

Somatic Cell Therapy: A Genetic Rescue for a Tattered Immune System?

ÉTUDE DE CAS / CASE STUDY

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Résumé

Le cas de M. Andrew Gobeau, le premier enfant à recevoir une thérapie génique expérimentale pour le déficit immunitaire combiné sévère (DICS), et une réflexion sur les implications éthiques associées à la recherche en thérapie génique.

Mots clés

cellules somatiques, la thérapie génique, la recherche expérimentale, les essais cliniques

Summary

The case of Andrew Gobeau, the first child to receive experimental gene therapy for severe combined immunodeficiency (SCID), and a reflection on the associated ethical implications of gene therapy research.

Keywords

somatic cell, gene therapy, experimental research, clinical trials

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Bryn Williams-Jones est l'éditeur en chef de la revue et directeur de thèse de Maude Laliberté.

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Conflicts of Interest

Bryn Williams-Jones is the Editor-in-chief of the Journal, and PhD supervisor of Maude Laliberté.

This case study, which is based on the PBS story "A Genetic Rescue for a Tattered Immune System?"[1], was initially published in shorter form on my website, Genethics.ca, in 2002 (<http://genethics.ca/somatictherapy.html>).

The Case

Andrew Gobeau was born in 1993 with a rare, normally fatal genetic disease – severe combined immunodeficiency (SCID).[2] SCID – which can take various forms – destroys much of the immune system, particularly the T cells, leaving newborns defenseless against infection.[3] There are a number of causes for SCID, but, in Andrew's case, he had two defective copies of the gene that codes for a critical enzyme, adenosine deaminase (ADA). Without the enzyme, the body fails to break down chemicals produced during normal metabolism that are toxic to T cells; and without T cells, there is no immunity, and with no immunity, death is inevitable.

A bone marrow transplant from a tissue-matched donor, usually a sibling, is the most common and effective treatment for SCID. Unfortunately, it is relatively rare that a person such as Andrew would find a matched donor, even within their family; as a result, they must be put on a waiting list to obtain a bone marrow transplant from an unrelated matched donor.[3] In 1993, however, a novel treatment –

experimental gene therapy – existed that offered the potential to keep Andrew alive. Working copies of the ADA gene would be inserted into the T cells, in cord blood stem cells, and then re-introduced into Andrew's system. But Andrew's condition meant that his stem cells also lacked a functioning ADA gene, so a modified virus would be used to insert a working ADA gene into these cells. The hope was that the virus would infect and then deposit the genes into enough cells to give Andrew a working immune system.

At only 4 days old, Andrew Gobeau became the first baby to receive gene therapy using cord blood cells.[4] Some of the cells did indeed take up the gene and began producing T cells with a functioning ADA gene. To insure Andrew's survival, though, he had to be given weekly injections of the missing ADA enzyme, at the time at a cost of \$2,200US per dose. These injections worked to clear the toxic metabolites out of his blood stream and allow the uncorrected T cells to survive. When Andrew was 18 months old, his doctor began tapering off the amount of enzyme in the injections, to see if the T cells that produce ADA could take over; and at four years old, he was cut off the enzyme altogether. For two months, things went well, but then Andrew caught a cold, which developed into a yeast infection of the mouth, something commonly found in immunocompromised patients. Andrew's immune system was crashing and it was necessary to resume the ADA treatment. The modified genes did not succeed in getting integrated into a sufficient number of cells to maintain the effect, and thus Andrew continues to need regular enzyme doses. The challenge for future research would be to find ways to get more cells to take up their message and keep producing the enzymes or other proteins critical for a patient's health.

Gene therapy for SCID again made the news in 2000, when two children in a clinical trial showed the development of functioning immune systems. But the clinical trial was stopped when two of the participants were found to have developed leukemia[5]. Ten years later – and 18 years since Andrew first received his treatment – and the early hopes of gene therapy for SCID are starting to show promise; most of the children in two recent studies had functioning immune systems, re-igniting the hope that a cure for SCID is near.[6]

Questions to consider:

1. Is the time and money involved in gene therapy research worth the investment given the still relatively low success rate of clinical trials? Should such economic issues not be a consideration? How would one decide?
2. Is experimental gene therapy ethically different from other novel treatments, in terms of how we should evaluate the balance of risks and benefits?
3. Does the potential benefit of gene therapy for SCID (or for other rare disease) to provide a permanent cure (instead of regular treatment) justify the risks that patients take (e.g., of developing leukemia, other cancers)?
4. What risks should Andrew, his family, and society at large consider with regards to the use of modified viruses as vectors for gene therapy?
5. Are families of children such as Andrew being given unreasonable hope that a cure is “around the corner” when they consent for their children to participate in clinical trials?

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