

Working Group on Sickle Cell Disease: Inflammation, Thrombosis and Vascular Injury

Held: October 28, 2009
Location: National Heart, Lung, and Blood Institute, NIH
6701 Rockledge Drive, 9th Floor, Conference Rooms 9100/9104
Bethesda, MD 20817 United States

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Agenda and Speakers Lists: See attached files.

Summary:

The working group discussed basic mechanisms of vascular injury, cell-cell and cell-protein interactions in sickle cell disease (SCD). The goal of the working group is to provide recommendations to help develop targeted Funding Opportunity Announcements in basic research that will increase the pipeline of SCD research leading to translational and clinical research.

The anticipated product of this meeting will be an RFA in “Mechanisms of Inflammation, Thrombosis and Vascular Injury in Sickle Cell Disease”. This RFA proposal would be brought forward in the next intra-NHLBI approval process for new Initiatives (early 2010), and the securing of funding would be the initial metric of success. The next metric would be the awarding of several (possibly 4 to 6) R01 grants under this RFA.

Recommendations:

- Investigate the mechanism(s) of SCD phenotype.
- Determine how cell-cell interactions regulate hemolysis in SCD. Cell-cell interactions include:
 - Reticulocytes-Leukocytes
 - Reticulocytes-Platelets
 - Platelets-Leukocytes
 - Microparticles-Target Cells (Reticulocytes, Leukocytes, and Platelets)
 - Interactions with Endothelial Cells
- Identify clinical features of SCD as an inflammatory state with and without hemolysis that result from reperfusion injury
- Examine how cell-cell interactions alter gene expression patterns in SCD.
- Understand SCD human physiology and measure physiological responses noninvasively in patients and SCD animal models.
- Identify and validate surrogate endpoints.
- Image what is going on during pain crises in SCD patients—i.e. RBC aggregation, blood flow regulation and evaluate responses to interventions.

- Investigate coagulation and/or endothelial cell activation and role of microparticles in acute vaso-occlusive SCD events.
- Compare SCD microvasculopathy and pathogenesis to TTP
- Investigate coagulation signaling mechanisms that promote lung injury, inflammation and vascular repair in SCD.
- Prepare for systems biology approaches to study SCD.
- A community of investigators who are in touch with each other should partner with experts in other fields such as engineering.
- Understand the role of the autonomic nervous system in SCD patients.
- Ensure that pilot studies can be launched and completed. Use efficacy rather than effectiveness studies for evaluation of promising ideas
- Identify and test novel therapeutic ideas.
- For all SCD clinical trials, identify what worked correctly and what went wrong.
- Use multi-modality therapy to treat SCD.
- If single-modality therapy is studied, an endpoint must include vascular efficacy.
- Focus on key morbidities/causes of mortality
- Attract the community of investigators from allied fields (interdisciplinary team)