POLYSOME PROFILING REVEALS DIFFERENT MOLECULAR CLUSTERS AND A NEW TARGET SIGNATURE FOR GLIOBLASTOMA

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Background

Glioblastoma (GBM) is among the most aggressive and least responsive tumor types to therapies. At present, data on gene expression in these tumors is based on the total mRNA expression, however, this approach provides little information about the cellular proteome. In view of this, the population of mRNAs that are actively being translated (polysome associated mRNA) more faithfully reflects protein expression and is thus closer to the true measurement of gene expression. Our aim was to investigate gene expression profiles and establish molecular groups with relevant biological signatures from polysome associated mRNAs from 47 GBM samples patients (Research Ethics Committee 1775/13 and 1692/12).

Methods

Polysome associated mRNAs isolated from flash frozen tissue was isolated and identified by polysome profiling followed by RNA-seq. GO analysis were performed for the enrichment of the sequenced-RNA.

Results

Total and polysomal mRNA data from the same sample do not cluster together, being more different from each other, than from different samples.

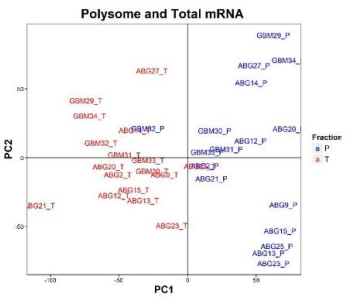
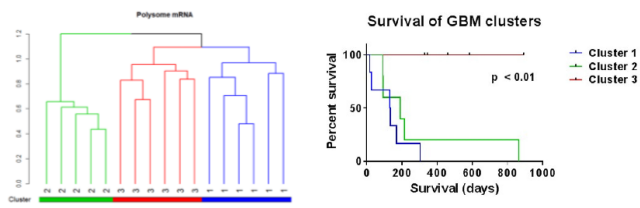


Figure 1. PCA plot of the glioblastoma samples. The graph shows the names of each sample. Principal component 1 separated total samples from polysomal samples.

Poly-mRNA data revealed a separation of the data into three groups with impact on survival (1, 2 and 3).

Figure 2. Clusters generated by the unsupervised analysis of the polysomal RNA data. The clusters are indicated by colors, according to the separation by PCA and survival relative to the clusters generated in the polysomal RNA analysis.



GO analyses confirm different biological processes for each of the groups.

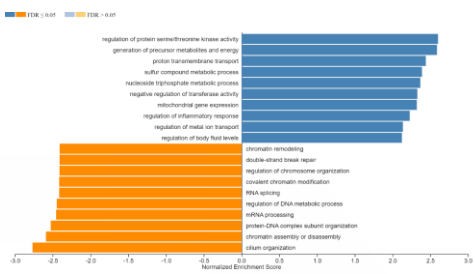


Figure 3. GO of the 1 x 2 + 3 group. The enriched and statistically significant biological processes of the group are represented in dark blue (FDR < 0.05).

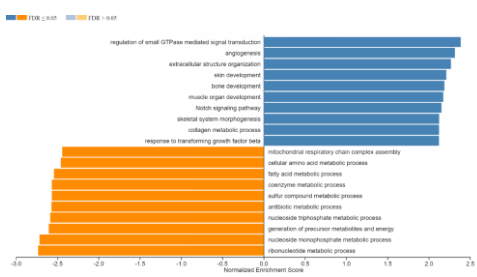


Figure 4. GO of the 3 x 2 + 1 group. The enriched and statistically significant biological processes of the group are represented in dark blue (FDR < 0.05).

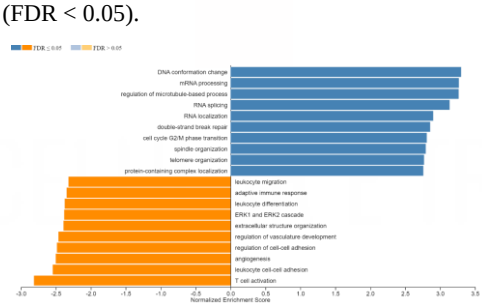


Figure 5. GO of the 2 x 1 + 3 group. The enriched and statistically significant biological processes of the group are represented in dark blue (FDR < 0.05).

Conclusions and Future Directions

- Differentially expressed genes include: *SPRY4, PDGFD, DUSP14, eIF6, RPUSD3 and MRPS18A*, increased in cluster MIT; *ARHGEF11, AGO2, SIPA1, STK11, VEGFA and NOTCH3*, increased in cluster ANG; and *DHX9, SMARCA5, SRPK2, KIAA1429, METTL14 and PCM1*, increased in cluster RNA.
- Our work a new molecular signature for GBMs, with potential to increase our knowledge of the disease and suggest new therapeutic approaches.

Support and Acknowledgements