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X-Linked Lymphoproliferative Syndrome

Gene Therapy and XLP

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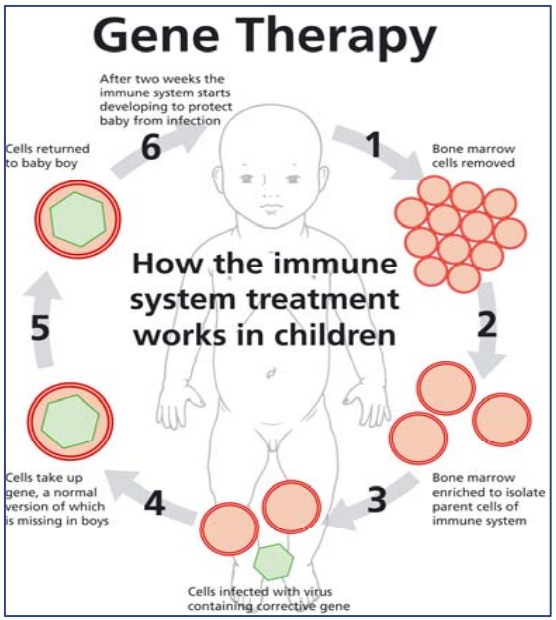
Introduction

Gene therapy is a hot topic today. It offers the potential of a whole new series of advanced treatments for a large number of medical conditions and cures for many diseases and there have been some successes in some areas, and some equally disappointing failures in others. The purpose of this leaflet is to outline how X-linked Lymphoproliferative Syndrome (XLP) sufferers could potentially benefit from this emerging science and to outline how this could work specifically for XLP.

X-Linked Lymphoproliferative Syndrome

XLP is a rare, often fatal disease that affects only boys and has profound damaging effects on the immune system. It is caused by an abnormal immune response to the Epstein-Barr (EBV) virus. In normal people EBV causes 'glandular fever' but in XLP, EBV infection may cause a number of different problems including overwhelming glandular fever, B cell lymphoma or poor immune function. The gene defective in XLP has been identified as *SAP*, a gene required for the correct function and growth of specific cells within the immune system. The only cure today for XLP is bone marrow transplantation. If a well matched donor is found, the chances of success are good but patients still undergo intensive chemotherapy and suffer from side effects of the transplant procedure. In boys who cannot find a good donor or who are very unwell coming into transplant, the chances of success are less good. Thus there is a need to develop alternative, safer ways of treating the disease. With the identification of SAP as the gene, there is the possibility to introduce a correct copy of the SAP gene into the patients own cells; a process termed 'gene therapy'. The past 5 years have seen the first successes for gene therapy in curing certain immune deficiencies and there is hope that similar approaches can be used to cure other conditions.



Gene Therapy

Gene therapy aims to transfer a healthy copy of the affected gene into the cells of a patient for therapeutic effect. For conditions such as XLP where the abnormalities are in the immune system, the gene needs to be targeted to bone marrow cells which will eventually grow into immune cells. A small number of other similar conditions have now been successfully treated using this technique. First bone marrow is extracted from the patient and then bone marrow (HSCs) stem cells are selected and purified. These cells are then cultured with a virus/vector that carries the corrective gene, in the case of XLP; the *SAP* gene. After a few days the gene will be integrated into DNA of the bone marrow cells. These gene modified cells will be returned to the patient where over the next few months they grow into a functional immune system.

Advantages of Gene Therapy

Today the only possible cure treatment for XLP is a bone marrow transplant BMT is accepted as a cure), replacing the faulty immune system. The table below outlines the main advantages of gene therapy over a bone marrow transplant.

Gene Therapy	Bone Marrow Transplant
Available to all	Available to only 70%
Repairs existing immune system	Replaces existing immune system
Limited risk of GVHD (Graft vs. Host Disease)	High risk of GVHD
Keep existing immunity	Low immunity for 2 years
Hospital stay 1 month	Hospital stay 2-3 months

But it is still early days.....

As an emerging science, gene therapy brings the potential to revolutionise many sectors of medicine including the treatment of XLP. But it is still an emerging science and whilst there have been some spectacular successes with other genetic disorders, there have also been sadly some cases where the therapy has not only failed but contributed to the death of the patient.

Conclusions

Gene therapy offers real hope for XLP affected families who cannot find suitable bone marrow donors and could become the treatment of choice for all XLP boys in the near future. However we are still some years off having a safe effective gene therapy treatment for XLP. The XLP Research Trust is committed to fund raising to ensure that gene therapy becomes a real possibility.