A New Approach: Gene Silencing

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Silencing the BCLA11A gene

- The BCL11A gene acts as an “off” switch to fetal hemoglobin production shortly after birth for most people
- While most people then switch to making healthy adult hemoglobin, people with sickle cell disease transition to making a mutated, sickled hemoglobin
- Silencing the BCL11A gene simultaneously increases fetal hemoglobin, which does not sickle and has potent anti-sickling characteristics, and directly reduces the creation of adult, sickling hemoglobin

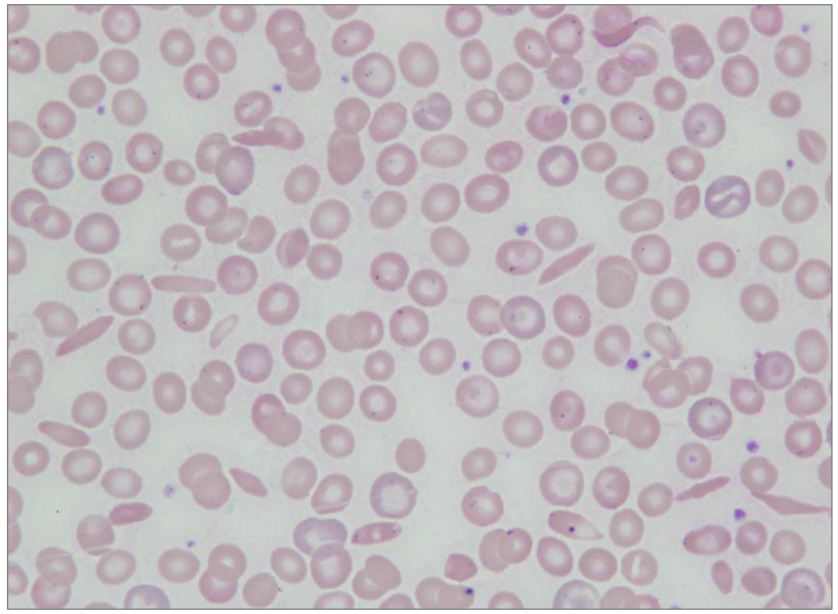
Ex vivo lentiviral vector approach

- Blood stem cells are removed from the body
- A lentiviral vector delivers instruction to the cell to silence or “knock down” the BCL11A gene product
- These genetically-modified cells are returned to the body

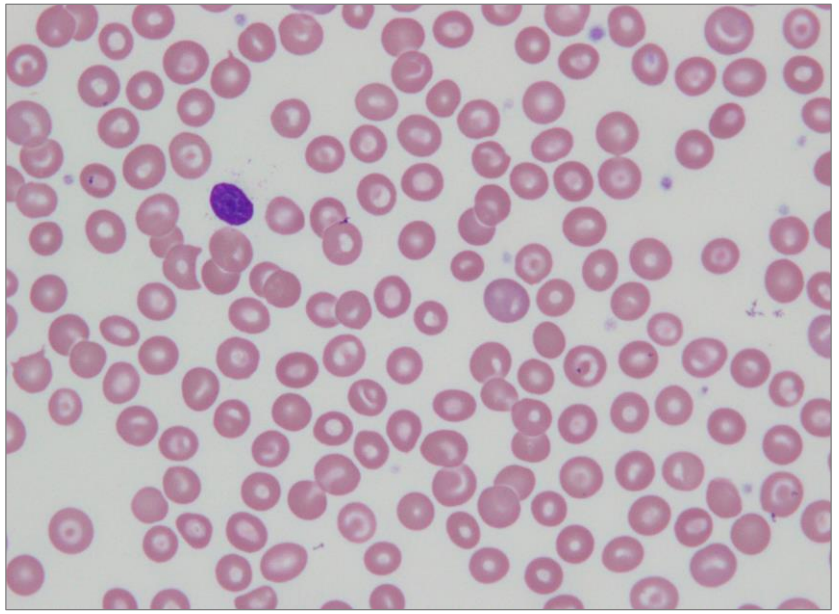
BCL-002: Reversal of Sickle Cell Phenotype

- No pain
- No respiratory or neurologic events
- No anemia
- No transfusions since engraftment

Pre-GT



6 months post-GT



Update

- Adult cohort complete
  - Kinetics of engraftment very similar in all patients
  - Kinetics of fetal hemoglobin production and reduced sickle hemoglobin production very similar in all patients
  - No adverse events attributed to gene therapy product
- DSMB interim review complete
- Age 12-18 cohort opened and enrollment already completed
- Age 2-12 now opening, many patients interested…….

Many interested families

- 51 families with children under age 12
- 23 adolescents
- 49 adults

- Worldwide interest:
  - U.S. (Rhode Island, Massachusetts, Minnesota, Texas, Indiana, Florida, Louisiana, New York, New Hampshire...)
  - International (UK, Canada, Nigeria, Kenya, Argentina…)

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