

Doctor Bobby Gaspar

Having trained at Kings College Hospital, I came to GOSH as a senior house officer in Immunology. I became very interested in primary immunodeficiencies and gained a PhD while working in the Molecular Immunology Unit. I continued training as an academic clinician and am now a senior lecturer/consultant in the same unit. My research programme includes clinical trials of gene therapy for severe immunodeficiencies and understanding the genetics and pathogenesis of immunodeficiencies such as XLP.



Funding body

- Primary Immunodeficiency Association

Collaborators

- GOSH: Kimberly Gilmour
- ICH: Mike Hubank, Adrian Thrasher
- INSERM429, Paris: Sylvain Latour
- UCL: Arne Akbar • University of Birmingham: Andrew Hislop

The silent killer

A devastating disease which can leave an apparently healthy boy fighting for his life has been the focus of Dr Bobby Gaspar's research.

"X-linked Lymphoproliferative syndrome (XLP) is clinically and academically a real challenge," says Dr Gaspar. It is an X-linked disease, which means it only affects boys, and then only those who have a problem with their immune system. "These children are born without any problems, making the disease more devastating. But when they get a virus – most commonly glandular fever – they can become very ill and can die."

Dr Gaspar explained that when a healthy person contracts glandular fever their glands swell, they have a fever and occasionally the liver can swell too. However, in a boy with XLP the symptoms can be very extreme – high fever, overactive glands, a very enlarged liver and, eventually, liver failure. At that point, XLP can be 95 per cent fatal. "They can also suffer from lymphoma in their gut or, following infection with the virus, their immune systems never fully recover and they get recurrent infections."

XLP is a very rare condition affecting only a few boys in every million. "It may be more common but it is not well recognised," explains Dr Gaspar. XLP was identified as a disease in 1975 and in 1998 the gene, known as SAP, was found to be the defective gene in boys with XLP. Dr Gaspar became involved with studying the disease following this identification. "We've recently been analysing blood from patients and looking at the expression of the protein – which may indicate the presence of XLP. It's allowed us to develop a quick way of making the diagnosis, enabling us to offer a national service."

Dr Gaspar and his team have been studying the immune system to work out the defect, and looking at the body's T-cells – necessary to fight viral infections such as glandular fever. "T-cells are very important for fighting viruses, especially Epstein Barr Virus (EBV) which causes glandular fever. In healthy individuals, EBV infects B-cells and causes them to grow abnormally, but because we have healthy T-cells, the growth of EBV-infected B-cells is well controlled. However in XLP sufferers, EBV-infected B-cells develop in an unregulated manner, their T-cells are very abnormal and, as a consequence, cannot control the growth of the EBV-infected B-cells. The T-cells may also be abnormal in fighting other viruses."

At present, a bone marrow transplant (BMT) is the only way forward for XLP treatment, but a BMT can be risky and weaken the child. However, Dr Gaspar and his team are looking to pursue gene therapy treatment – replacing or correcting the damaged SAP gene – which would correct the T-cells and make them fight infection. Experiments in a laboratory model have found that this treatment restored their function.

Dr Gaspar has been involved with gene therapy for other forms of immunodeficiency and has seen success in treating children using this approach. He hopes that his team can now start to develop gene therapy for XLP.

Joshua, Nathan, Luke and Daniel Hartley

In November 2003 four brothers from the Hartley family – Joshua 13, Nathan 11, Daniel eight and Luke five – were diagnosed with XLP or Duncan's Disease. The diagnosis was made at GOSH after Joshua caught a 'super bug' which his immune system could not fight.

Without a bone marrow transplant (BMT) the boys would be lucky to live through their teens. Joshua had a successful BMT at GOSH in June 2004 – his mum Allison the donor match – and despite some initial complications he has recovered well.

Daniel's bone marrow was matched with an unrelated donor and he underwent a BMT in November 2004. He made a steady recovery and returned home at the end of January 2005.

Luke and Nathan have also been found unrelated donor matches, and Nathan will have his BMT in April 2005, with Luke receiving his later in the year.

All boys will have been treated at GOSH and their prognosis for a healthy, normal life is promising.

