Research update from the MCM team (April 2023)

Summary: The MCM team's research into lung cancer biomarkers has identified 26 genes that are present with top scores across all the signature sizes considered. This update focuses on a potential biomarker gene called FARP1, which is linked to lung cancer metastasis.

Background

The Mapping Cancer Markers project aims to identify the markers associated with various types of cancer with the goal to identify biomarkers to detect cancer earlier, identify high-risk patients and customize treatment for individual patients. To date, over 818,200 CPU years have been donated to the project by WCG volunteers across the world. Thank you all for your support.

In our previous MCM project update, we started to introduce putative lung cancer biomarkers that are present with top scores across all the signature sizes considered. The first update focused on VAMP1, a gene linked to patient survival and differentially expressed in normal lung compared to lung cancer. This update highlights a potential biomarker gene called FARP1, which is linked to metastatic development.

New developments

The protein FARP1 encodes is a guanine nucleotide exchange factor that plays a role in dendritic formation and growth. FARP1 can be found in cell membranes, cytoplasm, synapses and dendrites (Uniprot). Since both VAMP1 and FARP1 are involved with synapses, we investigated whether the two proteins interact together. While they do not interact directly (IID; Integrated Interaction Database) they share two interacting partners, RAB6A and APBA1. RAB6A plays a role in neuron projection development, while APBA1 regulates APP (Alzheimer's disease amyloid precursor protein), and is thought to have a role in the secretion of synaptic vesicles.

Neither RAB6A nor APBA1 are present in the top 99th percentile, but they suggest that there is indeed a neuronal signal associated with our two proteins of interest – VAMP1 and FARP1. The importance of this finding is related to the difficult-to-study connection between lung cancer and one of its most frequent sites of metastasis: the brain[1]. Moreover, it has been shown that FARP1 is one of the key drivers of migration and invasion in lung cancer[2].

We thus decided to investigate further the importance of this gene using external datasets. FARP1 is a potential diagnostic biomarker, similar to VAMP1, as highlighted in Figure 1. Furthermore, FARP1 is differentially expressed in metastatic samples, strengthening the connection between the molecular function of this protein and the phenotype it can help develop.
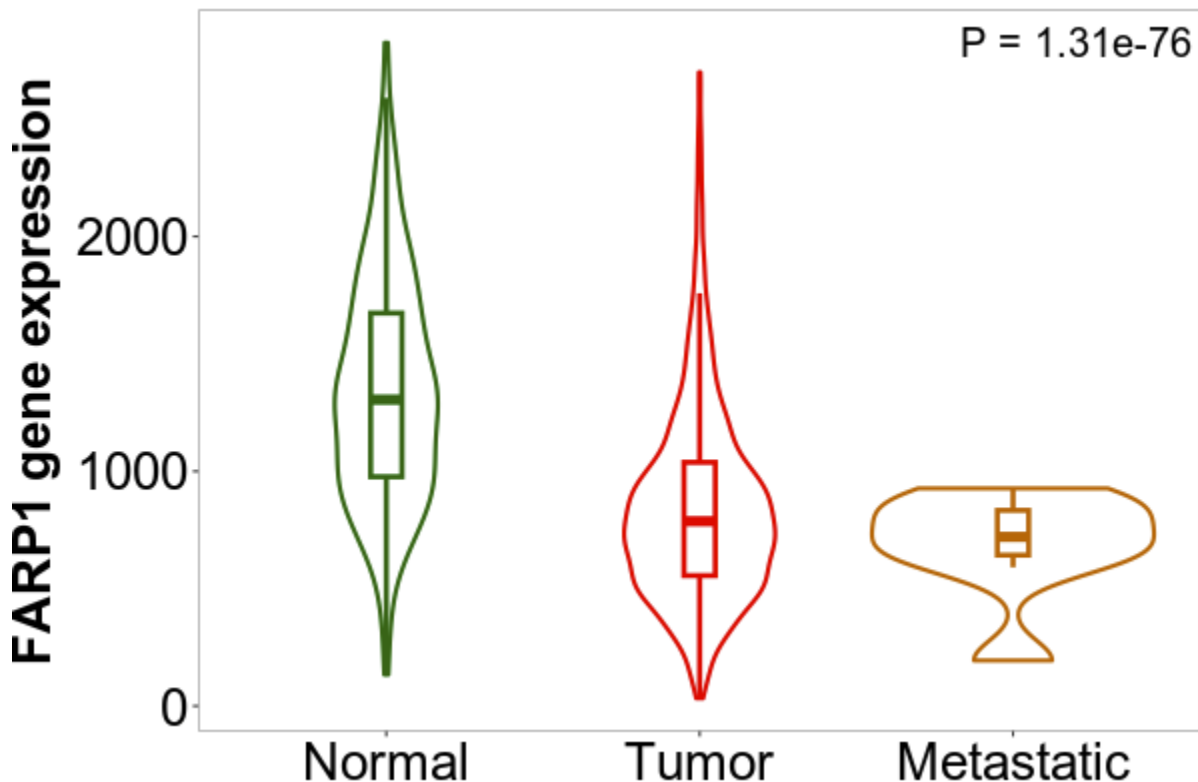
Figure 1. Expression of FARP1 in normal samples, lung cancer and metastatic samples.

cBioPortal shows that FARP1 is significantly linked to the patients' smoking status, and according to mirDIP, it is targeted by hsa-mir-105 (a microRNA specific to former smokers, similarly to VAMP1) and hsa-mir-150 (a microRNA specific to never smokers)[3]. The connection between smoking and lung cancer development is well established, but the molecular landscape behind such development is still not completely understood. Our signatures, derived from a dataset of patients with a history of smoking, can shed light on the molecular mechanisms and support researchers investigating the connection.

While we keep validating our results, we are excited about the impact our results can have on patient lives and research, computed by thousands of volunteers. Thank you for the contribution to this research.

WCG team

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