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Blood based genomic and proteomic biomarkers for cardiac transplantation: From discovery to clinical implementation

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Solid organ transplantation is often the only treatment for end stage organ failure and has shown a dramatic increase in outcomes over the past 20 years. However, acute graft rejection remains an important clinical concern and is an adverse predictor for long-term graft survival. The current gold standard diagnostic for acute rejections remains repeated tissue biopsies - highly invasive procedures with associated risks. Using advanced genomics, proteomics and computational biology, a series of blood based diagnostic biomarkers for acute heart allograft rejection have been developed and are currently being clinically implemented to monitor timely and effective therapeutic intervention to minimize graft damage and enable knowledgeable adjustment of immunosuppressive therapy. Using a series of blood samples from over 65 transplant recipients with or without acute rejection, panels biomarkers correlating with acute rejection were generated using leukocyte mRNA and whole genome microarrays and quantitative plasma proteomics. The biomarkers were then validated using a separate series of 85 single time point samples from a cross-Canada cohort of recipients. The resulting validated panel of 10 genes exhibit excellent performance with 100% sensitivity and 74% specificity and 0.85 AUC (100% NPV and 14% PPV), that increases to 100% sensitivity and 91% specificity and 0.91 AUC (100% NPV and 32% PPV) with the addition of 6 plasma proteins biomarkers. Multiplex assays for both genomic and proteomic biomarkers are currently being developed for FDA approval for implementation in clinical laboratories and routine transplant monitoring.

Biography

Robert McMaster received a B.Sc and M.Sc from the University of BC was awarded a D.Phil. from the University of Oxford. He joined the UBC Department of Medical Genetics in 1982, and served as Head of the UBC Department of Medical Genetics and Head of Medical Genetics for the Women's Health Centre for British Columbia, 2000-2010. Dr. McMaster was also Founding Director of the Immunity and Infection Research Centre at VCH Research Institute and Director of Transplant Immunology for British Columbia Transplant until being appointed in 2008 as Vice President, Research for VCH, Executive Director, VCH Research Institute, and Associate Dean of Research, Faculty of Medicine, UBC.

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