

## Supplementary materials

### A New Mechanism for Ginsenoside Rb1 to Promote Glucose Uptake, Regulating Riboflavin Metabolism and Redox Homeostasis

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## Contents

Abbreviation List.....	2
Figure S1. <sup>1</sup> H NMR Spectrum of Ginsenoside Rb1 .....	3
Figure S2. <sup>13</sup> C NMR Spectrum of Ginsenoside Rb1 .....	4
Figure S3. HR ESI MS spectrum of Ginsenoside Rb1 .....	5
Figure S4. Fluorescence microscopy images of ROS production (A) and cell death (B) in DM Zebrafish larvae treated with different concentrations of GRb1 .....	6
Figure S5. Fluorescence microscopy images of ROS production ((A) and cell death (B) in diabetic Zebrafish larvae treated with different concentrations of riboflavin. ....	7
Table S1. Primer sequences of the tested genes .....	9
Table S2. Differential expressed metabolites .....	9

## **Abbreviations List**

2-NBDG, 2-Deoxy-2-[(7-nitro-2,1,3-benzoxadiazol-4-yl) amino]-D-glucose

AO, acridine orange

CAT, catalase

DCFH-DA, 2,7-Dichlorodihydrofluorescein diacetate

FAD, flavin adenine dinucleotide

FC, fold change

FMN, flavin mononucleotide

GRb1, ginsenoside Rb1

GSH, Glutathione

GSH-Px, glutathione peroxidase

GSSG, glutathione disulfide

hpf, hour post fertilization

IGT, impaired glucose tolerance

KEGG, Kyoto Encyclopedia of Genes and Genomes

MDA, malondialdehyde

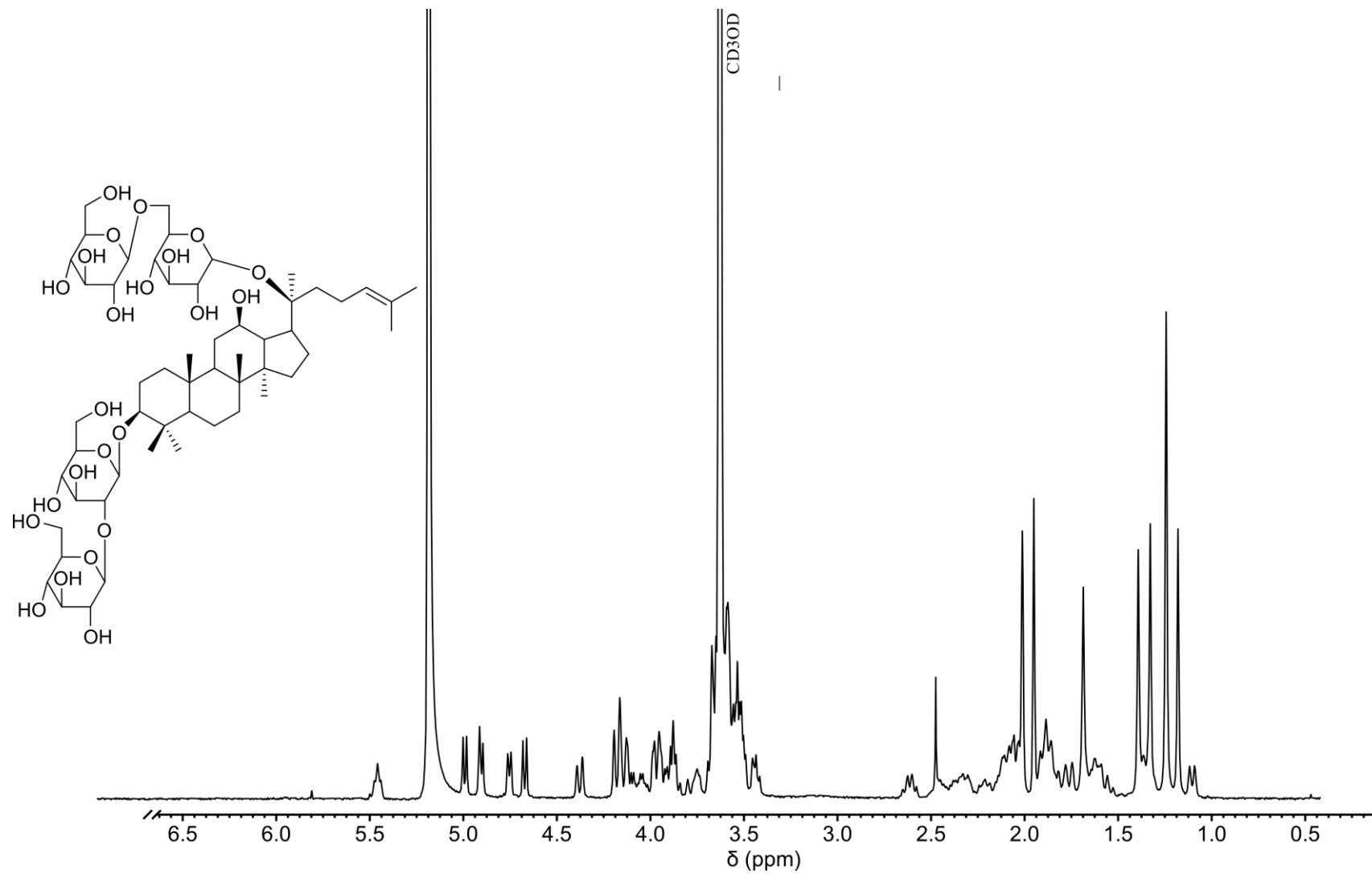
PCA, principal component analysis

PLS-DA, partial least squares discriminant analysis

PTU, N-Phenylthiourea

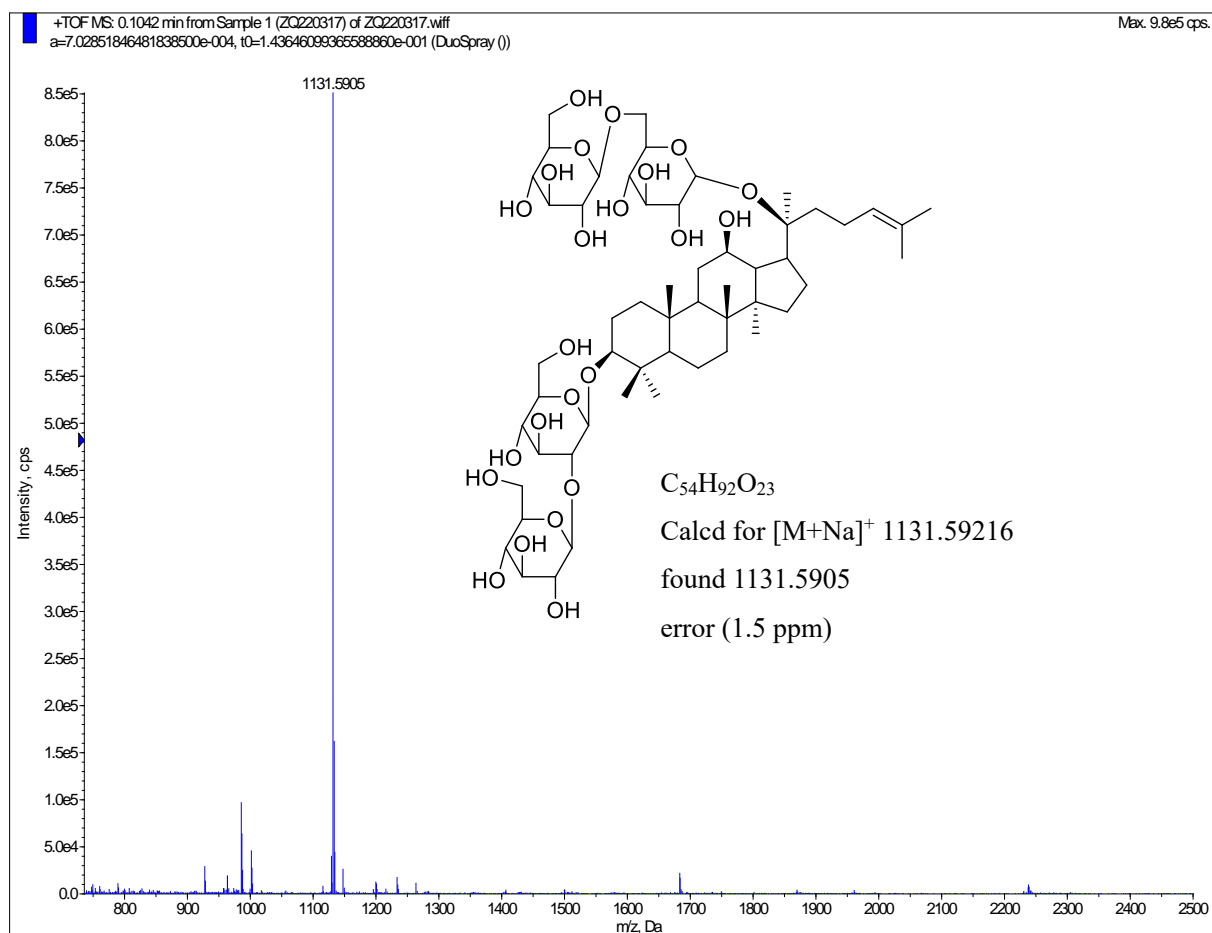
RFK, riboflavin kinase

RT-qPCR, real-time quantitative

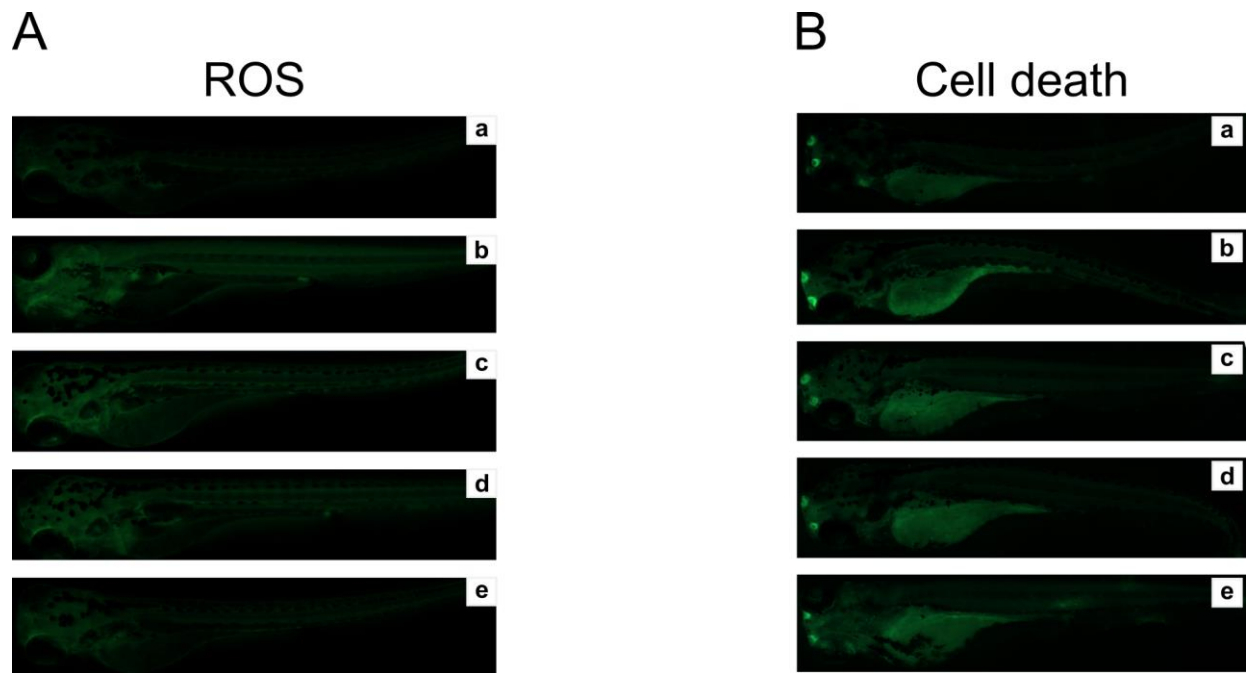


**Figure S1.**  $^1\text{H}$  NMR Spectrum of Ginsenoside Rb1

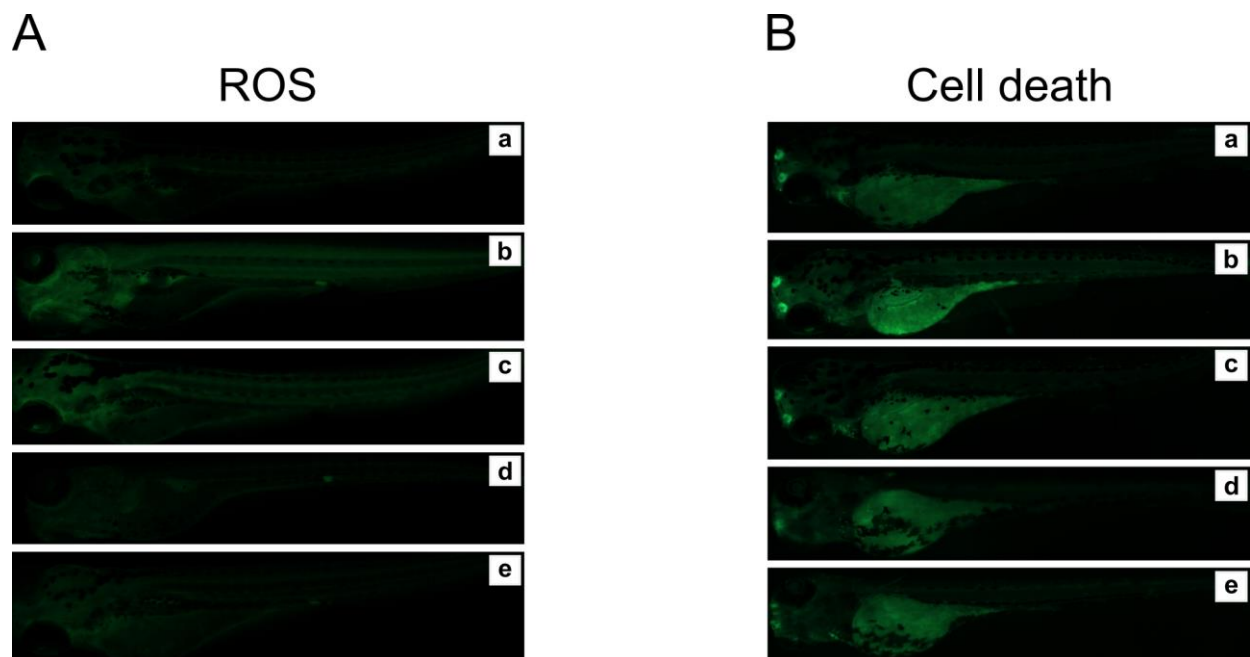




**Figure S3.** HR ESI MS spectrum of Ginsenoside Rb1



**Figure S4.** Fluorescence microscopy images of ROS production (A) and cell death (B) in DM Zebrafish larvae treated with different concentrations of GRb1. Control (a), model: 4% glucose + 0.2 mM alloxan (b), 20 µg/mL GRb1 (c), 60 µg/mL GRb1 (d), 100 µg/ mL GRb1 (e).



**Figure S5.** Fluorescence microscopy images of ROS production ((A) and cell death (B) in diabetic Zebrafish larvae treated with different concentrations of riboflavin. Control (a), model: 4% Glucose + 0.2 mM alloxan (b), 5  $\mu$ M riboflavin (c), 10  $\mu$ M riboflavin (d) and 20  $\mu$ M riboflavin (e).

**Table S1.** Primer sequences of the tested genes

<b>Gene</b>	<b>FP Sequence (5'-3')</b>	<b>RP Sequence (5'-3')</b>
<i>SLC52A1</i>	GAACGCTTTTACGTTGCGGT	GACCTGTCTCCAGTTACGCC
<i>SLC52A3a</i>	ATCTTTGGACAACCTCGTAGCACAG	GGCAGGAAGGTAACAGACGAAGTG
<i>SLC52A3b</i>	AGCGCTGCATTACTGTCACT	CCAAACCGCTGAGACCTTCT
<i>RFK</i>	GCATCTACTACGGTTGGGCA	TTCAGGGCGAATGTAGCCAG
<i><math>\beta</math>-actin</i>	F CGTGCTGTCTTCCCATCCA	TCACCAACGTAGCTGTCTTTCTG



**Table S2.** Differential expressed metabolites

KEGG ID	Metabolite name	Formula	RT/min	<i>m/z</i>	contrast
C00148	Proline	C <sub>5</sub> H <sub>9</sub> NO <sub>2</sub>	1.035	116.0693	G3 <i>vs.</i> G2, G4 <i>vs.</i> G2
C00408	L-Pipecolate	C <sub>6</sub> H <sub>11</sub> NO <sub>2</sub>	0.952	130.0853	G3 <i>vs.</i> G2, G4 <i>vs.</i> G2
C00047	Lysine	C <sub>6</sub> H <sub>14</sub> N <sub>2</sub> O <sub>2</sub>	0.948	147.1122	G3 <i>vs.</i> G2, G4 <i>vs.</i> G2
C09315	Umbelliferone	C <sub>9</sub> H <sub>6</sub> O <sub>3</sub>	6.988	163.0384	G3 <i>vs.</i> G2, G4 <i>vs.</i> G2
C01742	Palatinose	C <sub>12</sub> H <sub>22</sub> O <sub>11</sub>	6.520	360.1505	G3 <i>vs.</i> G2, G4 <i>vs.</i> G2
C10453	Eugenol	C <sub>10</sub> H <sub>12</sub> O <sub>2</sub>	4.932	165.0895	G3 <i>vs.</i> G2
C17957	Irigenin	C <sub>18</sub> H <sub>16</sub> O <sub>8</sub>	5.263	361.0858	G3 <i>vs.</i> G2
C00183	Valine	C <sub>5</sub> H <sub>11</sub> NO <sub>2</sub>	1.028	118.0853	G4 <i>vs.</i> G2
C01879	Pidolic acid	C <sub>5</sub> H <sub>7</sub> NO <sub>3</sub>	1.030	130.0490	G4 <i>vs.</i> G2
C00262	Hypoxanthine	C <sub>5</sub> H <sub>4</sub> N <sub>4</sub> O	1.418	137.0447	G4 <i>vs.</i> G2
C00064	Glutamine	C <sub>5</sub> H <sub>10</sub> N <sub>2</sub> O <sub>3</sub>	1.033	147.0765	G4 <i>vs.</i> G2
C00319	Sphing-4-enine	C <sub>18</sub> H <sub>37</sub> NO <sub>2</sub>	12.021	300.2901	G4 <i>vs.</i> G2
C00051	Glutathione	C <sub>10</sub> H <sub>17</sub> N <sub>3</sub> O <sub>6</sub> S	1.081	308.0891	G4 <i>vs.</i> G2
C00255	Riboflavin	C <sub>17</sub> H <sub>20</sub> N <sub>4</sub> O <sub>6</sub>	3.184	377.1455	G4 <i>vs.</i> G2