Title: Platelet transcriptome for early detection of kidney cancer

Abstract:
In renal cell carcinoma (RCC), the 7th most commonly diagnosed cancer in the U.S., time of diagnosis has a profound impact on survival. For stage I patients (localized non-invading tumor < 7 cm), the 5-year overall survival rate is 96%, compared to 23% for stage IV (metastatic) patients. There are currently no screening assays for RCC, hence it is often found incidentally and 30–40% of patients are still diagnosed with poor-prognosis, advanced (stage III or IV) RCC, which highlights the need for early detection and practical screening assays.

Once a small renal mass has been found by imaging, the treatment decision for surgery versus surveillance is made based on tumor features (histologic subtype, growth rate, tumor grade, which is a measure of tumor aggressiveness) and condition of the patient (age, comorbidities). However, information on tumor grade cannot be readily obtained through imaging or tumor biopsies, hence there is a need for a surrogate marker for tumor grade to aid in diagnosis and clinical management of small renal masses.

Platelets splice pre-mRNA deposited by megakaryocytes, which is the bone marrow cell type from which platelets are derived, splice it into mature mRNA, and translate it into protein. While the platelet transcriptome is remarkably stable over time in healthy individuals, platelets have been shown to respond to various disease states, including cardiovascular and autoimmune disease, and more recently, cancer, with likely disease-specific changes in the platelet transcriptome. However, platelet transcriptomic changes have never been specifically investigated in RCC or in early stage cancer or in high-grade tumors.

Hypothesis:
In this pilot biomarker discovery study, we use bulk platelet RNA sequencing to test the hypothesis that the platelet compartment responds to the presence of early stage RCC and/or aggressive RCC biology (i.e. high tumor grade) with specific changes in the platelet transcriptome.

Input Needs:
We would like to get feedback on the current data analysis strategy and come up with a consensus which results support our hypothesis. Furthermore, we need input on how to use the quantitative information from this pilot study to plan a validation study.

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