



Figure S1. Two dimensions proteome integral solubility alteration assay workflow for chemical target identification. Adapted from Lizano-Fallas et al., 2021.

Table S1. Database containing the information of each protein target (alternatives) for each criterion.

Protein name	Protein name abbreviation	Position in Ft (solubility alteration) ranking	Position in Fc p-value ranking	Number of diseases where it is involved	Number of reported negative effects on cells/organs when functionality is absent	Relevance of reported negative effects on cells/organs when functionality is absent	References	Number of pathways where it has participation	Relevance of pathways where it has participation	Number of functional and physical protein associations with other protein targets
General transcription factor 3C polypeptide 4	GTF3C4	1	1	0	0	NA	NA	1	Gene expression (Transcription): RNA Polymerase III Transcription	0
Protein FAM98B	FAM98B	2	7	0	0	NA	NA	1	Metabolism of RNA: tRNA processing in the nucleus	0
Heat shock protein beta-1	HSPB1	3	4	2	10	Charcot-Marie-Tooth axonal neuropathy; distal hereditary motor neuropathy; myopathy; reduced antioxidant capacity; decreased cell viability and increased the incidence of UVB-induced apoptosis; negative effect on cell growth in chinese hamster ovary cells; attenuated contractile force in human bladder smooth muscle cells; impact on calcium homeostasis and muscle energy	36-37, 46-53	4	Signal transduction: signaling by VEGF, extra-nuclear estrogen signaling and MAPK6/MAPK4 signaling; metabolism of ARN: regulation of mRNA stability by proteins that bind AU-rich elements	0

						metabolism; provokes an accumulation of GATA-1 and impairs terminal maturation in CD34+ human cells; ultrastructural abnormalities in the myofibrillar structure in mouse (e.g. destructured myofibrils and higher gaps between myofibrils)				
Ras-related protein Rab-1A	RAB1A	4	5	0	2	Synthetic lethal in a haploid human cell line (critical for the survival and/or growth of MDCK cells), Golgi stack and ribbon structures disruption, and endoplasmic reticulum (ER)-to- Golgi trafficking inhibition; perinuclear clustering of early endosomes and delayed transferrin recycling in MDCK cells	54-55	4	Vesicle-mediated transport: COPI- mediated anterograde transport, COPII- mediated vesicle transport and intra- Golgi and retrograde Golgi-to-ER traffic; metabolism of proteins: RAB geranylgeranylation	2
Myotrophin	MTPN	5	2	0	0	NA	NA	Protein not found in the sources	NA	1
Proteasome adapter and scaffold protein ECM29	KIAA0368	6	3	0	0	NA	NA	Protein not found in the sources	NA	1

Glyoxylate reductase/hydroxypyruvate reductase	GRHPR	7	8	1	1	Primary hyperoxaluria type II (PH2)	56	1	Metabolism of aminoacids and derivatives: glyoxylate metabolism and glycine degradation	0
Protein canopy homolog 3	CNPY3	8	6	1	1	Early-onset epileptic encephalopathies, including West syndrome	57	1	Immune system: trafficking and processing of endosomal TLR	0

Table S2. Pairwise comparison matrices for the alternatives at level 3 of the hierarchy for each criterion and the computed values of local priority vector, principal eigenvalue (λ_{\max}), consistency index (CI), random consistency index (RI), and consistency ratio (CR) for each matrix.

Position in Ft (solubility alteration) ranking	GTF3 C4	FAM9 8B	HSP B1	RAB1 A	MTP N	KIAA03 68	GRHP R	CNP Y3	Priori ty vector	Position in Fc p- value ranking	GTF3 C4	FAM9 8B	HSP B1	RAB1 A	MTP N	KIAA03 68	GRHP R	CNP Y3	Priori ty vector
GTF3C4	1	2	3	4	5	6	7	8	0.360	GTF3C4	1	7	4	5	2	3	8	6	0.502
FAM98B	1/2	1	2	3	4	5	6	7	0.259	FAM98B	1/7	1	1/4	1/3	1/6	1/5	2	1/2	0.073
HSPB1	1/3	1/2	1	2	3	4	5	6	0.188	HSPB1	1/4	4	1	2	1/3	1/2	5	3	0.247
RAB1A	1/4	1/3	1/2	1	2	3	4	5	0.135	RAB1A	1/5	3	1/2	1	1/4	1/3	4	2	0.183
MTPN	1/5	1/4	1/3	1/2	1	2	3	4	0.092	MTPN	1/2	6	3	4	1	2	7	5	0.400
KIAA0368	1/6	1/5	1/4	1/3	1/2	1	2	3	0.061	KIAA0368	1/3	5	2	3	1/2	1	6	4	0.318
GRHPR	1/7	1/6	1/5	1/4	1/3	1/2	1	2	0.039	GRHPR	1/8	1/2	1/5	1/4	1/7	1/6	1	1/3	0.041
CNPY3	1/8	1/7	1/6	1/5	1/4	1/3	1/2	1	0.026	CNPY3	1/6	2	1/3	2	1/5	1/4	3	1	0.134
λ_{\max} = 9.563										λ_{\max} = 8.551									
CI = 0.223										CI = 0.079									
RI = 1.41										RI = 1.41									
CR = 0.158										CR = 0.056									
Number of diseases where it is involved	GTF3 C4	FAM9 8B	HSP B1	RAB1 A	MTP N	KIAA03 68	GRHP R	CNP Y3	Priori ty vector	Number of reported negative effects on cells/organs/organ isms when functionality is absent	GTF3 C4	FAM9 8B	HSP B1	RAB1 A	MTP N	KIAA03 68	GRHP R	CNP Y3	Priori ty vector
GTF3C4	1	1	1/9	1	1	1	1/7	1/7	0.102	GTF3C4	1	1	1/9	1/5	1	1	1/3	1/3	0.100
FAM98B	1	1	1/9	1	1	1	1/7	1/7	0.102	FAM98B	1	1	1/9	1/5	1	1	1/3	1/3	0.100

HSPB1	9	9	1	9	9	9	5	5	0.968
RAB1A	1	1	1/9	1	1	1	1/7	1/7	0.102
MTPN	1	1	1/9	1	1	1	1/7	1/7	0.102
KIAA0368	1	1	1/9	1	1	1	1/7	1/7	0.102
GRHPR	7	7	1/5	7	7	7	1	1	0.708
CNPY3	7	7	1/5	7	7	7	1	1	0.708

$$\lambda_{\max} = 8.042 \quad CI = 0.006 \quad RI = 1.41 \quad CR = 0.004$$

HSPB1	9	9	1	7	9	9	8	8	0.853
RAB1A	5	5	1/7	1	5	5	3	3	0.369
MTPN	1	1	1/9	1/5	1	1	1/3	1/3	0.100
KIAA0368	1	1	1/9	1/5	1	1	1/3	1/3	0.173
GRHPR	3	3	1/8	1/3	3	3	1	1	0.297
CNPY3	3	3	1/8	1/3	3	3	1	1	0.297

$$\lambda_{\max} = 8.166 \quad CI = 0.024 \quad RI = 1.41 \quad CR = 0.017$$

Relevance of reported negative effects on cells/organs/organs when functionality is absent

Number of pathways where it has participation

	GTF3 C4	FAM9 8B	HSP B1	RAB1 A	MTP N	KIAA03 68	GRHP R	CNP Y3	Priori ty vector		GTF3 C4	FAM9 8B	HSP B1	RAB1 A	MTP N	KIAA03 68	GRHP R	CNP Y3	Priori ty vector
GTF3C4	1	1	1/9	1/5	1	1	1/9	1/9	0.097	GTF3C4	1	1	1/9	1/9	0	0	1	1	0.089
FAM98B	1	1	1/9	1/5	1	1	1/9	1/9	0.097	FAM98B	1	1	1/9	1/9	0	0	1	1	0.089
HSPB1	9	9	1	1/7	9	9	1	1	0.715	HSPB1	9	9	1	1	0	0	9	9	0.801
RAB1A	5	5	7	1	5	5	1/7	1/7	0.374	RAB1A	9	9	1	1	0	0	9	9	0.801
MTPN	1	1	1/9	1/5	1	1	1/9	1/9	0.097	MTPN	0	0	0	0	1	0	0	0	0.015
KIAA0368	1	1	1/9	1/5	1	1	1/9	1/9	0.097	KIAA0368	0	0	0	0	0	1	0	0	0.005
GRHPR	9	9	1	7	9	9	1	1	0.900	GRHPR	1	1	1/9	1/9	0	0	1	1	0.089
CNPY3	9	9	1	7	9	9	1	1	0.900	CNPY3	1	1	1/9	1/9	0	0	1	1	0.089

