MCM team has been researching GSDMB (July 2023 update)

Summary: We continue our work on characterizing lung cancer biomarkers identified in the MCM1 project. This update focuses on GSDMB, a gene associated with lung cancer survival and differentially expressed across multiple cancer types compared to normal tissues.

Background

Recognizing patterns in cancer patients can have many benefits, such as making it possible to detect signs of cancer in other patients and personalizing each patient's treatment to fit their specific cancer profile. Since November 2013, World Community Grid volunteers have donated over 820,800 CPU to the project, helping analyze research data on cancers and sarcomas at a speed never thought possible before. We are immensely grateful for the volunteers who continue to donate to this project, and help us accelerate the search for better biomarkers.

We continue our analysis of the most common biomarkers amongst lung cancer patients. Following discussion of the genes VAMP1 and FARP1 that were described in our <u>March</u> and <u>April</u> updates, here we focus on GSDMB.

GSDMB research

Gasdermin B (GSDMB) is a protein in the GSDM family, which share similar structures and typically play roles in cell proliferation and differentiation^[1]. The GSDM family are known for their role in triggering pyroptosis, a highly inflammatory type of cell death, which they accomplish by forming pores in cell membranes^[1]. GSDMB has also been identified to regulate epithelial cell growth independently of its role in pyroptosis (<u>Uniprot</u>). GSDMB is considered unique among the other members of its family, and its role in various types of diseases and cancers is relatively under-studied. It has been shown that genetic variants in GSDMB are linked to increased susceptibility to diseases like asthma and inflammatory bowel disease (IBD)^[2].

Similarly to VAMP1 and FARP1 genes, we investigated the role of GSDMB in lung cancer, and found that its presence has a protective role in lung cancer, as shown in Figure 1 (data from <u>KMplotter</u>).



Figure 1. Survival curves for patients with high and low expression of GSDMB.

Extending our observation beyond lung cancer, as it is an aim of our WCG project, we find that GSDMB behaves in a similar way in the majority of tested cancers, as visible in Figure 2. This suggests that GSDMB has an important role in carcinogenesis, and may play a role in hallmarks of cancer. This has been confirmed in the literature, where an association between GSDMB expression levels and cancers such as gastric cancer, breast cancer^[3], and bladder cancer^[4].



Figure 2. Expression of GSDMB in normal and cancer tissues for multiple cancer types.

Using Human Protein Atlas (<u>HPA</u>), we also identified strong prognostic value of GSDMB protein, as shown in Figure 3.



Figure 3. Prognostic value of GSDMB protein in renal (unfavourable), urothelial and cervical cancers (favourable).

Exploring GSDMB expression using the GTEx portal (<u>GTEx</u>), we identify which cells in the lung express it, as shown in Figure 4.



Figure 4. Single cell data from the GTEx portal show strong expression both in epithelial cells and immune cells.

If you have any comments or questions, please leave them in this thread for us to answer. Thank you for your continued support.

WCG team

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