

Biomolecular proteomics discloses ATP synthase as main target of the natural glycoside deglucoruscin.

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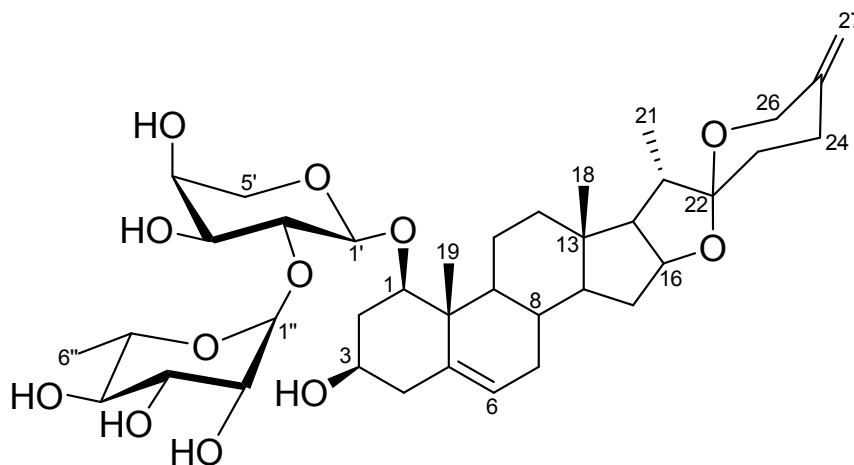


Table S1. ^1H and ^{13}C NMR data (CD_3OD , 400 and 100 MHz) of **DGR**

Position	$\delta_{\text{H}}^{\text{a}}$	$\delta_{\text{C}}^{\text{a}}$
1	3.35 ovl	84.6
2	1.67 ovl, 2.09 m	37.3
3	3.33 ovl	69.2
4	2.19 m, 2.25 ovl	43.5
5	-	139.6
6	5.55 br d (5.5)	125.9
7	1.52 ovl, 1.96 m	32.7
8	1.55 ovl	34.0
9	1.23 m	51.5
10	-	43.5
11	1.40 ovl, 2.55 ovl	24.8
12	1.22 m, 1.65 m	41.1
13	-	41.2
14	1.15 m	57.9
15	1.30 m, 1.98 m	32.9
16	4.43 m	82.5
17	1.74 ovl	64.1
18	0.82 s	17.1
19	1.09 s	15.3
20	1.90 m	42.9
21	0.94 d (6.9)	14.9
22	-	110.7
23	1.71 ovl	34.1
24	2.24 ovl, 2.53 ovl	29.5
25	-	145.2
26	3.82 d (11.8) 4.26 ovl	65.8
27	4.73 br s, 4.76 br s	108.9
$\alpha\text{-L-Ara}$		
1'	4.26 d (7.6)	101.0
2'	3.69 ovl	75.6
3'	3.63 dd (9.5, 3.0)	76.1
4'	3.74 ovl	70.8
5'	3.48 dd (12.0, 3.0) 3.85 dd (12.0, 2.0)	67.4
$\alpha\text{-L-Rha}$		
1''	5.28 br d (1.2)	101.6
2''	3.87 ovl	72.4
3''	3.68 ovl	72.1
4''	3.37 t (9.6)	74.2
5''	4.07 m	69.7
6''	1.24 d (6.1)	18.4

Ovl: overlapped signals; ^aCoupling constants are in parentheses and given in hertz.
 ^1H and ^{13}C assignments aided by COSY, HSQC and HMBC experiments.

Table S2: Proteins Identified as DGR partners in two different experiments. The list has been obtained comparing the proteins eluted from DGR modified resin and control matrix after cutting the entire gel lane in few slices .

Accession	Score	Mass	Matches	Match(sig)	Seq.	Seq(sig)	emPAI	Description
ACTB_HUMAN	1451	42052	66	61	10	8	1.73	Actin, cytoplasmic 1
TBB4B_HUMAN	1244	50255	58	55	10	10	2.18	Tubulin beta-4B chain
TBA1B_HUMAN	949	50804	43	35	10	9	1.55	Tubulin alpha-1B chain
ACTA_HUMAN	728	42381	29	24	8	6	1.11	Actin, aortic smooth muscle
TBA4A_HUMAN	587	50634	37	29	9	8	1.31	Tubulin alpha-4A chain
SERA_HUMAN	426	57356	13	12	6	6	0.74	D-3-phosphoglycerate dehydrogenase
ATPA_HUMAN	249	59828	8	8	3	3	0.3	ATP synthase subunit alpha, mitochondrial
EFTU_HUMAN	208	49852	6	5	3	3	0.37	Elongation factor Tu, mitochondrial
4F2_HUMAN	201	68180	5	3	3	2	0.17	4F2 cell-surface antigen heavy chain
AAAT_HUMAN	160	57018	9	5	3	2	0.2	Neutral amino acid transporter B(0)
BZW1_HUMAN	128	48184	9	6	5	4	0.55	Basic leucine zipper and W2 domain-containing protein 1
DCD_HUMAN	126	11391	5	4	2	2	1.49	Dermcidin
LAMP1_HUMAN	123	45367	4	4	1	1	0.12	Lysosome-associated membrane glycoprotein 1
KPYM_HUMAN	110	58470	6	4	4	3	0.31	Pyruvate kinase PKM
RSSA_HUMAN	107	32947	4	3	2	1	0.17	40S ribosomal protein SA
BASI_HUMAN	102	42573	4	4	1	1	0.13	Basigin
UGDH_HUMAN	90	55674	1	1	1	1	0.1	UDP-glucose 6-dehydrogenase
QCR1_HUMAN	75	53297	1	1	1	1	0.1	Cytochrome b-c1 complex subunit 1, mitochondrial
QCR2_HUMAN	74	48584	1	1	1	1	0.11	Cytochrome b-c1 complex subunit 2, mitochondrial
ACADV_HUMAN	67	70745	4	2	4	2	0.16	Very long-chain specific acyl-CoA dehydrogenase, mitochondrial
ECHB_HUMAN	65	51547	3	2	2	1	0.11	Trifunctional enzyme subunit beta, mitochondrial
HORN_HUMAN	56	283140	8	5	5	3	0.06	Hornerin
APMAP_HUMAN	55	46622	2	1	2	1	0.12	Adipocyte plasma membrane-associated protein
GPDM_HUMAN	52	81315	7	4	4	3	0.22	Glycerol-3-phosphate dehydrogenase, mitochondrial
ATPB_HUMAN	51	56525	2	1	2	1	0.1	ATP synthase subunit beta, mitochondrial

Accession	Score	Mass	Matches	Match(sig)	Seq.	Seq(sig)	emPAI	Description
TBB5_HUMAN	884	50095	30	29	11	10	2.21	Tubulin beta chain
TBA1B_HUMAN	818	50804	48	33	12	10	1.84	Tubulin alpha-1B chain
TBB4B_HUMAN	807	50255	29	27	11	10	2.19	Tubulin beta-4B chain
ATPB_HUMAN	559	56525	28	21	12	9	1.56	ATP synthase subunit beta, mitochondrial
ATPA_HUMAN	525	59828	29	21	10	9	1.22	ATP synthase subunit alpha, mitochondrial
TBA4A_HUMAN	358	50634	34	18	10	7	1.08	Tubulin alpha-4A chain
ARF1_HUMAN	249	20741	6	5	2	2	1.14	ADP-ribosylation factor 1
RS10L_HUMAN	223	20279	6	5	2	1	0.3	Putative 40S ribosomal protein S10-like
SRP54_HUMAN	206	55953	7	6	5	4	0.46	Signal recognition particle 54 kDa protein
EF1A1_HUMAN	195	50451	8	5	4	3	0.37	Elongation factor 1-alpha 1
ARF5_HUMAN	168	20631	7	5	2	2	1.15	ADP-ribosylation factor 5
RL12_HUMAN	100	17979	6	4	2	1	0.34	60S ribosomal protein L12
LYSC_HUMAN	82	16982	2	2	1	1	0.36	Lysozyme C
FSCN1_HUMAN	74	55123	10	4	5	2	0.21	Fascin
UGDH_HUMAN	72	55674	6	3	4	2	0.21	UDP-glucose 6-dehydrogenase
TCPB_HUMAN	67	57794	5	4	3	3	0.32	T-complex protein 1 subunit beta
BASI_HUMAN	64	42573	2	2	1	1	0.13	Basigin
MIF_HUMAN	61	12639	1	1	1	1	0.51	Macrophage migration inhibitory factor
SORCN_HUMAN	56	21947	4	3	2	2	0.62	Sorcin
ATPO_HUMAN	55	23377	5	3	3	3	0.97	ATP synthase subunit O, mitochondrial
TCPD_HUMAN	54	58401	3	2	3	2	0.2	T-complex protein 1 subunit delta
TRXR1_HUMAN	54	71832	1	1	1	1	0.08	Thioredoxin reductase 1, cytoplasmic
S10A7_HUMAN	51	11578	3	2	1	1	0.57	Protein S100-A7

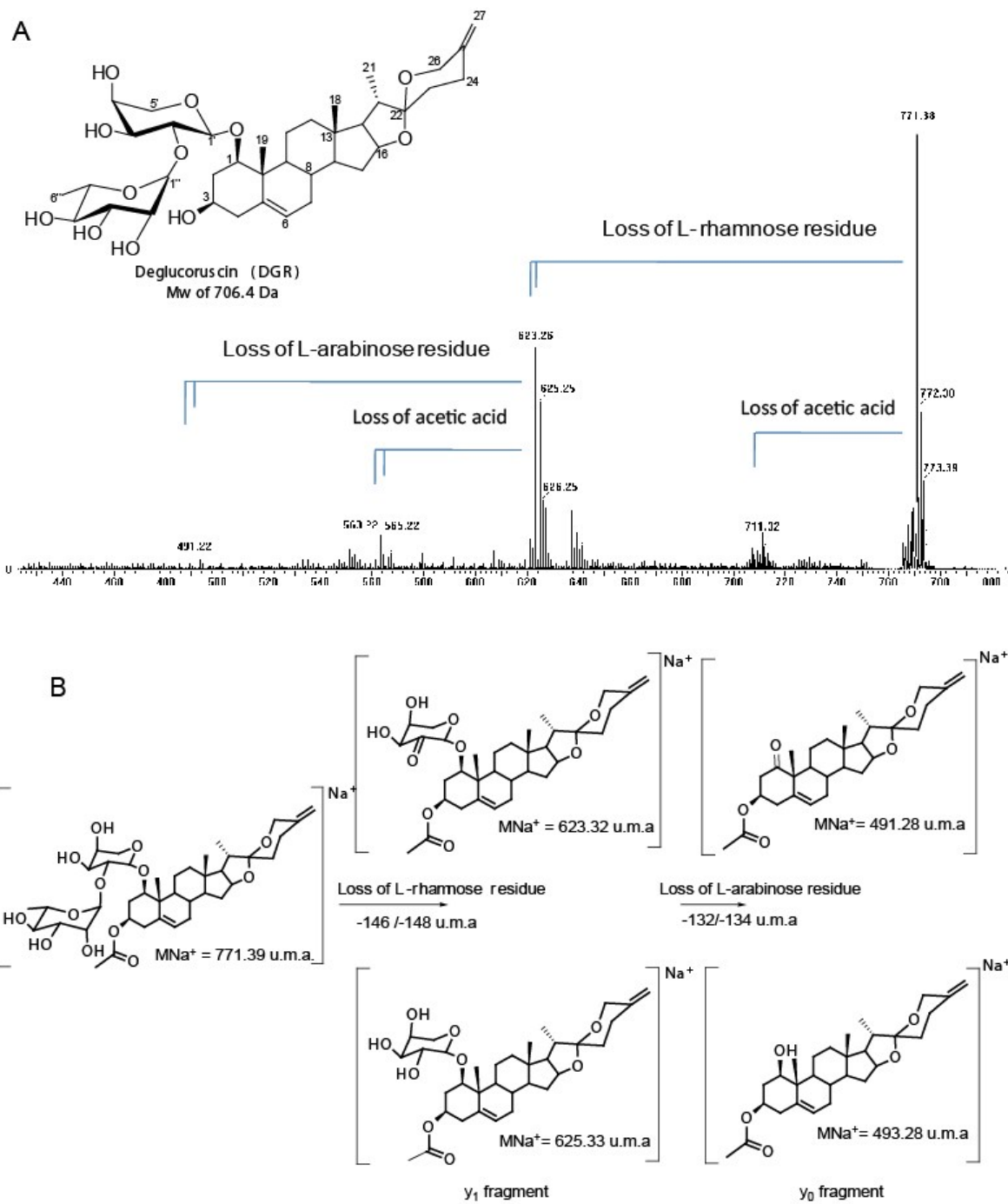


Figure S1: Panel A shows the MS/MS fragmentation of the acetylated DGR at m/z 771.4. Panel B shows the postulated fragmentation pattern based on the observed ion peaks, in accordance with Domon and Costello.

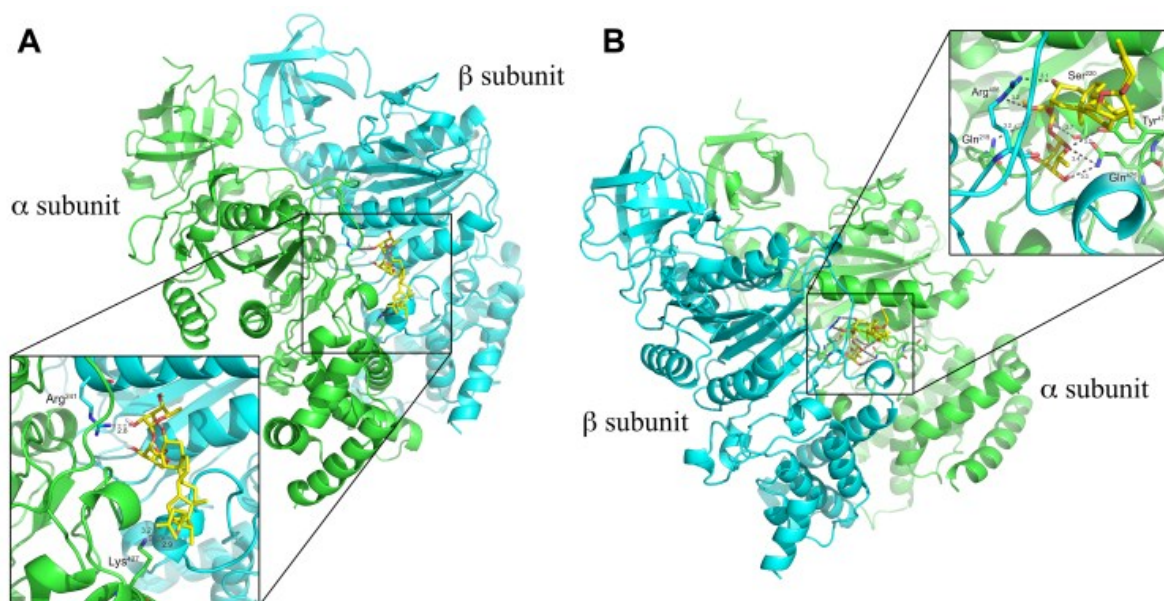


Figure S2: Molecular docking of DGR into the interface of tight binding subunits (A) and the interface of loose binding subunit (B). F1 subunits are shown as cartoons whereas the DGR is shown as sticks. In the boxes are reported amino acids involved in the H-bonds formation with the DGR.

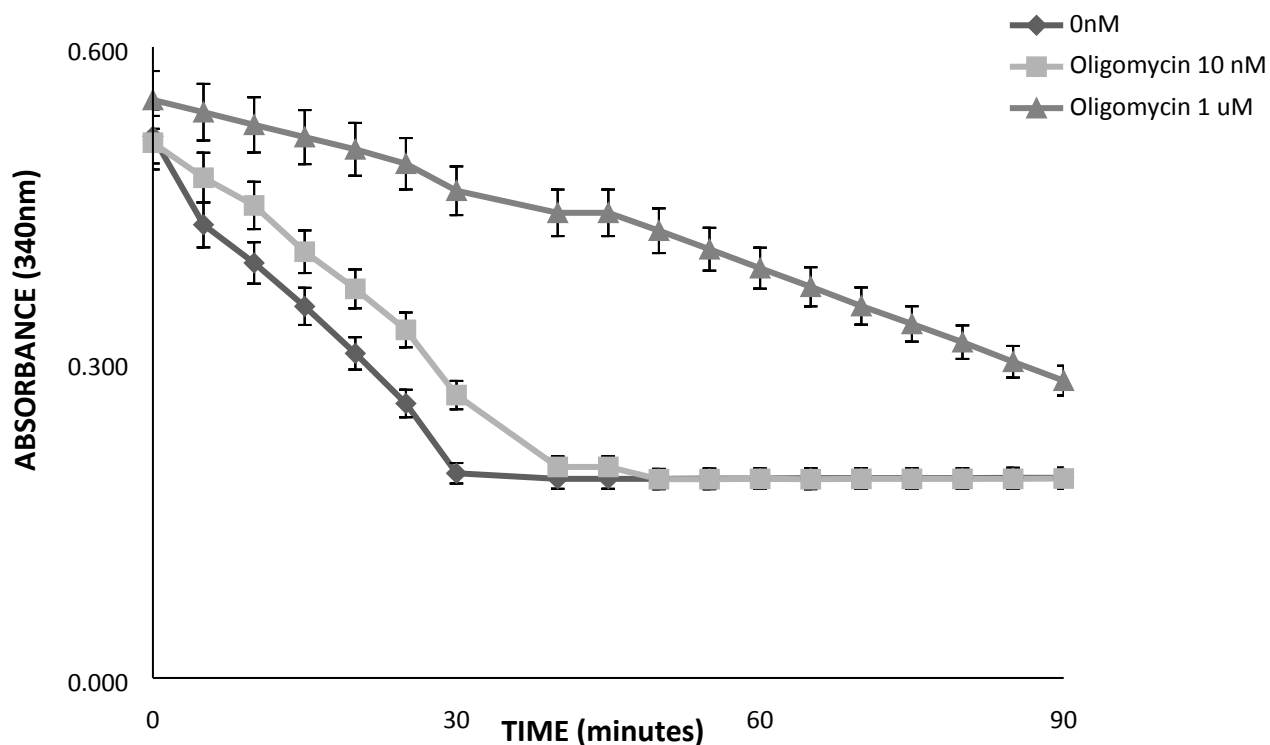


Figure S3: The ATP synthase inhibition by Oligomycin is reported measuring the intensity of the signal of NADH^+ at 340 nm during 90 min of reaction. The intensity of this signal is inversely proportional to the ATP synthase activity.