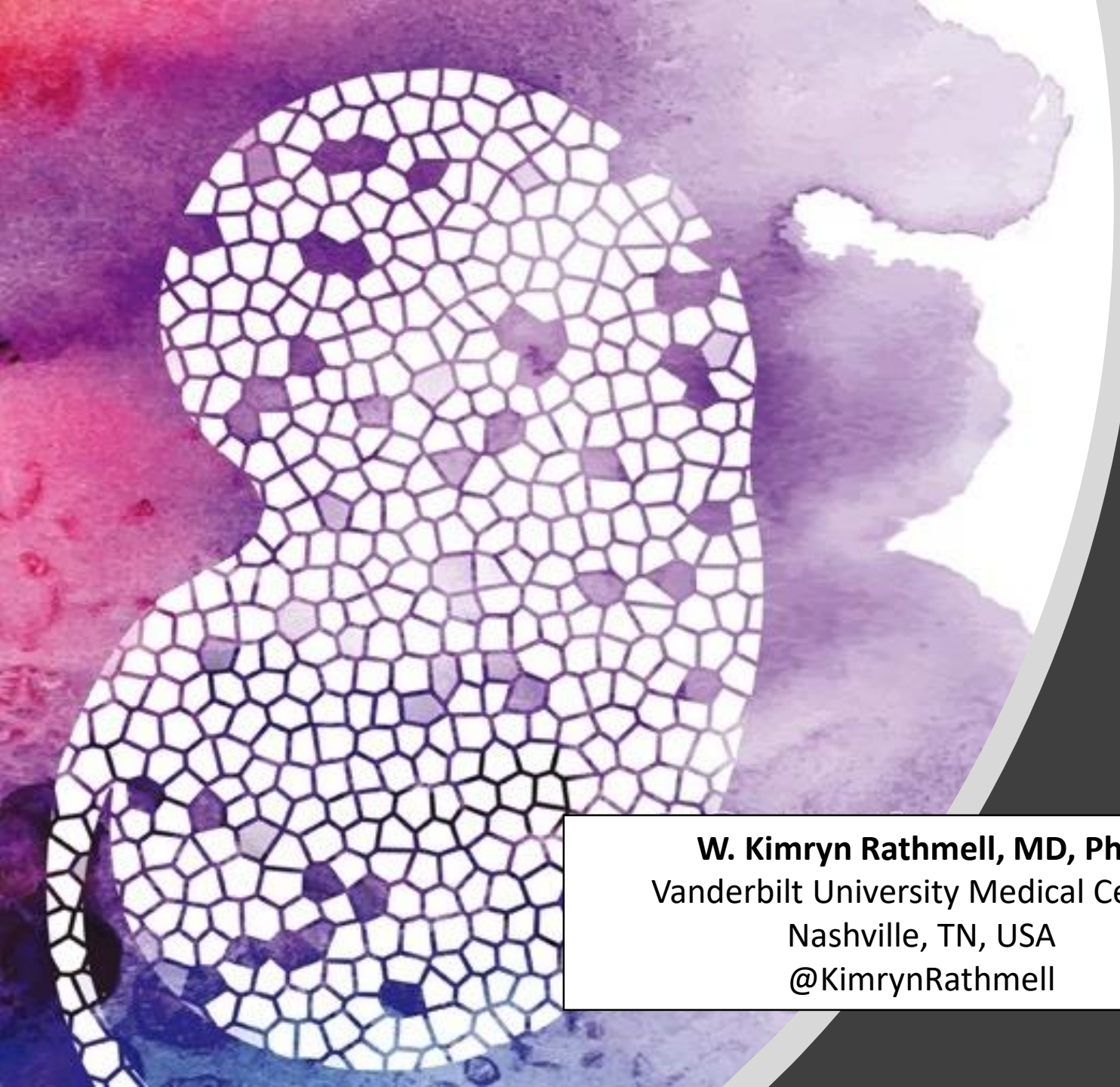




Novel surrogate biomarkers for immune therapy response and resistance

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Conflict of Interest Disclosures

I hereby declare: That I do not conduct activities that would involve a conflict of interest with CME-accreditable training, but that in the past 2 (two) years I have received the funding listed below from the following sources:

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Tissue

- Circulating
- Tumor heterogeneity
- Metastatic site
- Host immune capability
- Dormancy niche



What are we looking for in (an ideal) surrogate?

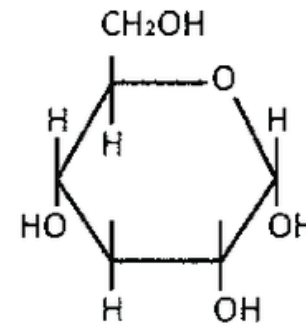
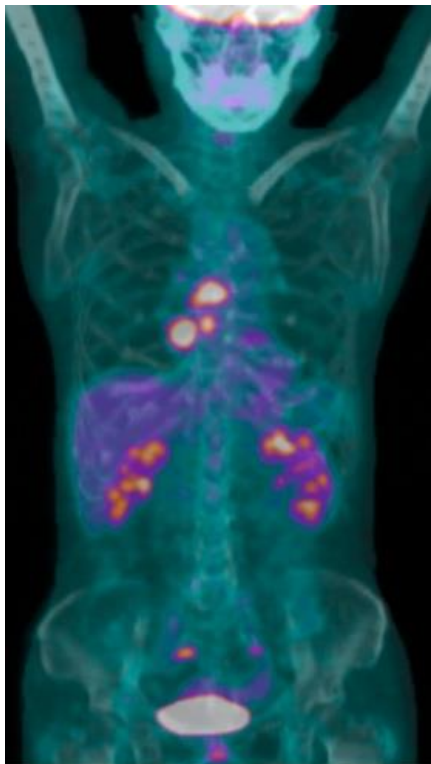
- Informative of the holistic disease “state”
- Accessible repeatedly and using a minimally invasive modality
- Defines host immune response
- Reliable estimate of tumor response
- Guides treatment choices through successive treatments



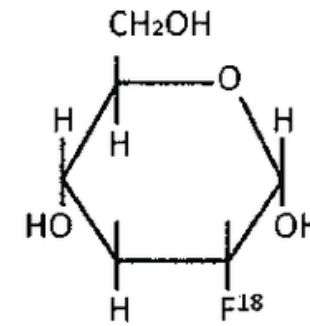
Imaging Immune Response

Opportunity to characterize immune response in and around metastatic sites
Opportunity to visualize the landscape of immune activation state

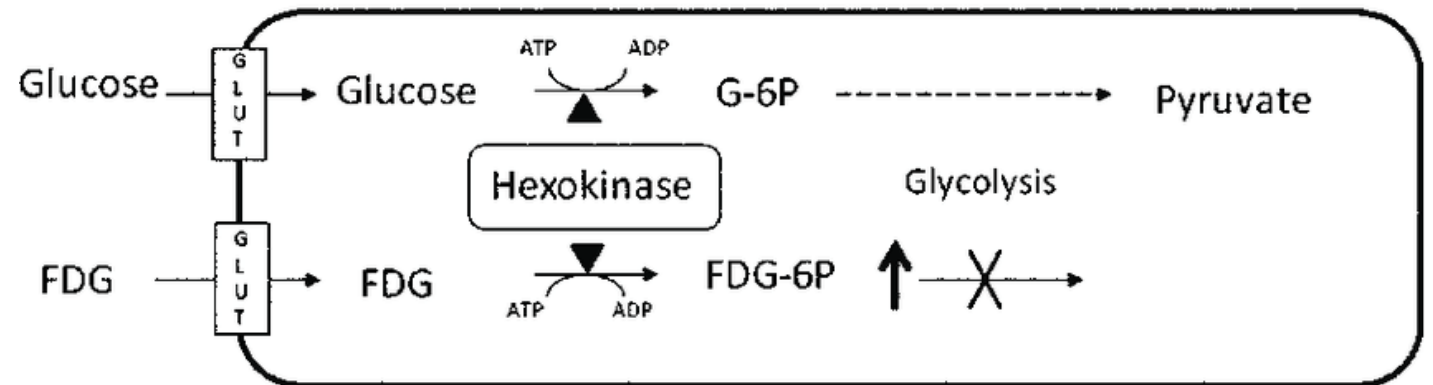
FDG-PET



Glucose

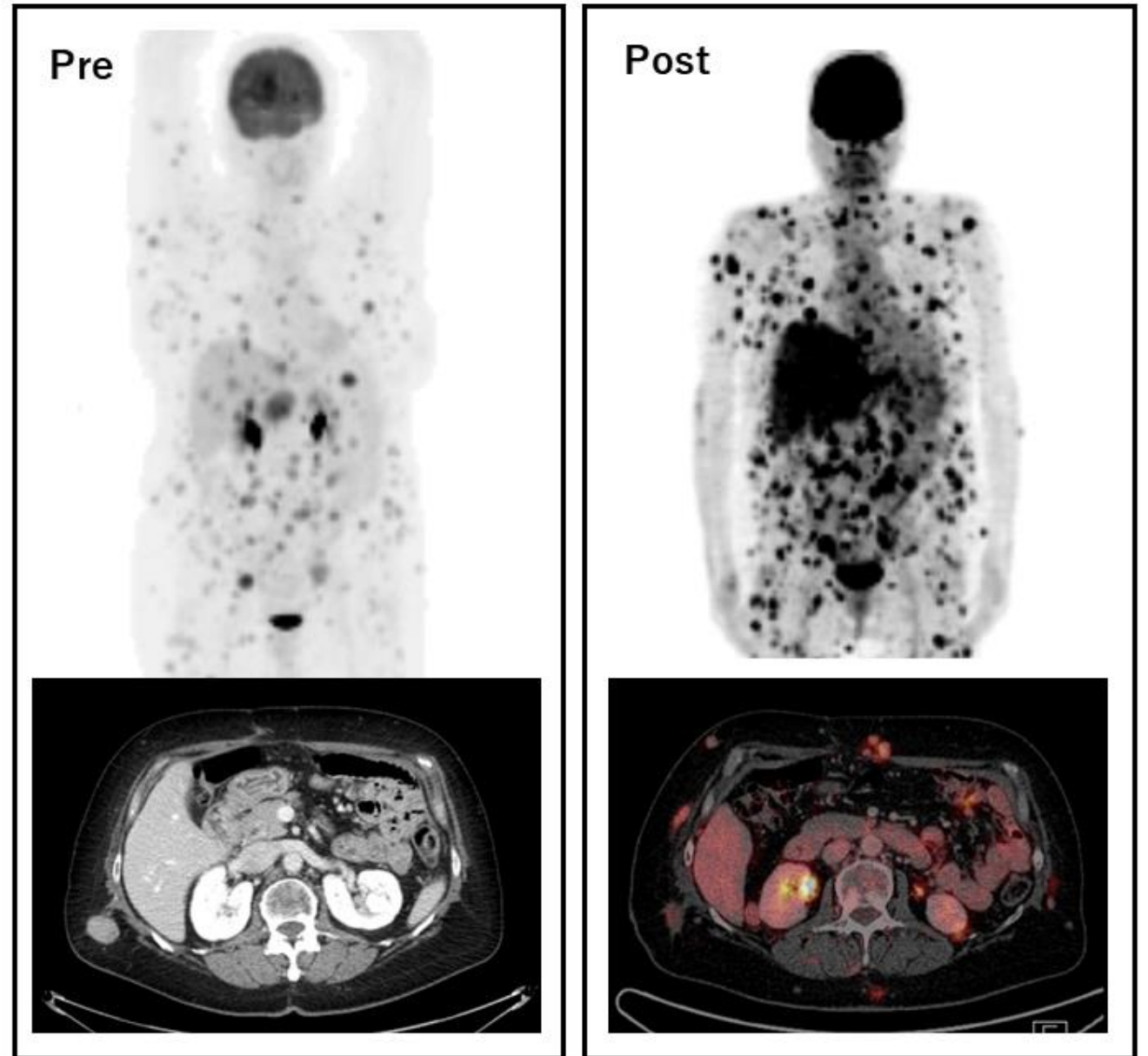


Fluorodeoxyglucose (FDG)



How do we think about PET scans in evaluating response to therapy?

<https://ecrtoday.myesr.org/highlights/experts-investigate-immunotherapy-in-oncology/>

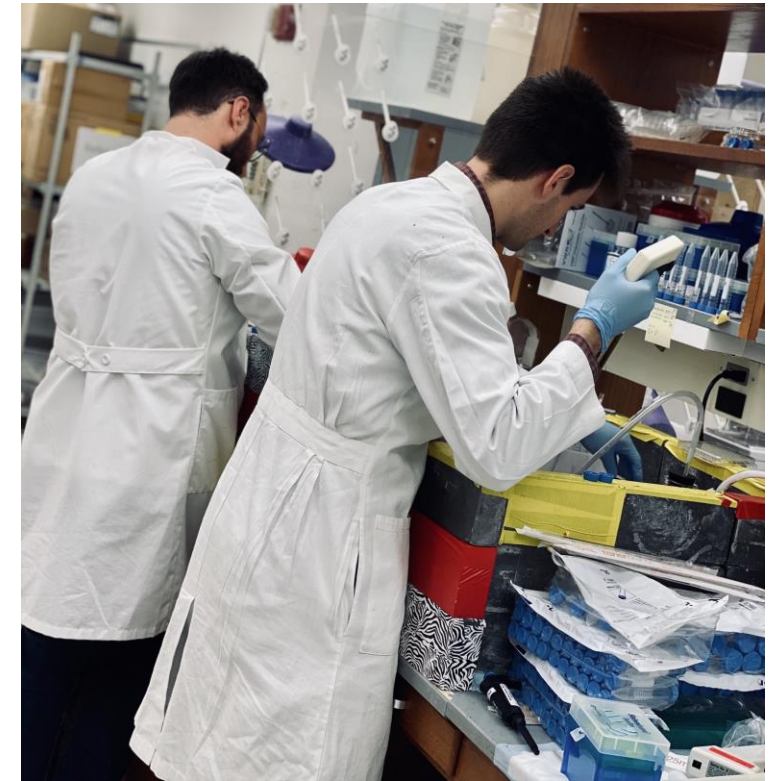
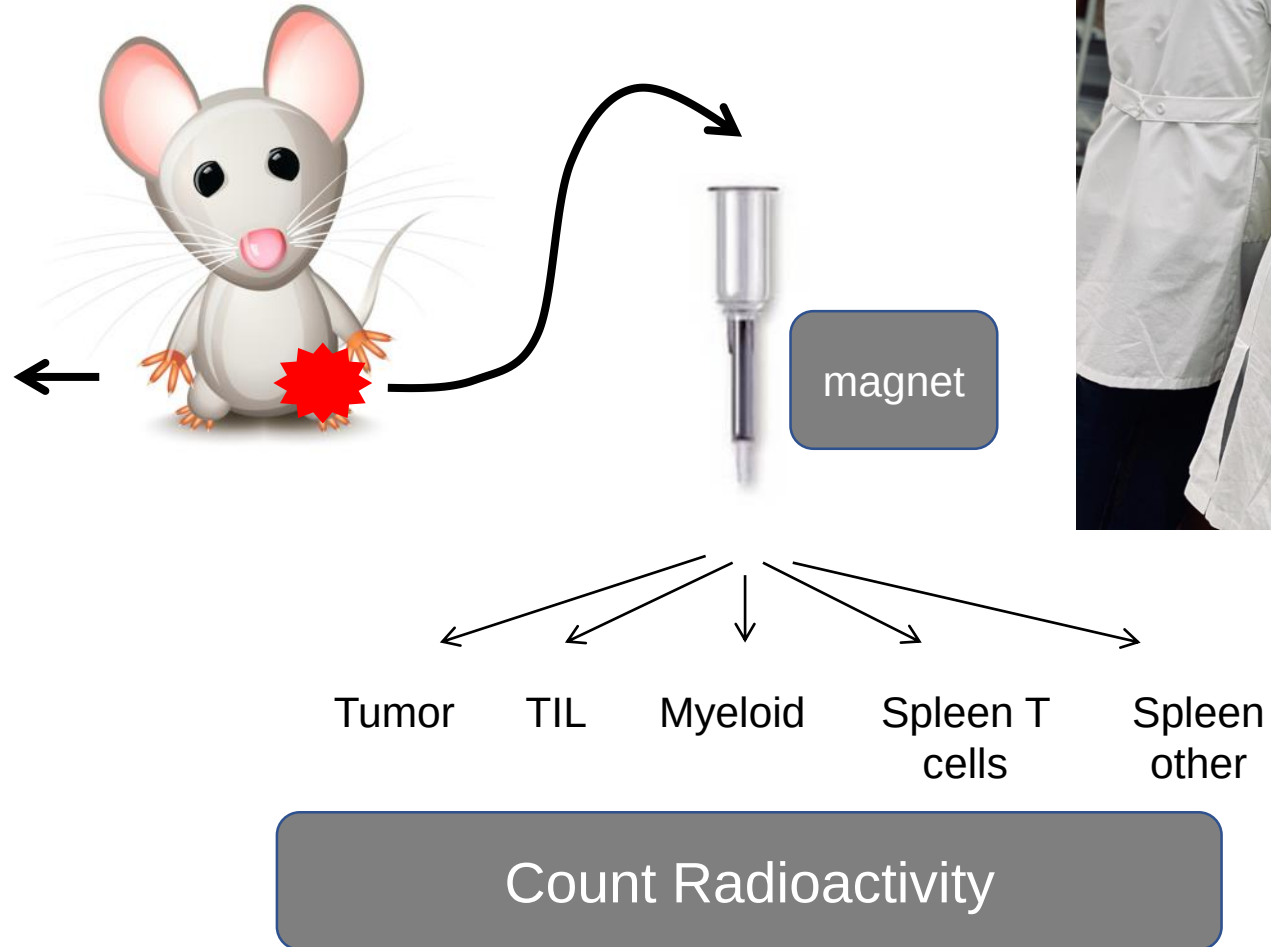


FDG PET: Which cells take up the glucose

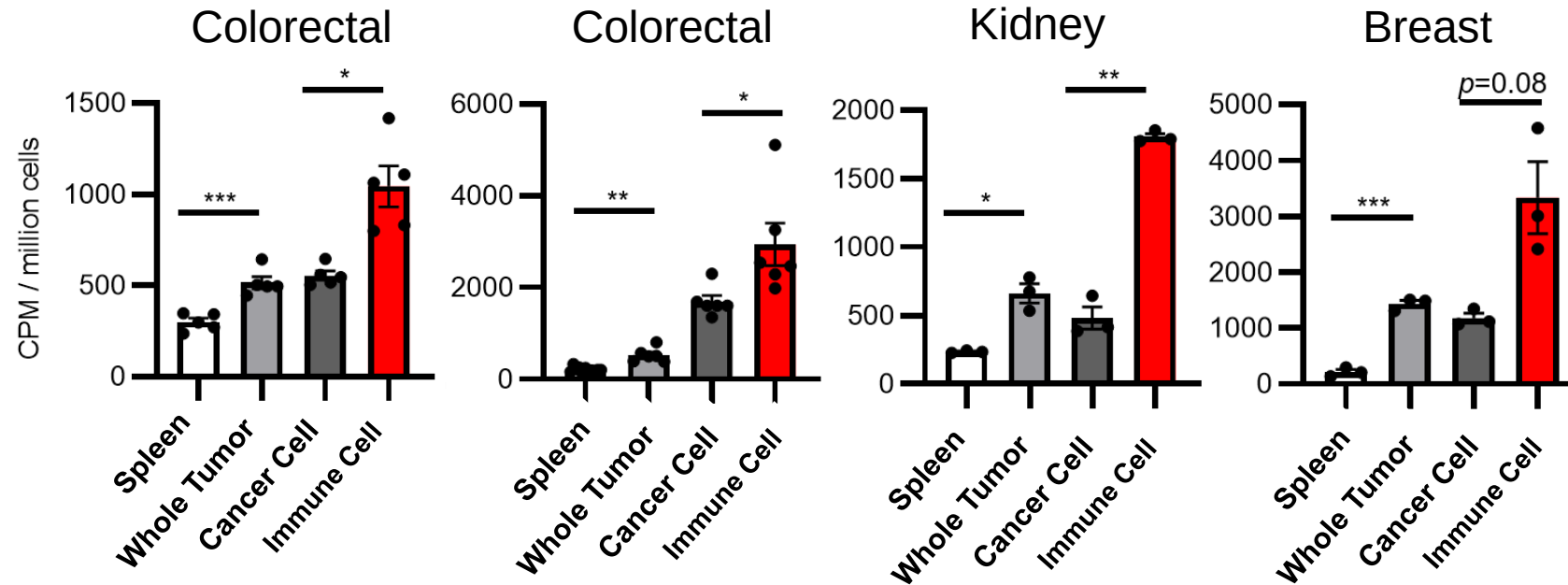
^{18}F -2DG PET



Sagittal View

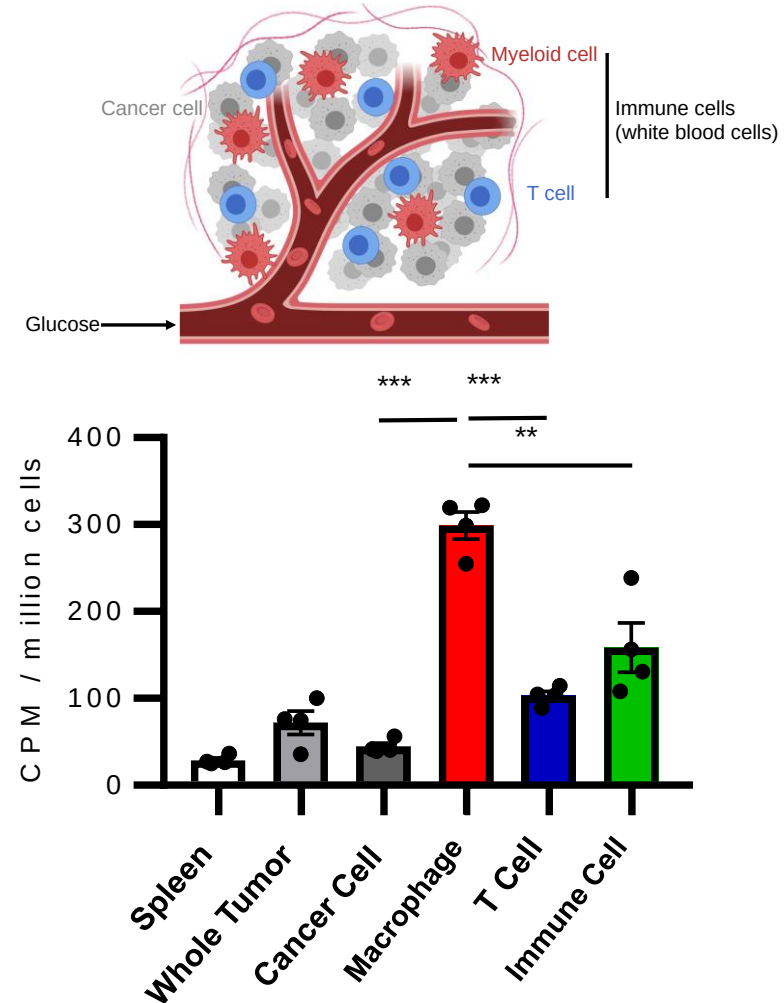


Myeloid Cells Uptake More Glucose Than Cancer Cells



CT26
E0771
RenCa—orthotopic
PyMT GEMM
AOM/DSS CRC

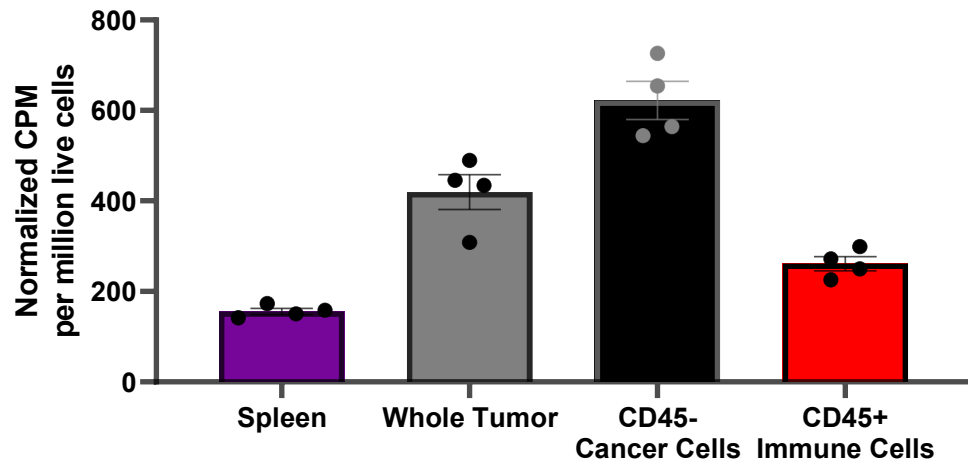
All with similar results



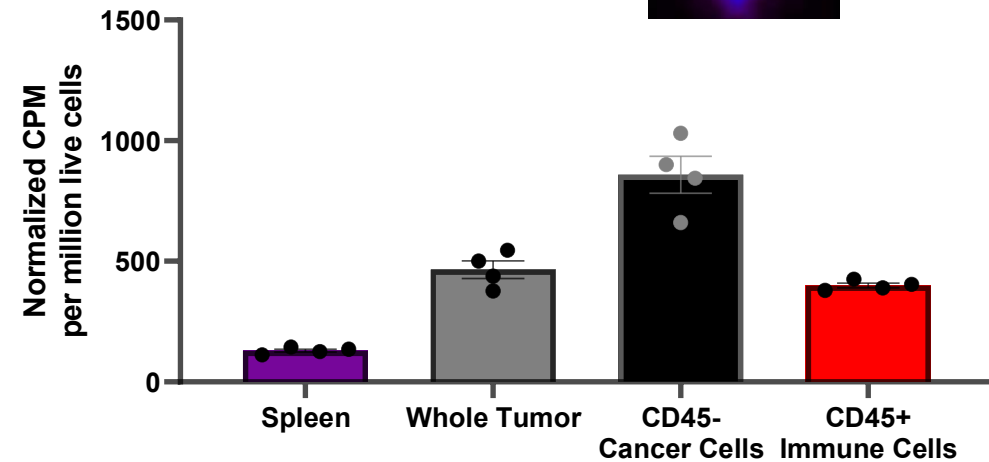
Unlike Glucose, Glutamine Uptake is Predominantly Cancer Cell-Mediated

- ^{18}F -Glutamine Avidity per 10^6 Cells

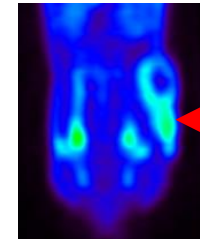
MC38



RenCa

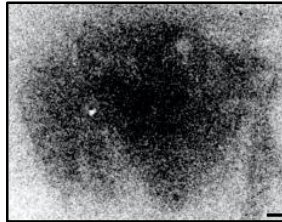


^{18}F -Gln PET



Subcutaneous MC38 tumor

^{18}F -Gln



Cancer cells consume fatty acids and glutamine in tumors.

Amount Per Serving
Calories 230

Total Fat 8g
Saturated Fat 1g
Trans Fat 0g

Cholesterol 0mg

Sodium 160mg

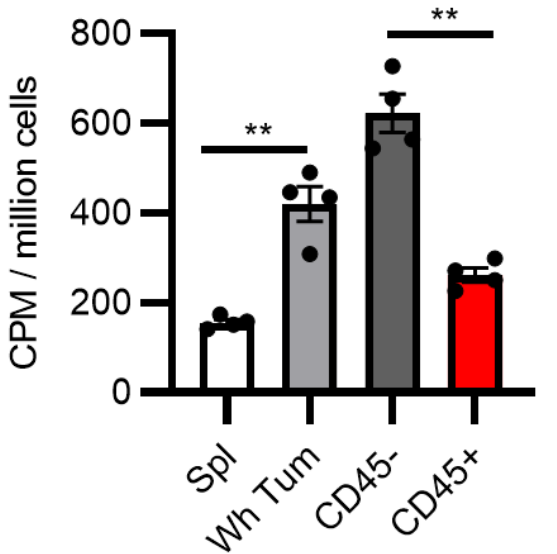
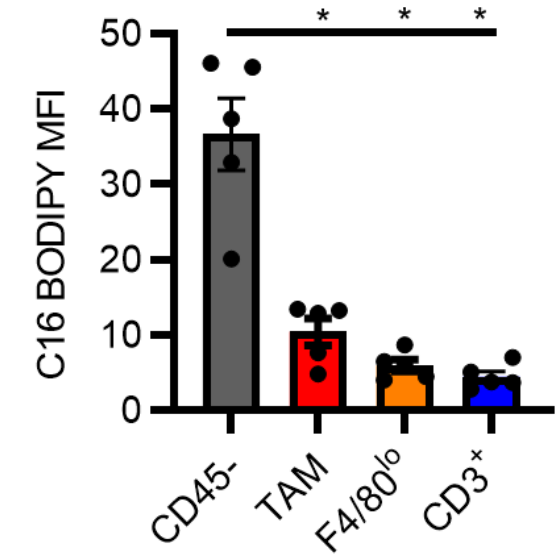
Total Carbohydrate 37g
Dietary Fiber 4g
Sugars 12g

Protein 3g

Fluorescent fatty acid

Radioactive ^{18}F -deoxyglucose
Immune cells

Radioactive ^{18}F -glutamine





Surrogate Biomarker

- Easily accessible
- Rapid analysis
- Quantitative
- Systemically informative (imaging or blood-based)

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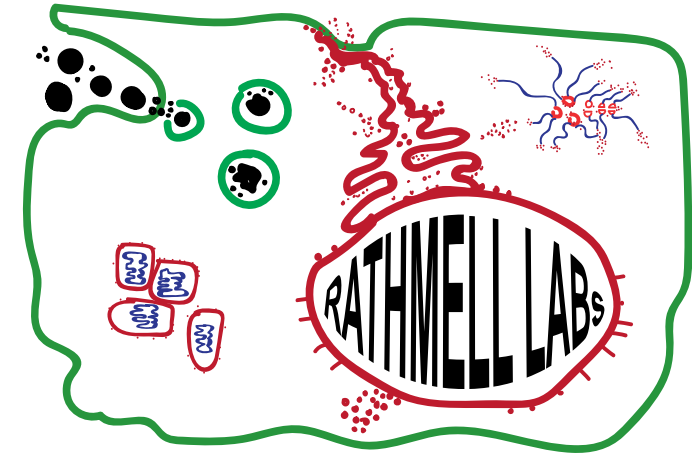
Zaid Hatem

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Rathmell Lab² 2022 Fall Retreat





Bullet points for discussion

- What is the best strategy to rapidly develop imaging biomarkers of immune response/resistance?
- Should or could we demand robust blood based analytics (or stored blood samples) from clinical trials?
- How should we prioritize biomarker discovery and validation from blood based platforms?
- Are there standards needed to facilitate functional imaging biomarker development?

Extra slides

Blood based measurement of host response

- Cytokine markers
- Inflammatory markers (LDH, CRP)
- Circulating immune cell subsets
- Complement
- Inflammasome
- Antigen presentation/immune function

Available now

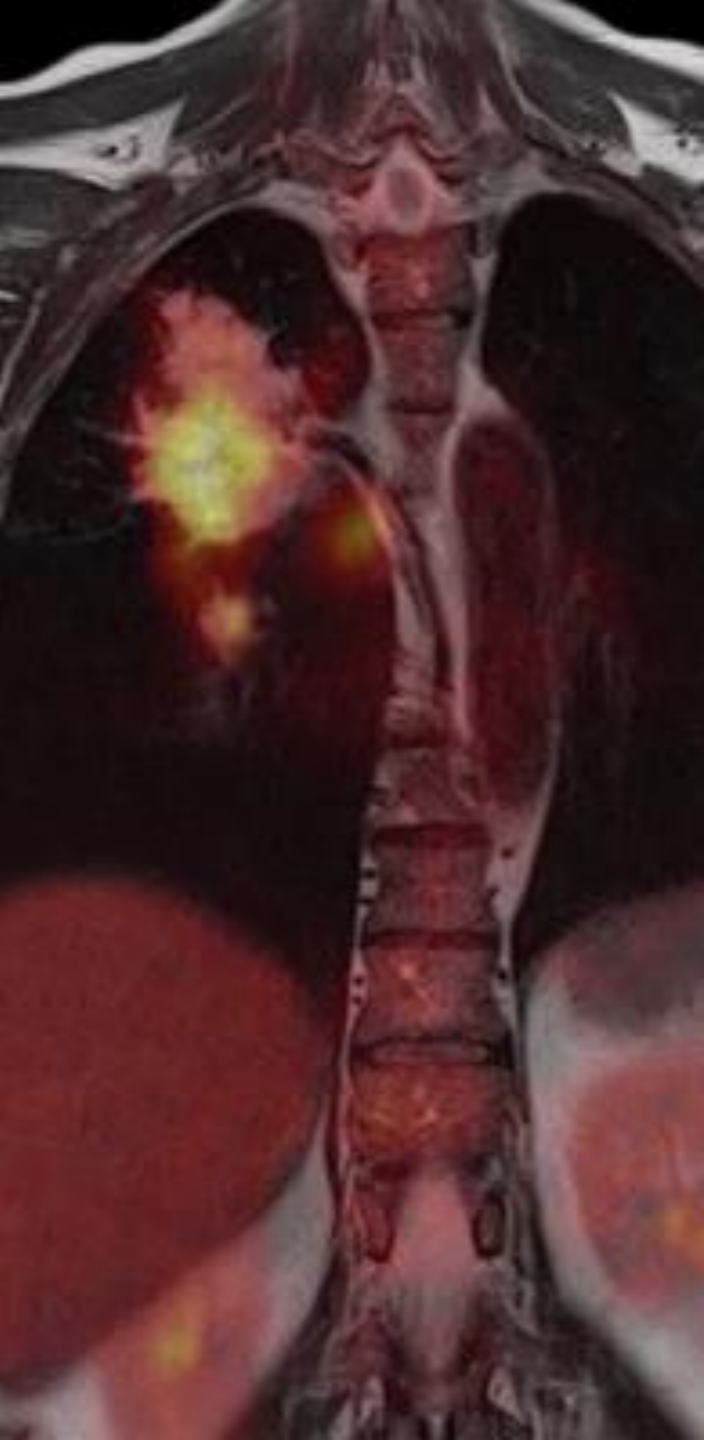
In development

Barriers:



- Nonspecific
- Internally variable
- Unclear potential*

*Antigen repertoire, circulating DNAs worth further investigation



Lung Cancer

Frafjord et al, Human Immunology, 2020

<https://www.itnonline.com/content/study-suggests-lung-cancer-survivors-receiving-too-many-pet-scans>

Tumour-associated macrophages

