Supplementary Methods

Untargeted metabolomics UPLC-MS^e method

A gradient mobile phase was used with a binary solvent system, which changed from 60% solvent A to 57% solvent A over 2 min, then to 50% solvent A at 2.1 min, then to 46% solvent A over 9.9 min, and then, after change to 30% at 12.1 min, to 1% solvent A over 5.9 min, then to 60% solvent A at 18.1 min and this was held for 2 min. The total run time was 20 min, and the flow rate was 0.4 mL/min. Solvent A consisted of acetonitrile/water(60/40) with 10 mM ammonium formate and 0.1% formic acid; solvent B consisted of isopropanol/acetonitrile (90/10) with 10 mM ammonium formate and 0.1% formic acid. The injection volume was 5 µL for negative mode and 2 µL for positive mode. Column temperature was kept at 55°C. The capillary voltage is 2 KV for positive mode and 1 KV for negative mode, cone voltage is 30 V, desolvation temperature, 550°C; desolvation gas flow, 900 L/h; source temperature, 120°C; mass acquisition range 50-1200 m/z.

Targeted UPLC-ESI-MS/MS method

Ganglioside GM3, GM1, and GD1 in cell samples were analyzed with the Waters Quattro (Premier) ultra HPLC system coupled to electrospray tandem mass spectrometry. The optimal signal for the ion pair of gangliosides was achieved in negative ion mode with the use of the following instrument settings: capillary voltage, 1.0 kV; extractor voltage, 1 V; radio frequency lens voltage, 0.2 V; entrance, −1; exit, 0; source temperature, 120°C; desolvation temperature, 400°C; desolvation gas flow, 600 L/h; and cone gas flow, 50 L/h. Cone voltage, collision energy, and ion dwell time were optimized for each isoflavone; helium was used as the collision gas. UPLC method was the same as used in untargeted metabolomics studies. Data were acquired and processed with Masslynx 4.1 software (Waters). Lactosylceramides and glucosylceramides with chain length C16-26 in cell samples were analyzed with the same Waters Quattro (Premier) ultra HPLC system coupled to electrospray tandem mass spectrometry. But the optimal signal for the ion pair of lactosylceramides and glucosylceramides was achieved in positive ion mode with instrument setting described above with necessary adjustment.

Ganglioside GD3 was quantified with the liquid chromatography system LC-20A (Shimadzu, Kyoto, Japan) coupled with 5500 QTrap mass spectrometry (ABI-SCIEX, Toronto, Canada) using multiple reaction monitoring (MRM). A Kinetex Phenyl-Hexyl (50× 4.6 mm, 2.6u, 100A) HPLC column (Phenomenex, Torres, CA) was used and typically 10 µL sample solution was injected. A gradient mobile phase was used with a binary solvent system, which changed from 40% solvent B to 100% solvent A over 6 min, then hold for 2 min, change to 40% solvent B over 1 min, and then this was held for 3 min. The total run time was 12 min, and the flow rate was 0.4 mL/min. Solvent A consisted of water with 10 mM ammonium formate; solvent B consisted of

acetonitrile. Because the available ganglioside standards only contain a portion of ceramide moiety lengths that detected in the cell extract, we adapted a theoretically expanded MRM approach in the quantification. Theoretical calculated precursor and fragment ions (SA ion as the major fragment ion for gangliosides due to its high intensity) were used to cover a larger range of carbohydrate structures.

Supplementary Table 1. Ganglioside compound transitions on UPLC-MS/MS.

Class	Ionization	Ceramide type	Precursor ion	Fragmentation ion	Cone (V)	Collision (V)
Ganglioside GM3	ESI-	(d34:1)	1151.1	290.2	100	60
		(d36:1)	1179.6	290.2	100	60
		(d38:1)	1207.7	290.2	100	60
		(d40:1)	1235.8	290.2	100	60
		(d42:1)	1263.8	290.2	100	60
		(d44:1)	1291.8	290.2	100	60
		(d34:0)	1153.7	290.2	100	60
		(d36:0)	1181.6	290.2	100	60
		(d38:0)	1209.6	290.2	100	60
		(d40:0)	1237.6	290.2	100	60
		(d42:0)	1265.6	290.2	100	60
		(d44:0)	1293.6	290.2	100	60
		(d34:2)	1149.7	290.1	100	60
		(d36:2)	1177.7	290.1	100	60
		(d38:2)	1205.7	290.1	100	60
		(d40:2)	1233.7	290.2	100	60
		(d42:2)	1261.7	290.1	100	60
		(d44:2)	1289.7	290.1	100	60
Ganglioside GM1	ESI-	(d34:1)	1517.0	290.2	100	60
		(d36:1)	1544.9	290.2	100	60
		(d38:1)	1573.0	290.2	100	60
		(d40:1)	1601.0	290.2	100	60
		(d42:1)	1629.0	290.2	100	60
		(d44:1)	1657.0	290.2	100	60
		(d34:0)	1519.0	290.2	100	60
		(d36:0)	1547.0	290.2	100	60
		(d38:0)	1575.0	290.2	100	60
		(d40:0)	1603.0	290.2	100	60
		(d42:0)	1631.0	290.2	100	60
		(d44:0)	1659.0	290.2	100	60
		(d34:2)	1515.0	290.2	100	60
		(d36:2)	1543.0	290.2	100	60
		(d38:2)	1571.0	290.2	100	60
		(d40:2)	1599.0	290.2	100	60
		(d42:2)	1627.0	290.2	100	60
		(d44:2)	1655.0	290.2	100	60

Class	Ionization	Ceramide type	Precursor ion	Fragmentation ion	Cone (V)	Collision (V)
Ganglioside GD1	ESI-	(d34:0)	904.4	290.2	40	45
		(d34:1)	903.4	290.1	40	45
		(d36:1)	917.4	290.1	40	45
		(d38:1)	931.4	290.2	40	45
		(d40:1)	945.4	290.2	40	45
		(d42:0)	960.4	290.1	40	45
		(d42:1)	959.4	290.1	40	45
		(d44:1)	904.4	290.2	40	45
Class	**Ionization**	**Ceramide type**	**Precursor ion**	**Fragmentation ion**	**DP (V)**	**Collision (V)**
Ganglioside GD3	ESI-	(d34:1)	720.99	290	70	40
		(d36:1)	734.91	290	70	40
		(d38:1)	748.93	290	70	40
		(d40:1)	762.94	290	70	40
		(d41:1)	769.81	290	70	40
		(d42:1)	775.95	290	70	40
		(d36:0)	735.92	290	70	40
		(d38:0)	749.94	290	70	40
		(d40:0)	763.95	290	70	40
		(d42:0)	777.97	290	70	40
		(d34:2)	719.89	290	70	40
		(d36:2)	733.91	290	70	40
Class	**Ionization**	**Ceramide type**	**Precursor ion**	**Fragmentation ion**	**Cone (V)**	**Collision (V)**
Lactosylceramide	ESI+	(d34:1)	862.7	264.3	25	30
		(d34:0)	864.7	264.3	25	25
		(d36:1)	890.7	264.3	25	28
		(d38:1)	918.7	264.3	25	28
		(d40:1)	946.7	264.3	25	30
		(d42:2)	972.8	264.3	25	30
		(d42:1)	974.8	264.3	25	30
		(d44:1)	1002.7	264.3	25	28
Glucosylceramide	ESI+	(d34:1)	700.6	264.4	25	30
		(d34:0)	702.6	264.4	25	30
		(d36:1)	728.8	264.4	25	30
		(d38:1)	756.9	264.4	25	30
		(d40:1)	785.1	264.4	25	30
		(d42:2)	808.8	264.4	25	30
		(d42:1)	810.8	264.4	25	23
		(d44:1)	838.8	264.4	25	30