Dr Gerry McLachlan, The Roslin Institute, University of Edinburgh

Title: Respiratory Gene Therapy : Time to Deliver?

Abstract

Cystic Fibrosis is a genetic disease caused by mutations in the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) gene. Over 2000 mutations have been identified that have variable functional implications on the CFTR protein and the resulting disease phenotype. The rationale for developing gene therapy as a potential treatment is that, if successful, it would benefit patients with any type of mutation. The formation of the UK CF Gene Therapy Consortium (GTC), combining the expertise of three groups in the UK, has made a significant impact on progress. The combined resources enabled a thorough program of preclinical development work in animal models including inhalation studies in the sheep lung that allowed evaluation of safety and efficacy in a clinically relevant manner. These studies supported progression to the large-scale multi-dose clinical trial of the "Wave 1" non-viral gene therapy by inhalation in CF patients (2015) which reached its primary endpoint with patients who received therapy having a significant, if modest benefit in lung function compared with those receiving a placebo. The trial is the first ever to show that repeated doses of a gene therapy can have a meaningful effect on the disease in terms of the lung function of patients. The GTC are now in the preclinical development phase of a "Wave 2" product that uses a modified lentivirus to deliver DNA which we believe has significant advantages over the "Wave 1" product.

Biography

Dr McLachlan a Group Leader at The Roslin Institute. He gained a BSc Hons in Biochemistry and Immunology (1988) from the University of Strathclyde and completed his PhD at the Department of Medicine and Therapeutics, University of Aberdeen (1992). His early postdoctoral research in the lab of Prof David Porteous at the MRC Human Genetics Unit, Edinburgh involved the characterization of a Cystic Fibrosis (CF) Knock-Out Mouse model and the development of Gene Therapy for CF. He was awarded a Wellcome Trust Research Fellowship in 1998. Dr McLachlan continued in the field of CF Gene Therapy as a Senior CF Trust Research Fellow (in 2002) within the UK Cystic Fibrosis Gene Therapy Consortium (GTC) https://www.cfgenetherapy.org.uk/ and is now a member of the Consortium Strategy Group and a current Board member of the British Society for Gene and Cell Therapy (BSGCT). The main focus of his research has been developing and utilising the sheep lung as a model for pre-clinical development of CF gene therapy protocols to evaluate both safety and efficacy of candidate gene transfer agents. He has developed an interest in other models of respiratory disease/biology and in particular the application of large animal models, building on the considerable expertise developed through the GTC. Dr McLachlan is committed to advising early career scientists through his role as Divisional Postgraduate convenor and membership of the Roslin Institute Career Development Committee and the Early Career Development and Collaboration sub-

committee of BSGCT. As a STEM Ambassador, he has a strong track record in public engagement. This includes activities at the Edinburgh International Science Festival, British Science Association; Science Week and workshops, talks and careers events at a number of local Primary and High Schools.