Scientists and doctors alike have considered gene therapy a potential panacea since it was first postulated on in the 1970s. If harnessed correctly, gene therapy could provide real cures for an array of ailments from cancers to Parkinson’s [1] to Tay-Sachs [2]. The common thread in these is that a cell’s genome is altered in a very specific way that is detrimental to the organism’s physiology. In gene therapy, the idea is that by using a vector (usually a virus) we can return the cell’s genome to a healthy state by delivering a functional gene to the patient. Unfortunately, perfecting this technique has been a several decades long dance with failure and many have begun losing faith. Thankfully, the tides appear ready to turn in our favor.

One such sign that gene therapy is gearing up for mainstream medicine is a recent clinical trial for the treatment of Wiskott-Aldrich syndrome (WAS), which was highlighted in the most recent release of the Journal of the American Medical Association. WAS is a rare genetic immunodeficiency in which a gene active in immune progenitor cells is mutated and produces a dysfunctional protein, which leads to a litany of physiological abnormalities, including dysfunctional platelets, decreased antibody production and non-functional T-cells. Patients with the syndrome suffer from skin and blood cell problems, and if left untreated, patients tend to die in their teenage years, or earlier. All of these pathologies are caused by a single gene mutation, which makes it an excellent candidate for gene therapy. Currently, the best treatment is a bone marrow transplant, however, these are risky and finding a genetic match is difficult.

In the study [3], 7 patients had some of their own hematopoietic stem cells (the aforementioned immune progenitor cells that reside in the bone marrow) removed and exposed to a vector containing the functional gene. Next they were reinserted into the bone marrow with the hope that the mature cells derived from these modified progenitors would be healthy B and T cells. Myeloablative chemotherapy (killing of all bone marrow cells) was performed before the modified cells were returned to ensure that the only stem cells in the patient’s bone marrow were the genetically modified ones.

Although the sample size was very small, the results were extremely promising. Of the 7 patients to receive the treatment 6 were still alive at their most recent follow up (mean of 27 months post treatment). According to the researchers the 7th patient died from complications from an infection that preceded treatment. Furthermore, the 6 living patients saw significant improvement in associated pathology. Eczema, a constant in the life of a WAS patient, had resolved in all 6
patients, and they were all able to cease blood clotting supportive therapy. Furthermore, no vector related toxicity was observed in any of the patients, which is a problem that has marred previous gene therapy attempts. Hospitalizations were also down among the six, from a median of 25 days in the 2 years prior to gene therapy to a median of 0 days in the 2 years after the treatment.

Moving forward, the researchers acknowledge a need to increase their sample size, but the results make them hopeful. There is also hope for sufferers of other genetic diseases that involve cells derived from bone marrow stem cells to use this same method of functional gene delivery. One in particular is sickle cell anemia, a disease that is characterized by a dysfunctional version of the gene for hemoglobin and which affects 1 in 5,000 Americans.

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