermediates such as calcium, H_2S, ROS and NO. Inflammatory signals can also engage nuclear hormone receptors or inflammasome components to regulate metabolism. Blue= hormone, Yellow= lipid-related signal, Red= chemokine, Grey= cytokine.

Ligand	Receptor	Selected references
Adiponectin	Adiponectin Receptor (AdipoR1/2)	141-144
Advanced Glycation End Products (AGE)	Receptor for AGEs (RAGE)	145-147
Basic Fibroblast Growth Factor (bFGF)	Fibroblast Growth Factor Receptor 1c (FGFR1c)	148
Bile acids (e.g. cheno-deoxycholic acid, CDCA)	G protein coupled bile acid receptor (TGR5/GPBAR1)	149-153
Cannabinoids	Cannabinoid Receptor 1 (CB1R)	154, 155
Cannabinoids	CB2R	156-158
C-C motif chemokine ligand-2 (CCL2)/ Monocyte chemo-attractant protein-1 (MCP-1)	C-X-C chemokine receptor (CXCR)/ C-C chemokine receptor 2 (CCR2)	159-162
CCL3/4/5	CCR5	163
CD40 Ligand (CD40L)	Cluster of Differentiation 40 (CD40)	164-166
Ciliary Neurotrophic Factor (CNTF)	GP130/IL6R	167-171
C-X-C motif chemokine ligand 1 (CXCL1)	CXCR2	172
CXCL5 (RANTES)	CXCR2	172-174
CXCL14	CXCR4	175
Erythropoietin (EPO)	Erythropoietin receptor (EPO-R)/ Beta common receptor (BCR)	176-180
Fatty Acid Binding Protein 4 (FABP4/aP2)	?	181-184
Fatty acid hydroxyl fatty acid (FAHFA)	?	185
Free Fatty Acids (FFAs)	Toll Like Receptors (TLRs)	186-188
Fibroblast Growth Factor 21 (FGF21)	FGFR1c	189-195
FGF23	FGFR1c/Klotho	196,197
Gastric Inhibitor Peptide (GIP)	Gastric Inhibitory Peptide Receptor (GIPR)	198-203
Glucagon Like Peptide-1 (GLP-1)	Glucagon like peptide-1 receptor (GLP1R)	204,205
Heme oxygenase	?	206-210
High Mobility Group Box 1 (HMGB1)	RAGE	211
Interferon gamma (IFNγ)	Interferon gamma Receptor (IFNGR)	212-214
Interleukin 1beta (IL-1β)	Interleukin 1 receptor (IL-1R)	215-217

Interleukin 1 receptor antagonist (IL-1Ra)	IL-1R (antagonized)	218-220
IL-4	IL-4R	221-223
IL-5	IL5R/BCR	224
IL-6	IL-6R/ Glycoprotein 130 (GP130)	225-229
IL-7	IL-7R	230
IL-8/CXCL8	CXCR1/2	231, 232
IL-10	IL-10R	233-237
IL-13	IL-13Ra/IL-4R	238-240
IL-17	IL-17R	241-243
IL-18	IL-18R	244-246
IL-22	IL-22R	247-249
IL-23	IL-23R	247
IL-24	IL-24R	247
IL-33	IL-33R	250, 251
IL-37	IL-18Ra	252
Leptin	Leptin Receptor (LepR)	253-257
Lipopolysaccharide (LPS)	TLR4/CD14	258-261
Leukotriene B4 (LTB4)	Leukotriene B4 Receptor 1 (BLT1)	262, 263
Lysophosphatidylcholine	Scavenger Receptor A (SR-A)	264
Macrophage Migration Inhibitory Factor (MIF)	CD74/CD44	265-267
Mono/poly Unsaturated Fatty Acids (MUFAs/PUFAs)	G protein coupled receptor (GPRs)	268-272
Netrin	Uncoordinated 5 (Unc5)	273
Omega-3 fatty acids (n-3 fatty acids)	GPR120	274-277
Oncostatin	Oncostatin M receptor (OSMR)/ GP130	278-281
Osteocalcin	G Protein coupled receptor family C group 6 member A (GPRC6A)	282, 283
Osteopontin	CD44	284-287
Oxidized LDL (OxLDL)	CD36	288-291
Pancreastatin	Pancreastatin Receptor (PSTR)	292-294
Retinal Binding Protein 4 (RBP4) (retinol)	Stimulated by retinoic acid- 6 (STRA6)	295-297
Resistin	Adenyl cyclase associated protein 1 (CAP1)	298-300
ResolvinD1	Lipoxin A4 Receptor (ALX)	301, 302

Short Chain Fatty Acid (SCFA)	GPR40, 41, 43	268, 303-306
Semaphorin (Sema3)	PlexinD1	307
Sfrp1/5	Frizzled (antagonized)	308, 309
Tumor Necrosis Factor (TNF)	Tumor Necrosis Factor Receptor (TNFR)	310-323
UDP sugars	GPR105	324
?	GPR21	325, 326

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