Identifying the function of VSIG4 as seen in the tumor microenvironment of Glioblastoma

Dr. Courtney Crane /Crane Lab
Ben Towne Center for Childhood Cancer Research, Seattle Children's Research Institute
Neurological Surgery Student Summer Program
Cienna Slattery
Glioblastoma (GBM)

- Most aggressive primary brain tumor
- 5 year survival rate less than a 10%
- Invasive nature makes it impossible to completely remove surgically
- Immunotherapies have failed to provide a survival benefit due to
  - Blood Brain Barrier
  - Tumor Microenvironment
  - Immune privileged organ
Tumor-associated macrophages (TAMS)

- The most abundant immune cell in GBM
- Initiate development of pro-tumor microenvironment
- Key in communication between the innate and adaptive immune system
VSIG4

The Crane lab performed a single cell RNA sequencing of TAMs and found that the protein VSIG4 is significantly upregulated in GBM TAMs (in vivo)

- Increased VSIG4 is also correlated with poor patient prognosis

- The Crane lab found that upon the treatment of macrophages with GBM supernatant, VSIG4 expression increased in vitro via qPCR
The experiment: mRNA analysis (by Nanostring)

Question
Does the overexpression of VSIG4 lead to changes in global gene expression?

Groups:
1. Control human macrophages (n=3)
2. VSIG4-overexpressing human macrophages (n=3)
Changes in glucose and glutamine metabolism

- Upregulation of GLUL (glutamine Synthetase)
- Downregulation of GAPDH (glyceraldehyde-3-phosphate dehydrogenase)

Tumor Cell

Glucose metabolism

Glutamine metabolism

TAM

Glucose metabolism

Glutamine metabolism

TAM supports tumor cell survival
Conclusions and future directions

VSIG4 plays a crucial role in TAM survival and due to VSIG4’s role in TAM survival, it is a strong candidate for further study.

Using this information, we can:

- Run further experiments on VSIG4 examining the molecular factors causing its overexpression.
- Examine other genes that may have a role in shifting TAMs to a fatty acid metabolism.
- Engineer immunotherapies targeting VSIG4.
- Block the upregulation of VSIG4 in TAMs.
Acknowledgements

**Crane Lab**
Courtney Crane, PhD
Stephanie Balcaitis
Katie Brempelis, PhD
Harrison Chinn
Courtney Cowan
Amira Davis
Jennifer Gardell, PhD
Shannon Kreuser
**Nicole Lieberman, PhD**
Ciana Lopez
Lisa Matsumoto
Brooke Prieskorn

**Neurological Surgery Summer Student Program**
Dr. Ellenbogen
Mrs. Ellenbogen
Jim Pridgeon
Dr. Christine Mac Donald
Julie Bould
Sylvia Zavatchen

**Grants**
NIH NINDS 5R25NS095377-04
Summer Research Experience in Translational Neuroscience and Neurological Surgery

UW Neurological Surgery Donors, Faculty, Staff, and Residents