

Sickle Cell Pain: IPRCC Analysis of Current NIH Research

Wally R. Smith, MD
IPRCC Member

*Harvey Luksenburg, MD
Program Chair*

Sickle Cell Disease Overview

- Rare Autosomal Recessive Hb'pathy (100,000 in US)
- Begins as purely acute-on-chronic, multi-local vaso-occlusive, ischemic and inflammatory pain
- Phenotype transformation to central and/or peripheral neuropathic pain?
- Mechanisms of phenotype transformation?
 - Summative ischemia on neurons?
 - Genetic predisposition (different than 6 beta Hb Val->Glu)
 - threshold effect?,
 - Timing?
- Mechanisms shared in common with other syndromes?
- Approaches to Rx (besides HU and transplant)
 - Opioid?
 - non-opioid chemical?
 - Other, including biobehavioral?

Chronic SCD Pain

- Phenotypic features in common with conditions that exhibit features of central sensitization syndromes?
 - IBS
 - chronic LBP
 - chronic headache

Overview of the portfolio

- Currently 30 grants
- Distributed throughout 6 Institutes
 - NHLBI 23
 - NINR 2
 - NINDS 1
 - NCCAM 1
 - NICHD 1
 - NCMHD 2

Highlights of the Portfolio: Methods

- Total no. SCD grants < any other condition
 - Rare disease
 - relatively recent interest in this field
- Basic and translational research < other conditions

Highlights of the Portfolio: Topics

- Pain outcome assessments and measures 13%
- Health disparities in pain, pain management, and access to care” 11%
- Genetics and genomics of nociception and pain 7%
- Medical management of pain 7%
- Pharmacological mechanisms and treatment 7%
- Development and validation of animal models 9%
- Total 54%

Gaps & Opportunities: Research areas needed or untapped

- Missing studies characterizing SCD pain phenotype(s) or diagnosis/case definitions
 - Ischemic nociceptive
 - neurological
 - inflammatory
 - Biobehavioral
 - psychosocial
- Missing studies developing analgesics, device, and therapy delivery systems targeted at these mechanisms.

Gap Analysis (cont'd)

- Under-representation:
 - How genetic or other mechanisms alter the SCD pain phenotype
 - Opioid response analysis and studies of new, non-opioid therapeutics
- Areas with 0→2 grants:
 - Pain education, pediatrics, -omics of pain, non—pharmacological mechanisms, and unique populations.
- Lower numbers of grants:
 - pain education, non-pharmacological mechanisms, and biobehavioral and and psychosocial mechanisms
- Higher percentage of grants:
 - pain outcome assessments, health disparities, access to care, pain and women's and minority's health research

Relevance to other pain conditions and opportunities to collaborate

- Recent collaboration sought between investigators from NHLBI & investigators from NINDS, NICDR, NINDS, NCCAM, and NIDA
 - Example studies: OPERA (NIDCR) and MAPP (NIDDK)
- Questions
 - How are the pain phenotypes in SCD similar to those of other syndromes?
 - Is the pain phenotype in SCD static or age-dependent and evolving?