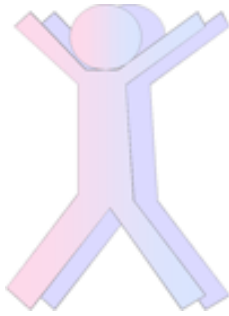


AlloStem - A World-Wide Joint Venture that will Change the Treatment of Haematopoietic Malignant Disorders



An exciting new research programme, AlloStem, funded by the European Commission and led by Professor Alejandro Madrigal (Scientific Director of The Anthony Nolan Trust), hopes to transform the treatment of leukaemia and to significantly increase the chance of survival for many patients. After a two-year-long application process and strong competition from Europe's most eminent research groups, a grant of eight million euros from the European Commission (EC) has enabled the creation of 'AlloStem'; a consortium of leading immunologists and clinical scientists dedicated to improving cancer therapies. This grant represents a watershed in European Union medical research funding and will be the largest grant the EC has ever awarded to an immunotherapy programme.

There have been important advances in the treatment of leukaemia and other haematological malignancies over the last 30 years, including improvements in chemotherapy and the use of other agents such as interferon and engineered antibodies targeting tumour-associated motifs. Despite these advances, haematopoietic stem cell transplantation (HSCT) remains the only therapy that can result in long-term disease free survival for many patients; especially those patients who suffer a relapse following initial chemotherapy. However, at present, allogeneic HSCT can carry some post-transplant complications, mainly due to recurrence or progression of the primary disease, graft versus host disease (GvHD) and infections due to immuno-protection deficiency. The AlloStem project aims to increase the number of patients that could benefit from HSCT with the use of immunotherapy. This will involve allogeneic HSCT with subsequent delivery of specific immune effector cells isolated from the donors and then expanded. Hence, the scientific and technological objectives of this project are to develop new immunotherapy strategies based on the prediction and modulation of the immune response. The outcomes hoped-for are to:

1. reduce the risk of GvHD
2. generate selective anti-tumour immune responses
3. provide protective immunity against opportunistic infections
4. extend applicability to a larger proportion of patients

These strategies may also be of use to treat other non-malignant haematological and autoimmune diseases. Thus, our deliverables will aim to develop: - novel methods to facilitate the anti-tumour effects of allogeneic stem cell grafts - methods for vaccination with novel antigens (peptides) - technology to generate specific immune cells reactive against tumours and infectious agents for active and adoptive immunotherapy - new methods for increasing short- and long-term engraftment potential of haematopoietic stem cells from different sources to generate stable chimerism as a basis for immunotherapeutic intervention and to make the procedure available for a wider spectrum of patients.

AlloStem is a joint research venture focussing on the development of new technologies in the field of stem cell transplantation and the transformation of these new technologies into clinical applications. The teams participating in this project include 29 centres-of-excellence from 13 different countries across the world. With the addition of a group of Associate Partners, AlloStem represents over 50 scientific and clinical research groups from 19 different countries. These groups comprise of leading clinicians and scientists in the fields of stem cell biology, immunogenetics, transplantation, cell processing and immunotherapy. With the wider implications of the new therapies in mind, AlloStem has incorporated advisory committees of experts in law, ethics, social science and policy regulations, together with representatives of patients and donor organisations. This represents an interactive and complementary network that, unique to this field, combines the competence and the technical skills to achieve its ambitious goals.

The groups involved have excellent performance-related backgrounds in trans-European collaborative studies and have delivered significant clinical and scientific advances over a period of more than 20 years. For example, Professors Fred Falkenburg and Els Goulmy of the Leiden University Medical Centre have made important contributions in demonstrating how donor cells, specific for genetic differences between donor and recipient, can be effective in eliminating leukaemia. Prof. Manuel Fernandez of the Hospital Puerta de Hierro (Madrid) is a leading expert in the use of different sources of stem cells for out-bone-marrow transplants. Prof. Herman Einsele (Tubingen) is, likewise, a leading expert in applying the techniques of immunotherapy to common viral diseases observed in transplant recipients and together with Prof. Franco Locatelli (Pavia) is developing therapies for the treatment of fungal diseases.

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