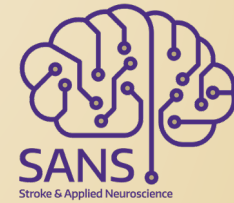


Endovascular biopsy for patient-specific genetic analysis of aneurysm rupture risk

- > Mohamed Magassa, Nghi Quan, Do Lim, Sam Levy, Christian Mandrycky, Chris Young, Cory Kelly, Ying Zheng, Michael Levitt, Louis Kim
- > Summer Student Program Student Presentations and Graduation, Department of Neurological Surgery, University of Washington. August 9th, 2019
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Background



Intracranial Aneurysms

An intracranial aneurysm is the outpouching of a deformed blood vessel within the human brain

Statistics:

- Approximately **2-3%** of people will develop an aneurysm
- Aneurysms are fatal in about **40%** of cases



Symptoms: Severe headaches, nausea/vomiting, vision impairment

Contributing factors to Aneurysm Formation/Growth/Rupture:



Traditional Treatments

aneurysm clipping



Surgical
Clippings



Endovascular
Coils & Stents

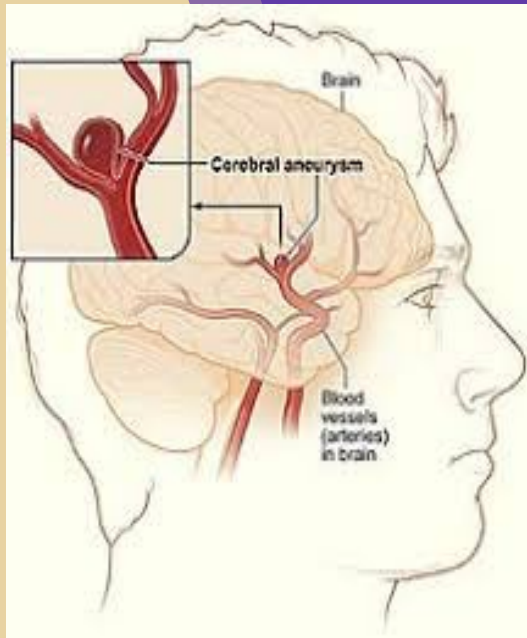
Best treatment for
aneurysms

Situational



Modern Treatments

Hypotheses & Aims



Hypotheses

- 1) There are specific endothelial markers of vascular dysfunction and differential hemodynamic stress are dysregulated during aneurysm formation
- 2) The Level of gene expression is dependent on the aneurysm's risk profile as defined by the **PHASES** aneurysm risk score

Aims

Aim 1: Collect endothelial cells during endovascular treatment of low-risk and high-risk aneurysms.

Aim 2: Perform targeted transcriptome measurement of collected endothelial cells by single-cell RNA sequencing (RNA-Seq).

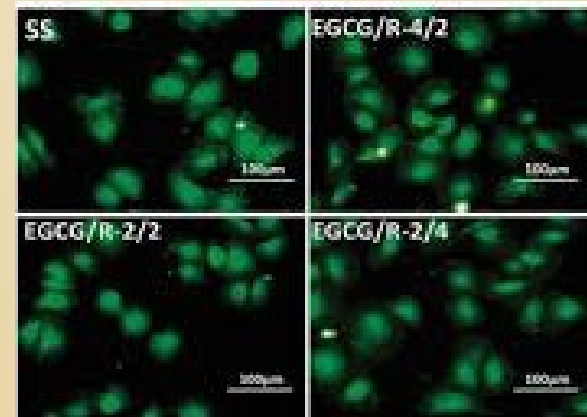
Aim 3: Compare the differential profile of key vascular factors of aneurysmal endothelial cells in unruptured, ruptured low- and high-risk aneurysms.

Methods

1. Patient Consent/ Biopsy Cells



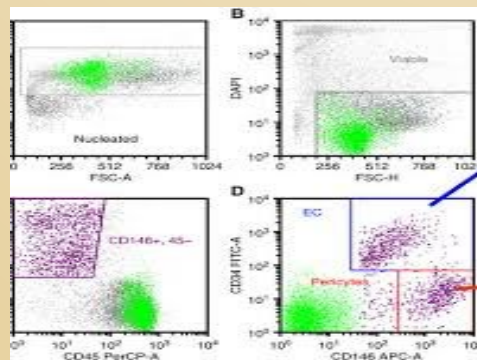
- Centrifuge cells
- Lyse red blood Cells
 - Stain cells



2. Cell Counting

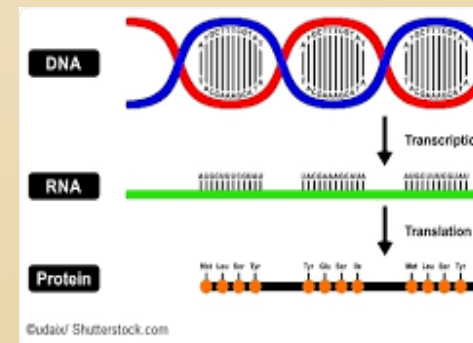
Methods

- Endothelial cell receptors
- Fluorescent marker
- Flow cytometry machine



3. Flow Cytometry

4. RNA Sequence



- Protein Abundance
- Protein Function

Results

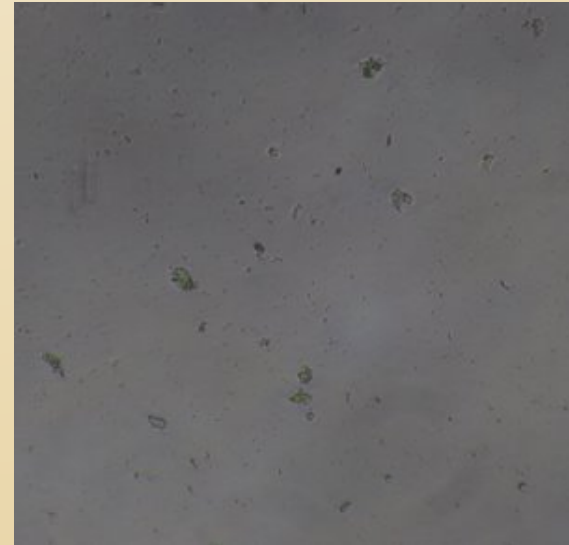
Study ID (EBx=SLU, PCx=SCRI)	Date of Baseline Procedure	Procedure Type	Blood 1	Blood 2	Tube 1		
					Label	Device	Dev. Location
B001		coiling of recurrent R PCom aneurysm	Blue Cap	Blue Cap	A	Axiom Prime 3x4	Aneurysm Dome
B002			Blue Cap	Blue Cap	A	First coil: ev3 Axiom Prime 7x20	Aneurysm Dome
B003		Balloon assisted coil embolization	Blue Cap	Blue Cap	A	Coil (not first): 3x6 360 soft	Basilar
B004							

Biopsy devices from three patients

- EB001 – **Recurrent** PCoA ---> First coil
- EB002 – **Ruptured** ACoA ---> First and second coil
- EB003 – **Ruptured** BA Tip ---> Third coil

Results

EB002 – Cx 5 Days



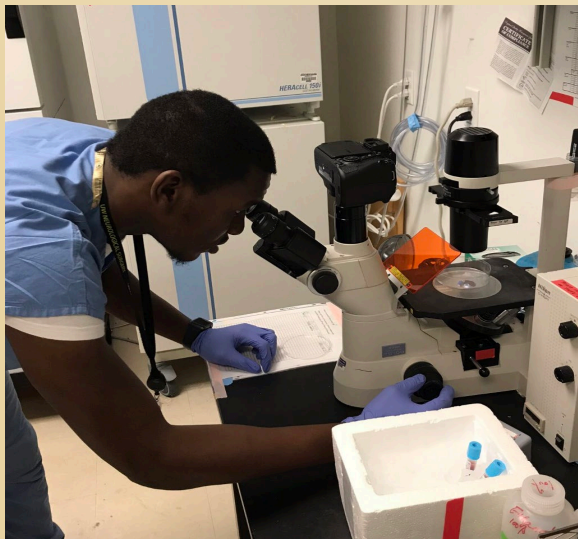
Lessons learned from
Cooke et al.:

1. Diameter of coils
2. First coil
3. Natural cell yield

Endovascular Biopsy - "In Vivo Cerebral Aneurysm Endothelial Cell Sampling and Gene Expression Analysis"

Dr. Daniel Cooke

- There is limited data describing endothelial cell (EC) gene expression
- EB was performed in 10 patients (5 ruptured, 5 non-ruptured).
- A total of **437 ECs** was collected and **94** of which were aneurysmal endothelial cells



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- > **Sylvia Zavatchen & Julie Bould**
- > **Mentors: Louis Kim, Michael Levitt, Cory Kelly**
- > **Lab Members: Sam Levy, Do Lim, Hannah Haugh, Keiko Prijoles; the Stroke and Applied Neuroscience Center Lab and Dr. Zheng's Cardiovascular Bioengineering Lab.**
- > **References:**
 - > Daniel L. Cooke¹ & David B. McCoy² & Van V. Halbach¹ & Steven W. Hetts¹ & Matthew R. Amans¹ & Christopher F. Dowd¹ & Randall T. Higashida¹ & Devon Lawson³ & Jeffrey Nelson¹ & Chih-Yang Wang¹ & Helen Kim¹ & Zena Werb¹ & Charles McCulloch¹ & Tomoki Hashimoto¹ & Hua Su¹ & Zhengda Sun¹. Endovascular Biopsy: In Vivo Cerebral Aneurysm Endothelial Cell Sampling and Gene Expression Analysis. 2018.
 - > Philippe Bijlenga, MD, PhD; Renato Gondar, MD; Sabine Schilling, PhD; Sandrine Morel, PhD; Sven Hirsch, PhD; Johanna Cuony, MS; Marco-Vincenzo Corniola, MD; Fabienne Perren, MD; Daniel Rüfenacht, MD; Karl Schaller, MD. PHASES Score for the Management of Intracranial Aneurysm. 2017.