

Table S22. GeneIndexer interrogation of RXFP3 ‘control’ interactome. Latent Semantic Indexing (LSI)-based informatic platform GeneIndexer (<https://geneindexer.com/>) is able to measure the degree of association of biomedical gene symbol identifiers of proteins with input interrogator concept terms through unbiased Cosine Similarity Score analysis. We cross-interrogated the obtained RXFP3 ‘control’ interactome dataset, with the following age-related syntactic concepts (Aging): *Neurodegeneration (ND)*, *Cognitive impairment (CI)*, *Senescence (S)*, *Parkinson’s Disease (PD)*, *Amyotrophic lateral sclerosis (ALS)*, *Alzheimer’s Disease (AD)*; and non-age-related terms (non-Aging): *Tuberculosis (TB)*, *Spina Bifida (SB)*, *Asthma (A)*, *Tourette syndrome (TS)*, *ADHD*, *Achondroplasia (AP)*. GeneIndexer extracts all gene-to-word relationships from the literature using LSI, which we then averaged per interrogator term and per interrogator group, *i.e.* ‘Aging’ vs. ‘non-Aging’. Here a cosine similarity score larger than 0.2 typically specifies an explicit association, while a score lower than 0.2 indicates an implied relationship, a cutoff score was set at 0.1.

| Gene | Aging | | | | | | Non-Aging | | | | | |
|------------------|-------|-------|-------|-------|-------|-------|-----------|-------|-------|-------|-------|-------|
| | ND | CI | AD | S | PD | ALS | TS | AP | A | ADHD | TB | SB |
| PHB | 0.150 | 0.118 | 0.146 | 0.203 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| PSMB6 | 0.138 | 0.000 | 0.107 | 0.000 | 0.156 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.169 | 0.000 |
| HNRNPA2B1 | 0.123 | 0.111 | 0.000 | 0.100 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| RXFP3 | 0.111 | 0.105 | 0.105 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| PSMAS5 | 0.200 | 0.150 | 0.272 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| RPL13A | 0.106 | 0.124 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.144 | 0.000 |
| RPL14 | 0.101 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| DNAJA1 | 0.221 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| RPL4 | 0.124 | 0.127 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| RPL21 | 0.000 | 0.159 | 0.106 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| RPL11 | 0.000 | 0.000 | 0.000 | 0.153 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| RPL23 | 0.000 | 0.000 | 0.000 | 0.103 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| MAP4 | 0.141 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| RPS26 | 0.131 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| RPL34 | 0.108 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| HSPA8 | 0.136 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 |
| TCP1 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.102 |
| RPLPO | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.000 | 0.173 |

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|--------------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|-------|--|
| | | | | | | | | | | | | |
| Average CSS | 0.099 | 0.050 | 0.041 | 0.031 | 0.009 | 0.000 | 0.000 | 0.000 | 0.000 | 0.017 | 0.015 | |
| Average CSS | 0.038 | | | | | | 0.005 | | | | | |