Biomarker of Venous Thromboembolism

Cliff Takemoto M.D.
Pediatric Hematology
The Johns Hopkins University
Disclosures

No relevant Disclosures
Goals of Project

Use mass spectroscopy to identify biomarkers of thrombosis

Identify and quantify proteolytic fragment with coagulation activation

Use signatures of coagulation activation peptides to assess thrombotic and bleeding risk
What is Proteomics?

- **Digest fragments**
- **IONIZE**
- **Separate peptides**
- **Biomarker Discovery**

- Plasma
- Mass/charge (m/z)
Patients with thrombosis for biomarker discovery

Venous Thrombosis:
- Pre-Anticoagulation
- On Anticoagulation
- Post Anticoagulation

Venous Malformation:
- Pre-sclerotherapy
- Post-sclerotherapy
How to make clot

Venous malformation

Percutaneous sclerotherapy with ETOH

catheter

catheter

clot
Optimizing Fragment detection

Goal:

Detect and Quantitate Proteolytic Fragments

Is there a “signature” of coagulation activation?
Novel view of coagulation activation?

Goal:

Detect and Quantitate Proteolytic Fragments

Is there a “signature” of coagulation activation?

Proteolytic fragment signature inform about thrombotic or bleeding risk?
Optimizing Fragment detection

- **plasma**
  - innovin
  - actin
  - protime
  - aPTT

**Mass spectroscopy**

**Proteins detected**
- Fibrinogen
- FII
- FV
- FIX
- FX
- FXI
- FXII
- Antithrombin
- Protein S
coagulation protein concentration

Proteins detected:
- FII
- FV
- FIX
- FX
- FXI

Not detected:
- FVIII
- FVII
Activation of thrombin

control

prothrombin

PT activated

PTT activated
Ongoing Studies

1. Detection of predicted fragments with activation: FIX, FV, FX, antithrombin, protein C

2. Discovery of novel proteolytic substrates with coagulation activation

3. Validation and quantitation of proteolytic substrates in disease states
Acknowledgements

Proteomics Core
Zongming Fu
Allen Everett

Pediatric Hematology
Stephanie Brandal

Support from 340B
Jim Casella

JHU Laboratory
Jayesh Jani
Tom Kickler