Research Update from the MCM Team (February 2024)

Summary
We continue our work on characterising lung cancer biomarkers identified in the MCM1 project. This update focuses on a transcriptional corepressor TLE3.

Terminology

- **Transcription factor:** A protein that binds to DNA to control the rate at which DNA is transcribed to messenger RNA.
- **Transcriptional corepressor:** A protein that indirectly represses expression of genes by binding to transcription factors.
- **Sheehan's syndrome:** Postpartum anterior pituitary hormone deficiency due to necrosis of the pituitary gland. This is usually the result of massive hemorrhage during or after delivery.

Background

Identifying molecular markers and their combination (signatures) enables us to detect disease earlier (diagnostic signatures) and stratify patients into subgroups based on disease progression patterns (prognostic signatures), potentially leading to identifying which patients may benefit from what treatment (predictive signatures). The Mapping Cancer Markers project analyses data sets with millions of data points collected from patients with cancers and sarcomas to find such diagnostic, prognostic and predictive signatures.

Since November 2013, World Community Grid volunteers have donated over 887,100 CPU years to the project, helping analyse data on lung and ovarian cancer and sarcoma, much more thoroughly than otherwise possible. We are immensely grateful for this continued support.

Further characterising the 26 top-scoring genes in lung cancer, we have already discussed VAMP1, FARP1, GSDMB, ADH6, IL13RA1, and PCKSK5 in previous MCM updates. Here, we outline information on TLE3.

TLE3 Research
TLE3 encodes a protein called transducin-like enhancer protein 3, which is a transcriptional corepressor that binds to several transcription factors (Uniprot). TLE3 has been implicated in immune functions. Studies have suggested that TLE3 promotes memory B cell development[1] and is involved in the maintenance of intestinal immune homeostasis[2]. One study also found that TLE3 expression was significantly increased in patients with Sheehan's syndrome compared to controls[3].

TLE3 was found to have a protective role in lung cancer, in line with the genes we have previously presented (Figure 1).

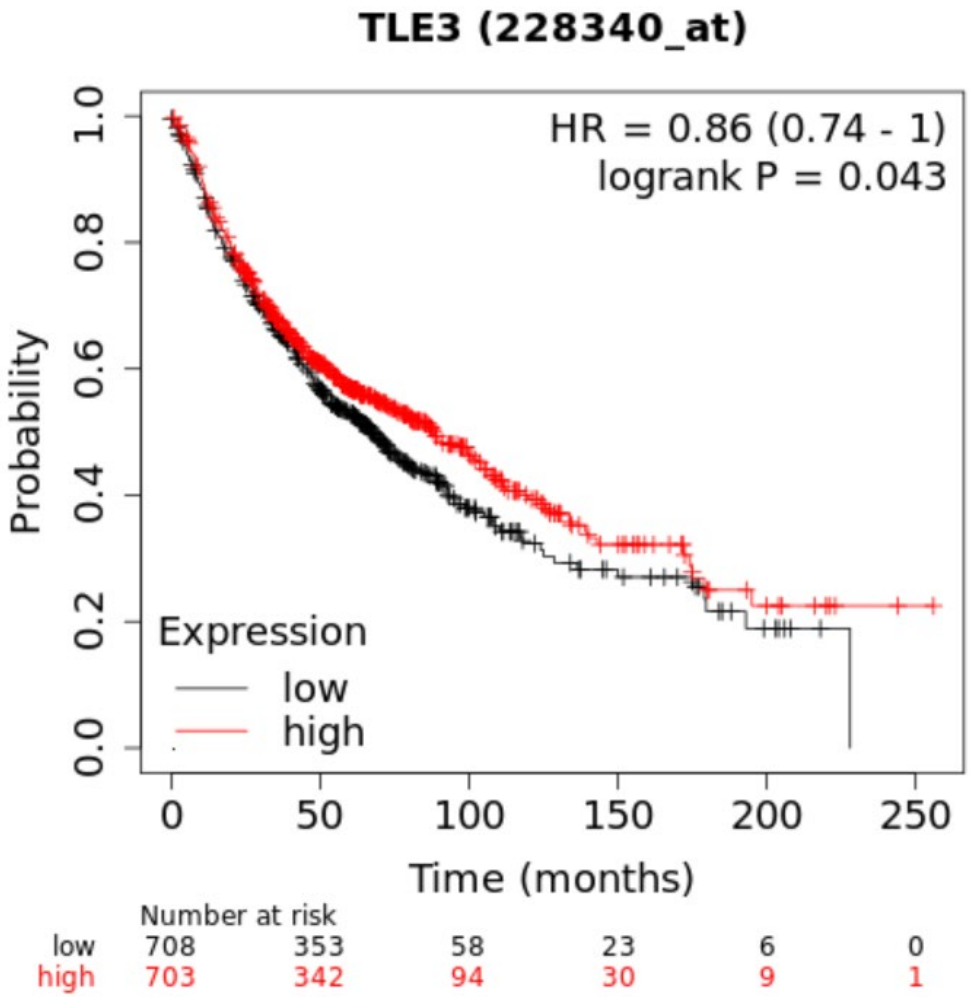

Figure 1. Survival curves for patients with high and low expression of TLE3 (KMplot).

This overall survival trend is even stronger for females, as depicted in Figure 2.

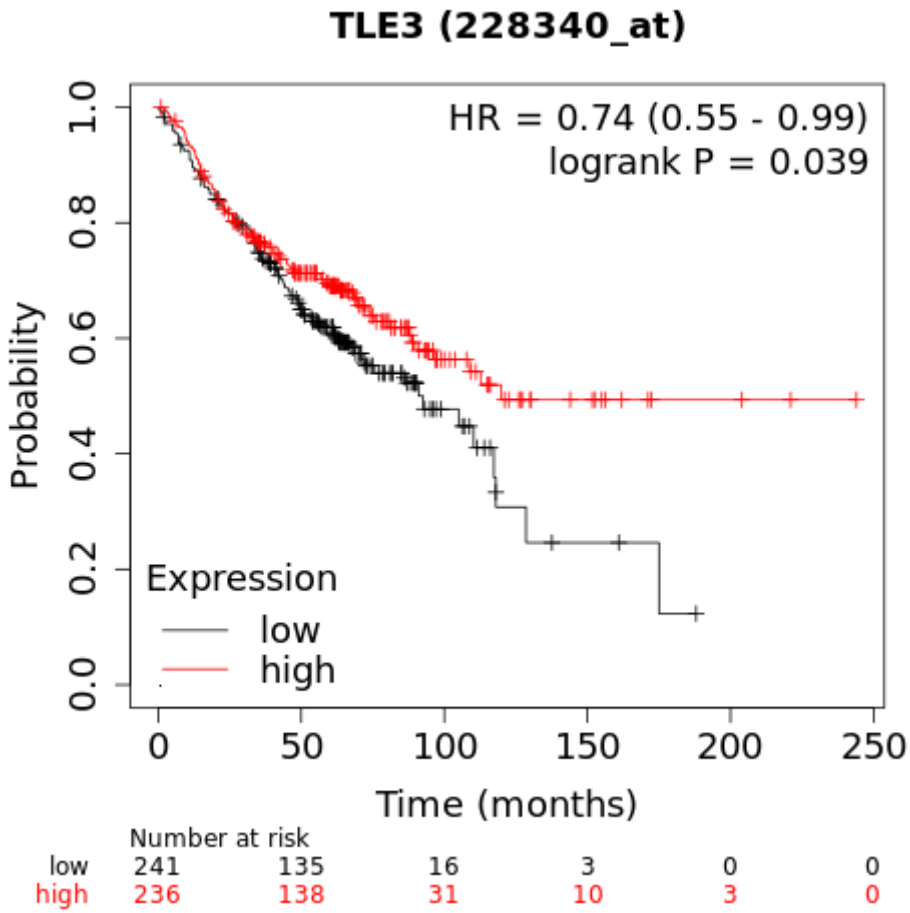

Figure 2. Survival curves for female lung cancer patients with high and low expression of TLE3 (KMplot).

We investigated further to see whether TLE3 expression was also associated with other cancers. As shown in Figure 3, comparing cancer to normal tissue, TLE3 is differentially expressed across most cancers (highlighted with red font). Within the literature, TLE3 expression has been associated with melanoma[4], rhabdomyosarcoma[5], ovarian cancer responsiveness to treatment[6], breast cancer prognosis[7] and responsiveness to treatment[8].

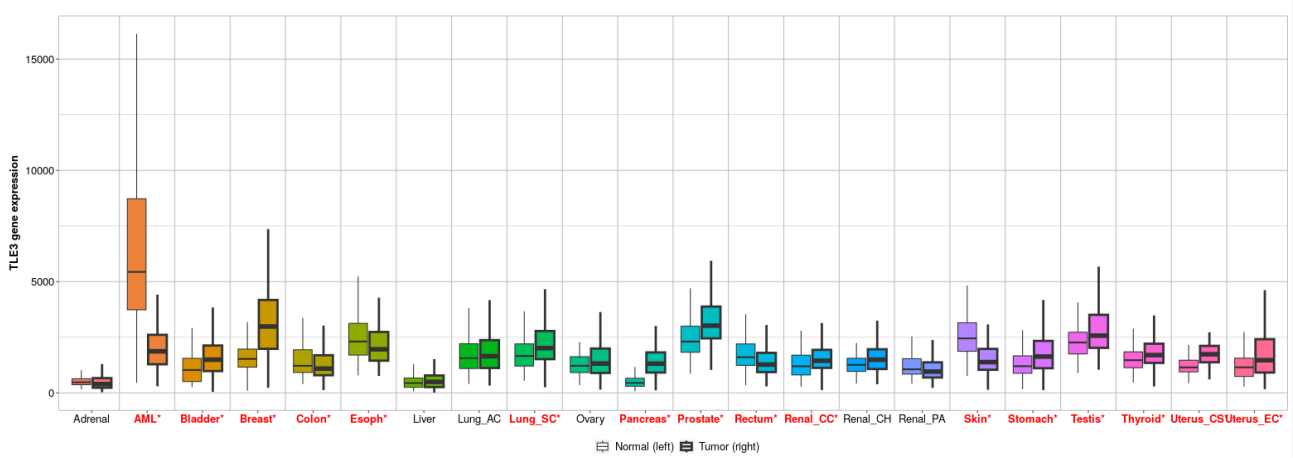

Figure 3. Expression of TLE3 in normal and cancer tissue for multiple cancer types. Red text represents a significant difference between expression in cancer tissue compared with normal tissue (TNMplot).

If you have any questions or comments, please leave them in this thread for us to answer!

WCG Team

References

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