Small molecule strategies interdicting the polymerization of deoxygenated sickle hemoglobin for the treatment of sickle cell disease

**Two types of small molecule strategies**
1. Shift RBC hemoglobin production to fetal hemoglobin (HbF)
2. Chemically modify sickle hemoglobin (HbS) to inhibit its polymerization

**HbS polymerization**
- Deoxygenation
- Acidosis
- HbS concentration
- Hydration

**RBC rigidity**
- Endothelial damage
  - Coagulation pathway activation
  - Aspirin 7 etc. ?
- Vaso-occlusion

**RBC adhesion**
- Inflammation pathway activation
- Selectin inh. etc.

**Hemolysis**
- Anemia
- Erythropoietin ?

**Tissue hypoxia**
- Multi-organ damage early death
- PCN, vaccines, wound care, dialysis etc.
- Pain
- Analgesia

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