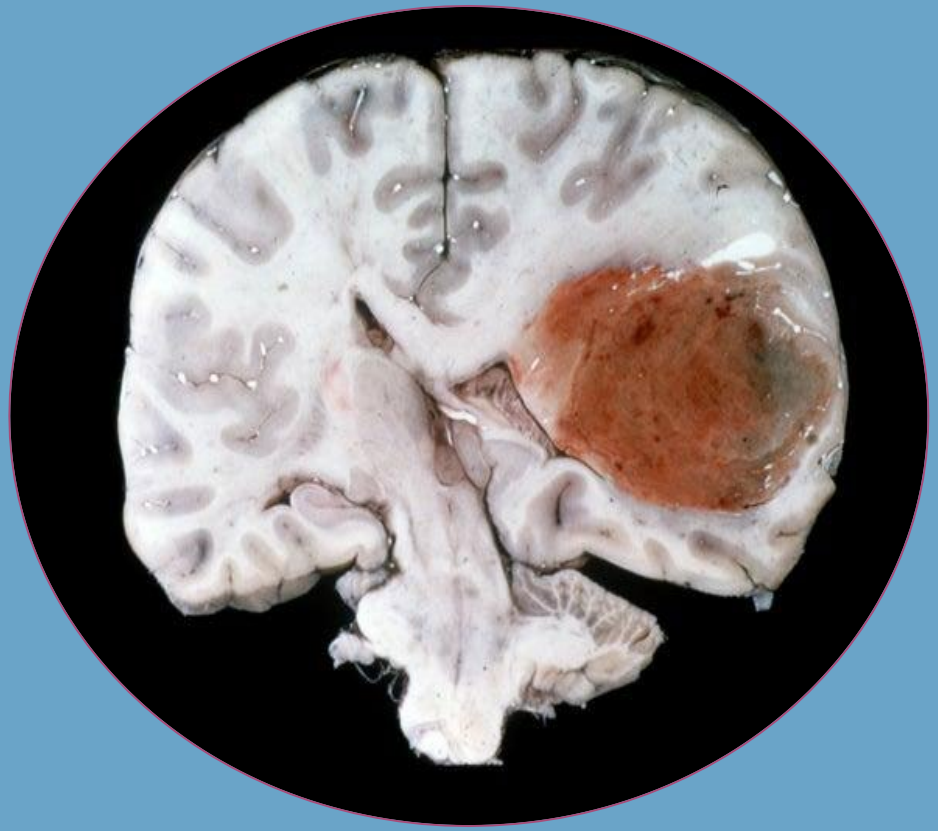
Identifying the function of VSIG4 as seen in the tumor microenvironment of Glioblastoma

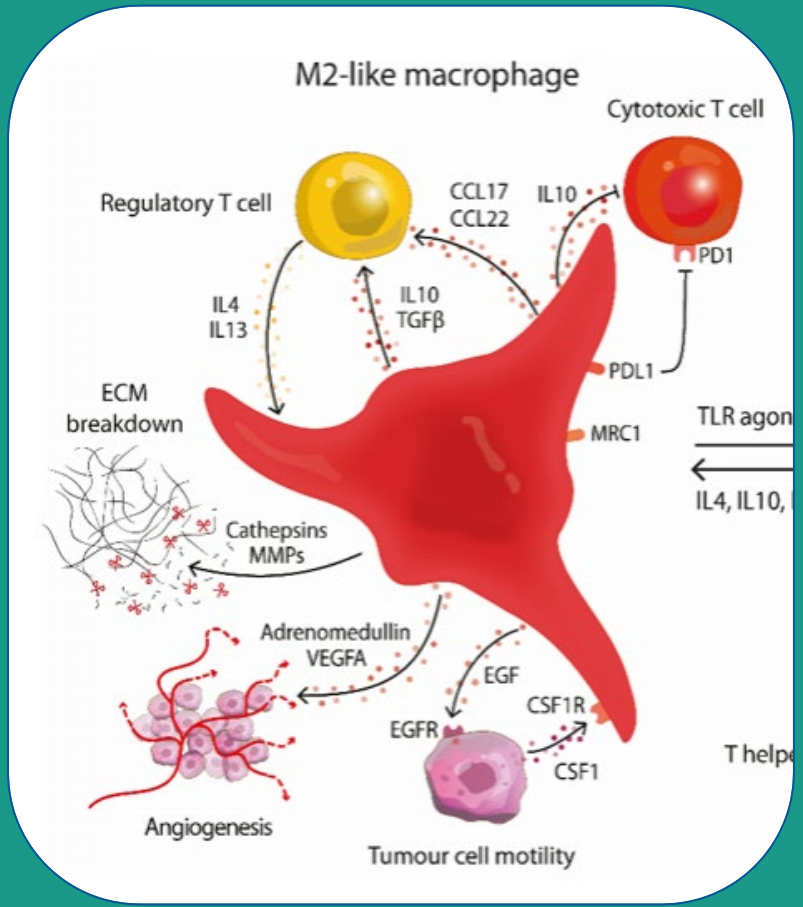
Dr. Courtney Crane /Crane Lab
Ben Towne Center for Childhood Cancer Research, Seattle Children's Research Institute
Neurological Surgery Student Summer Program
Cienna Slattery



Scientificamerica.com

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)

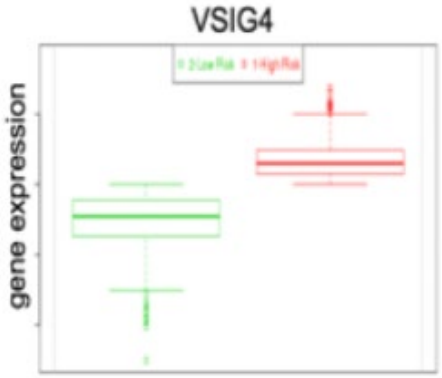
- The most abundant immune cell in GBM
- Initiate development of pro - tumor microenvironment
- Key in communication between the innate and adaptive immune system

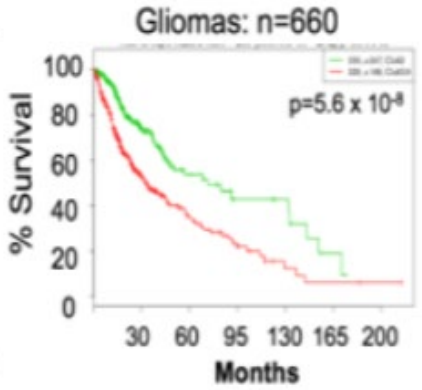
VSIG4

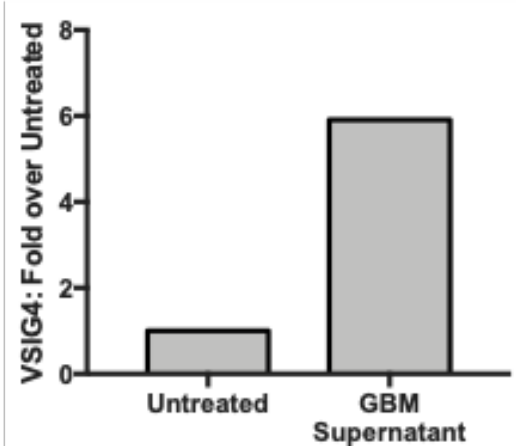
The Crane lab performed a single cell RNA sequencing of TAMs and found that the protein VSIG4 is significantly upregulated in GBM TAMs (in vivo)

- 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

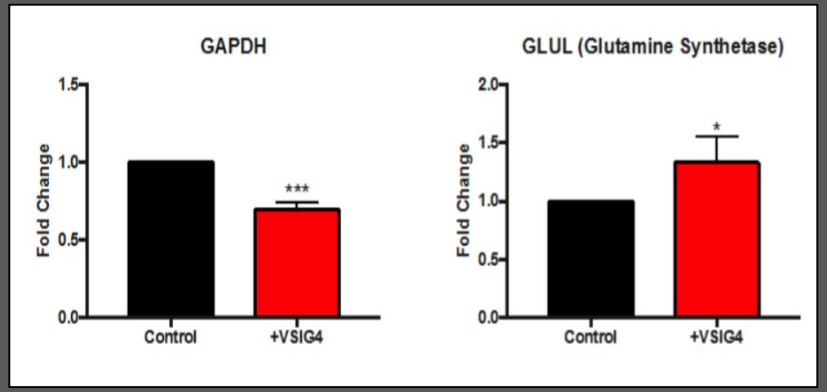
Does the overexpression of VSIG4 lead to changes in global gene expression?

Groups:

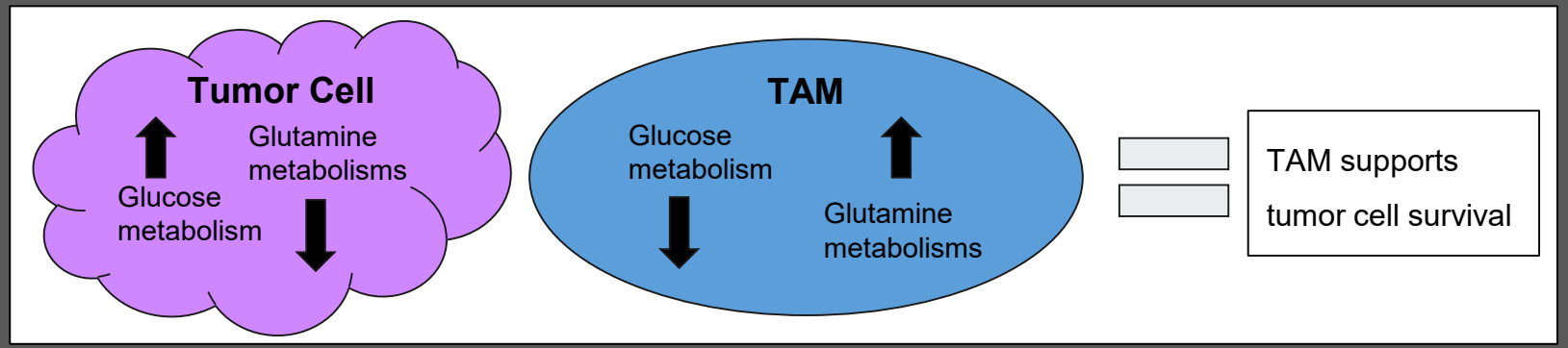
1. Control human macrophages (n=3)
2. VSIG4overexpressing human macrophages (n=3)

Nanostring.com

Changes in glucose and glutamine metabolism



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



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
UW Neurological Surgery Donors, Faculty, Staff, and Residents

Grants

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