Homologous recombination — a genetic blueprint to cure sickle cell anemia and 6,000 other diseases

Colleagues tease Dr. Matthew Porteus about his "Ferrari," their informal moniker for the costly beige box on his lab counter.

But inside the plain exterior, 1,000 blood cells per second are corralled like kids at recess and ushered single-file through a special laser. A sensor registers the light passing through each cell and keeps track of green cells (formerly mutated cells that have been repaired) and plain cells. This simple tally measures the efficacy of some very sophisticated research which holds the hope of new gene therapy treatment for more than 6,000 diseases (and millions of people), ranging from sickle cell anemia, which affects thousands of children like Christopher and Devan Tippitt, to severe combined immunodeficiency (bubble-boy disease).

Sequence differentiations in each person's DNA sequence are what blueprint the myriad forms of human life. Many differences are beneficial, but in some cases, the mutation of a single gene in the wrong place can give rise to one of more than 6,000 monogenic diseases, occurring in one in 200 live births. Under the direction of Dr. Porteus, a hematologist on the medical staff at Children's and assistant professor of Pediatrics and Biochemistry at UT Southwestern, the Porteus lab is engaged in — and inspiring other labs worldwide to engage in — research into how to exploit a cell's own maintenance pathways to correct these mutations.

"The approach most people take to gene therapy is to try to introduce a non-mutated copy of the gene somewhere into the DNA sequence and hope that it propagates itself," Dr. Porteus said. "That might work, but a more ideal approach that's far less intrusive to the body would be to go in and correct that specific mutation, leaving everything else untouched, and that's what we're trying to perfect using a process called homologous recombination."

Auto-repair mechanism

With homologous recombination, an auto-repair mechanism within the body's own genetic maintenance pathway is activated, whereby the DNA is corrected to the way it was before mutation.

"We have a world of smart scientists out there, and if I can give them a blueprint, they can develop the cures for their specific areas of expertise," Dr. Porteus said. "The exciting thing about research is that you never know which day is going to be the day that something finally works."