



Dr. David Haylock
Associate Professor, Australian Stem Cell Centre (Australia)

Abstract

Cellular products to improve haemopoietic stem cell transplantation

Allogeneic and autologous haemopoietic transplantation is now a routine and important part of treatment for many haematological and non-haematological malignancies. Since first introduced there have been significant advances made to improve transplant outcomes including reduced intensity conditioning regimes, the advent of mobilized blood stem cell transplants, the use of G-CSF to assist in neutrophil recovery and better immunosuppressive agents to treat and minimize graft versus host disease. Despite these important innovations, transplant related mortality remains a major risk. Severe neutropenia and thrombocytopenia in the first few days to weeks post transplant remains as a clinical concern for a significant number of patients, especially those who have cord blood transplants.

One obvious approach to improve haemopoietic recovery following haemopoietic stem cell (HSC) transplantation is to supplement the graft with additional HSC and or *ex vivo* generated cells. The later has been tested clinically by a number of investigators and demonstrate that the rate of neutrophil and platelet recovery can be hastened by transplantation with a mixed population of *ex vivo* cultured cells. Collectively these clinical studies demonstrate that the cell dose and cell type transfused correlate with outcome. In general terms, the more precursor cells that are transplanted the faster the rate of haemopoietic recovery and the shorter the period of neutropenia and thrombocytopenia. There is abundant data describing the proliferative potential of HSC *in vivo* and *in vitro*. An ongoing challenge for experimental haematologists is to devise *ex vivo* culture systems that harness the extensive proliferative potential of HSC so that large numbers of haemopoietic cells can be generated from limited numbers of HSC. This is well exemplified with cord blood HSC: they have extensive haemopoietic potential and given the right culture conditions could generate very large numbers of immature and mature cells for the clinic. There is a need for culture systems that replicate some of the features of the HSC niche so that HSC might be expanded in number and also for non-static culture systems that facilitate growth of haemopoietic cells at very high cell density. This presentation will cover the underpinning rationale for generating “smart” surfaces for propagation of HSC and provide examples of how this can be achieved with combinations of immobilized biological ligands.

Biography

Associate Professor David N Haylock has extensive knowledge and expertise in the biology of human haemopoietic stem and progenitor cells. He made the initial observation that haemopoietic recovery following high dose induction chemotherapy for acute myeloid leukaemia was associated with a dramatic increase in the level of circulating haemopoietic progenitor cells. In collaboration with Drs Juttner and To, he pioneered autologous transplantation with mobilised blood progenitor cells, a technique that has since revolutionised haemopoietic transplantation. During the last decade, Associate Professor Haylock has focused on ex vivo manipulation of haemopoietic stem and progenitor cells for therapeutic purposes. His studies include describing the requirement of simultaneous stimulation by combinations of soluble recombinant haemopoietic growth factors for division of primitive human haemopoietic progenitors.

From 2000-2005, as Head of Experimental Cell Therapy at the Peter MacCallum Cancer Centre, Associate Professor Haylock lead Australia's first clinical trial with ex vivo expanded CD34+ cells in the setting of repetitive high dose chemotherapy for metastatic breast cancer. He was appointed as the Director of the Major National Research Facility Division of the Australian Stem Cell Centre in 2004 and continues to participate in fundamental research on haemopoietic stem cells and the haemopoietic stem cell niche in collaboration with Associate Professor Susie Nilsson. Associate Professor Haylock is currently a member of the scientific steering committee overseeing the Bioconsortium component of the CRC for Polymers which is synthesizing and testing innovative polymer based materials and surfaces for propagation of embryonic and adult stem cells.