

**Cluster 1– mRNA/protein pairs both at high abundance:** Multiple genes known to have long-lasting proteins (*NUP205*, *NUP93*, *NUP107*, *NUP155*)<sup>1</sup> were present in cluster 1((**Figure 7**, red) and (**Supplementary Figure 6(a)**)). The scatterplots for pairs in this cluster (n = 855) show mRNA and protein at high abundance (**Figure 7(b)**-red). This cluster is enriched in genes with GO terms indicative of involvement in continuous cell processes and cell microenvironment maintenance. The members of this cluster predominantly support basic cell functionality such as transport and metabolic processes. Examples of enriched functionality include Golgi vesicle transport (FDR  $1.4e^{-9}$ ) and protein localization (FDR  $3.9e^{-15}$ ). Enrichment results are listed in **Supplementary folder 1**.

**Cluster 2 - Moderate to high transcript levels and limited protein production:** Cluster 2 pairs have a scagnostic pattern indicative of protein degradation or lack of protein but in presence of a relatively constant amount of mRNA (**Figure 7(a) and 7(b)**, blue). Protein abundance might be limited or negligible due to inhibited translation, rapid proteosomal degradation, or because the protein itself has a short life span. An example from this cluster is the *LOXL4* gene-protein pair (**Supplementary Figure 6(b)**)). The *LOXL4* mRNA has a half-life of 20.29 hours and a much shorter protein half-life of 2.45 hours<sup>2</sup>. This cluster (n = 830) contains groups of gene-protein pairs responsible for short-term, mitosis-related cell processes (regulation of cell cycle FDR  $8.1e^{-3}$ ). This cluster also contains the highest percentage (8%) across the scagnostics clusters of transcription factors identified using a consensus list<sup>3</sup>. Targeted proteosomal degradation is known to be a regulatory mechanism for mitotic cell cycle genes and transcription factors<sup>4</sup>. The enrichment results are listed in **Supplementary Folder 1**.

**Cluster 3 - Cell line-specific transcription and translation:** A small percentage of mRNA/protein pairs with both transcript and protein levels dependent on cell line are grouped in Cluster 3 (n = 125) (**Figure 7**, black). Employing a custom two-module extraction (detailed in **Supplementary Appendix 1 File**) enabled us to identify only the mRNA-protein pairs presenting possible cancer specificity by showcasing discordant high mRNA expression and protein abundance. The entire list (without pruning) of Cluster 3 members and information obtained after two-module extraction is provided in **Supplementary File 1**. Examples of genes in this cluster (after pruning) along with supporting literature evidence<sup>5-9</sup> are illustrated in **Supplementary Figure 6(c)**.

**Cluster 4 – Moderate to high transcript abundance and cell line-specific translation:** In Cluster 4, transcript levels are relatively similar across cell lines, but protein abundances are varied (**Figure 7(a)**, green). Examples from this cluster (n = 485) include the gene-protein pairs of HBS1L and POLD3 (**Supplementary Figure 6(d)**)). When analyzed with the data from the NCI-60 miRNA dataset, these two presented significant protein abundance to miRNA expression correlation with miRNAs hsa-mir-32 and hsa-mir-765 (Spearman correlation 0.618 and 0.429 respectively). These pairings can also be independently verified from existing experimental data included in the miRTarBase database<sup>10</sup> which list these genes as targets for the corresponding miRNAs. We hypothesize that genes in this cluster are likely regulated by miRNAs that selectively downregulate translation of certain genes in certain cell lines. We mapped highly expressing miRNAs in these subgroups, found by the mixture modeling and bi-clustering, to the genes/proteins in this cluster (without pruning) for which translation is selectively turned off, and we report these mappings in **Supplementary Folder 2**.

## References

1. Toyama BH, Savas JN, Park SK, et al. Identification of long-lived proteins reveals exceptional stability of essential cellular structures. *Cell*. 2013;154(5):971-982. doi:10.1016/j.cell.2013.07.037

2. Schwanhaussner B, Busse D, Li N, et al. Global quantification of mammalian gene expression control. *Nature*. 2011;473(7347):337-342. doi:10.1038/nature10098
3. Vaquerizas JM, Kummerfeld SK, Teichmann SA, Luscombe NM. A census of human transcription factors: function, expression and evolution. *Nat Rev Genet*. 2009;10(4):252-263. doi:10.1038/nrg2538
4. Desterro JMP, Rodriguez MS, Hay\* RT. Regulation of transcription factors by protein degradation. *Cell Mol Life Sci*. 2000;57(8):1207-1219. doi:10.1007/PL00000760
5. Sanchez-Aguilera A, Rattmann I, Drew DZ, et al. Involvement of RhoH GTPase in the development of B-cell chronic lymphocytic leukemia. *Leukemia*. 2010;24(1):97-104. doi:10.1038/leu.2009.217
6. Falkenius J, Lundeberg J, Johansson H, et al. High expression of glycolytic and pigment proteins is associated with worse clinical outcome in stage III melanoma. *Melanoma Res*. 2013;23(6):452-460. doi:10.1097/CMR.000000000000027
7. Wiestner A, Rosenwald A, Barry TS, et al. ZAP-70 expression identifies a chronic lymphocytic leukemia subtype with unmutated immunoglobulin genes, inferior clinical outcome, and distinct gene expression profile. *Blood*. 2003;101(12):4944-4951. doi:10.1182/blood
8. Toiyama Y, Inoue Y, Yasuda H, et al. DPEP1, expressed in the early stages of colon carcinogenesis, affects cancer cell invasiveness. *J Gastroenterol*. 2011;46(2):153-163. doi:10.1007/s00535-010-0318-1
9. Kohn KW, Zeeberg BM, Reinhold WC, Pommier Y. Gene expression correlations in human cancer cell lines define molecular interaction networks for epithelial phenotype. *PLoS One*. 2014;9(6). doi:10.1371/journal.pone.0099269
10. Hsu S Da, Lin FM, Wu WY, et al. MiRTarBase: A database curates experimentally validated microRNA-target interactions. *Nucleic Acids Res*. 2011;39(SUPPL. 1). doi:10.1093/nar/gkq1107