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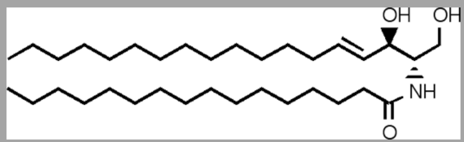
Supplementary information S2. Sphingolipid species and key cellular functions

Sphingolipid species	Function		Reference
Ceramide 	Cell death	↑C18-ceramide in chemotherapy-induced cell death in human head and neck squamous cell carcinomas (HNSCC)	(1,2)
		↑C16-ceramide via CerS activation induced by a variety of cell stressors Exogenous C16-ceramide ↑C16 and C24-ceramide in neutrophils	(3-15)
		↓C16-ceramide via CerS6 downregulation in human head and neck squamous cell carcinomas (HNSCC)	(16,17)
		↑C16-ceramide induced by acid ceramidase inhibition	(18,19)
		Exogenous C16-ceramide ASMase-dependent C16-ceramide generation	(20)
	Cell differentiation	↑Total ceramides	(21,22)
	Stimulation of cell migration/ invasion in cancer cell	↓C16-ceramide via downregulation of *LASS6* during epithelial-to-mesenchymal transition (EMT)	(23)
		↑Ceramides in arsenic trioxide (ATO) in hepatocarcinoma HCCLM3 cells	(24)
	Cell proliferation	↑C24 and C24:1-ceramide via overexpression of CerS2	(8,25)
	Cell cycle arrest	Exogenous C2- or C6-ceramides	(26-28)
	Senescence	↑Total ceramide Exogenous C8-ceramide	(29-31)
	Necrosis	↑Total ceramides	(32)

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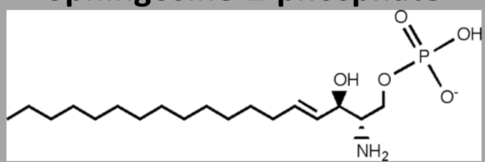
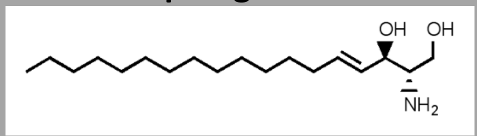
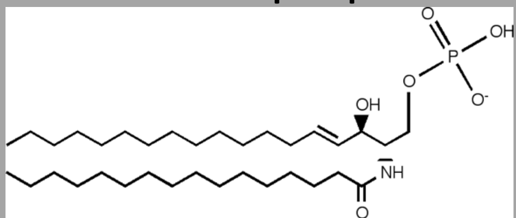
		Exogenous C2- or C6-ceramides	
	Necroptosis	Exogenous C16-ceramide	(33)
		↑C16-ceramide in TNFα-treated cells	(34-36)
	Autophagy	↑ceramide due to cell stressor Exogenous C2- or C6-ceramides and tamoxifen-treated cell	(37-39)
		↑C16-ceramide	(40,41)
	Mitophagy	↑C18-ceramide via CerS1 activity	(42)
	Cytoskeleton rearrangement	↑Total ceramides via activation of aSMase or exogenous bSMase	(43-46)
	Insulin resistance and cellular metabolism	↑Total ceramides in high fat diet HFD administration and/or palmitate treatment via CerS, nSMase or aSMase activity ↑C16-ceramide due to CerS6 upregulation upon HFD Exogenous C2- or C6-ceramides	(47-52)
Sphingosine-1-phosphate 	Cell survival	↑S1P	(13,53,54)
	Autophagy	Exogenous S1P ↑S1P via overexpression of SK1 during cell starvation	(55-58)
	Inflammation	↑S1P in TNFα-treated cells ↑S1P in S1P lyase-deficient mice ↑S1P via upregulation of SK1	(59-66)

	Cell migration and invasion	↑S1P via SK2 activation during EGF stimulation ↑S1P via overexpression of SK2 or ACER2 ↑S1P via SK1 mRNA and/or protein expressions in cancer cells Exogenous S1P	(67-71)
	Cytoskeleton rearrangement	↑S1P in bSMase/bCDase-treated HeLa cells ↑S1P in EGF-treated cells Exogenous S1P ↑Total ceramide via activation of aSMase in cisplatin-treated cells	(43-45,72)
Sphingosine 	Apoptosis	↑Sphingosine in cancer cells induced by environmental stress, chemotherapeutic treatment and apoptotic stimulus Exogenous sphingosine treatment ↑Sphingosine via SK inhibition	(73-79)
	Cell cycle arrest	↑Sphingosine during DNA damage ↑Sphingosine via upregulation of ACER2 Exogenous sphingosine	(79-81)
	Cell differentiation	↑Sphingosine via upregulation of haCER1 and ACDase in human epidermal keratinocytes Exogenous sphingosine	(22,82)
Ceramide-1-phosphate 	Cell migration	↑Ceramide-1-phosphate by upregulation of CerK Exogenous ceramide-1-phosphate treatment	(83-86)
	Cell proliferation	Exogenous ceramide-1-phosphate ↑Ceramide-1-phosphate in cells overexpressing CerK ↑Ceramide-1-phosphate production in cells culture in medium supplemented with FBS	(84,87,88)
	Inhibition of apoptosis	Exogenous ceramide-1-phosphate	(89-91)

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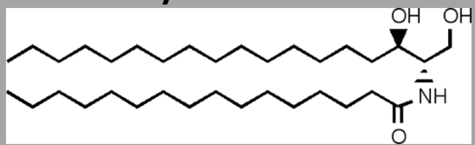
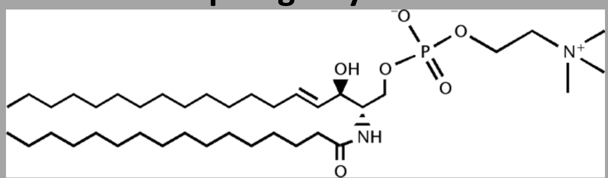
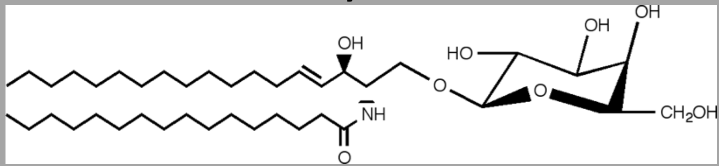
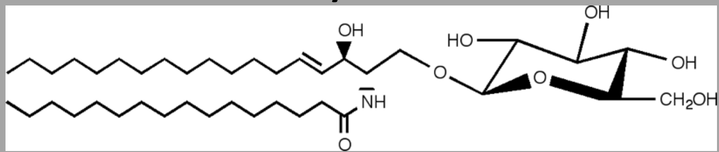
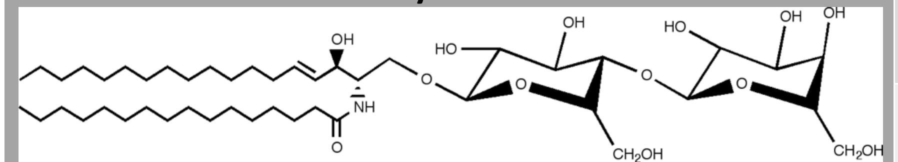
	Regulation of inflammation	Exogenous ceramide-1-phosphate ↑Ceramide-1-phosphate via CerK upregulation upon IL-1β or TNFα treatment, or stimulation of resting macrophages with macrophage-colony stimulating factor (M-CSF)	(92-99)
Dihydroceramide  	Cell cycle arrest	↑Total dihydroceramides via downregulation of DEGS1 gene	(100)
	Apoptosis	↑C16-dihydroceramide	(100,101)
		↑C16-dihydroceramide in fenretinide-treated cells	(102-104)
		↑C22 and C24-dihydroceramide in T-Cell acute lymphoblastic leukemia cell lines	(105)
	Inhibition of cell growth	↑C16-dihydroceramide induced by the sphingosine kinase 2 inhibitor ABC294640 in TRAMP-C2 cells	(106)
		↑Total dihydroceramides via downregulation of DEGS1 gene or DEGS2 or direct treatment with dihydroceramides	(107-109)
	Autophagy	↑Total dihydroceramides	(107,110, 111)
		↑C16-dihydroceramide in resveratrol-treated in human gastric cancer cell line HGC-27	(101)
Sphingomyelin  	Cell growth	↑Sphingomyelin via SMS1 overexpression Exogenous sphingomyelin ↑Sphingomyelin via basic fibroblast growth factor (bFGF)-dependent stimulation of SMS	(112-114)
	Cell adhesion	↑Sphingomyelin in cells treated with phorbol-ester stimulated cell adhesion ↓Sphingomyelin by nSMase treatment caused detachment	(115,116)

Galactosylceramide 	Inflammation	↑Galactosylceramides in GALC mutant mice Exogenous galactosylceramide treatment stimulates Natural Killer T (NKT) cell	(117-120)
	HIV-1 infection	Binding of human immunodeficiency virus type I (HIV-1) gp120 to galactosylceramide (GalCer) HIV-1 infection in CD4-/GalCer+	(121,122)
Glucosylceramide 	Multidrug resistance in cancer cells	↑Glucosylceramides via GCS overexpression in multiple multidrug-resistant (MDR) tumors and cancer cell lines	(123,124)
	Inflammation	↑Glucosylceramides caused by mutations in the GBA gene (Gaucher disease)	(125)
	Cell adhesion	↑Glucosylceramides via GCS overexpression ↑Glucosylceramides in cells treated with 12-O-tetradecanoylphorbol-13-acetate	(116,126,127)
	Cell differentiation	↑Glucosylceramides in cells treated with 12-O-tetradecanoylphorbol-13-acetate	(128,129)
Lactosylceramide 	Cell proliferation	↑Lactosylceramides due to upregulation of LCS activity	(130-132)
	Cell adhesion	↑Lactosylceramides due to upregulation of LCS activity Exogenous lactosylceramide treatment	(133-135)
	Angiogenesis	↑Lactosylceramides upon vascular endothelial growth factor (VEGF) treatment Exogenous lactosylceramide	(136,137)
	ROS generation	Exogenous lactosylceramide	(138,139)
	Inflammation	Exogenous lactosylceramide ↑Lactosylceramides via upregulation of LCS activity in lipopolysaccharide (LPS) and interferon-gamma (IFN-gamma) treated cells ↑Lactosylceramides upon cigarette smoke	(127,140,141)

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