

Jeffrey D. Kendall

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Mentor: Clifford J. Steer, M.D.,
Department of Medicine

Sleeping Beauty and Sickle Cell Disease: Constructing a Gene Therapy Vector Employing Sleeping Beauty Transposon with the Potential for Future Clinical Therapeutic Use

Sickle cell disease (SCD) is a genetically inherited disorder caused by a single point mutation in the β -globin gene sequence, resulting in a glutamic acid to valine substitution. Hemoglobin, the oxygen carrying molecule in erythrocytes (red blood cells), is a tetrameric protein composed of two α -globin subunits and two β -globin subunits. Mutated β -globin subunits cause hemoglobin molecules to polymerize with one another in the deoxygenated state, causing erythrocytes to sickle and lose their elasticity. Vasoocclusion, painful “crises,” anemia, and infarction arise in the thousands of individuals affected by SCD worldwide. Gene therapy may potentially offer an approach to successfully treat genetic disorders such as SCD.

In my laboratory, we are investigating the use of a novel nonviral vector system employing the *Sleeping Beauty* transposon (*SB-Tn*) to insert wild-type β -globin gene into the human genome. My project has consisted of the molecular engineering and construction of a gene plasmid vector incorporating *SB-Tn*. The plasmid contains two “reporter” genes: DsRed (a gene encoding a red fluorescing protein) and luciferase (a gene encoding an enzyme that induces bioluminescence). When β -globin gene is delivered to hematopoietic stem cells by the *SB-Tn* system, the reporter genes allow expression to be monitored. Researchers are working to develop vectors that deliver genes safely and effectively. It is our hope that the *SB-Tn* system will further demonstrate that it can serve as such a vector.

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