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

Funding Acknowledgements

NIH/NINDS 1R25NS095377 (PI: Ellenbogen)
NIH/NINDS R01NS088072 (PI: Kim)
NIH/NINDS R01NS105693 (PI: Levitt)
The AANS Dempsey Award (PI: Levitt/Young)
The Bee Foundation (PI: Kim)
Medtronic, Stryker, and Philips-Volcano investigator-initiated unrestricted educational grants
The Stroke & Applied NeuroScience Center donors
Background

Intracranial Aneurysms

An intracranial aneurysm is the outpouching of a deceased 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

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

2. Cell Counting

- Centrifuge cells
- Lyse red blood Cells
- Stain cells
Methods

3. Flow Cytometry
- Endothelial cell receptors
- Fluorescent marker
- Flow cytometry machine

4. RNA Sequence
- Protein Abundance
- Protein Function
Results

Biopsy devices from three patients

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

Lessons learned from Cooke et al.:

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

Dr. & Mrs. Ellenbogen
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:
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 Rufenacht, MD; Karl Schaller, MD. PHASES Score for the Management of Intracranial Aneurysm. 2017.