Venue: PYRAMID 1
22nd August 2007
1515-1630 hr

**Symposium 4B: New treatment strategies**

## S4B-1. Monoclonal antibodies to harness tolerance processes in transplantation and autoimmunity

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Abstract not available at time of printing.

## S4B-2. Arsenic trioxide in cancer therapy

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Arsenic trioxide ($As_2O_3$) for leukemia treatment has been known for over a century. The recent rekindling of the interest in $As_2O_3$ is due to its high efficacy in acute promyelocytic leukemia (APL). $As_2O_3$ induces remissions in over 90% of newly diagnosed or relapsed cases of APL. Important side effects include prolongation of QT interval, leucocytosis, and the APL differentiation syndrome. Combined use of $As_2O_3$ and all trans retinoic acid (ATRA) has been found to be more efficacious in relapsed and newly diagnosed cases. To overcome the problems associated with intravenous-$As_2O_3$ administration, an oral formulation of has been prepared. Oral-$As_2O_3$ gives similar bioavailability as compared with intravenous-$As_2O_3$. Importantly, because of a low peak plasma concentration of arsenic after oral-$As_2O_3$ as compared with intravenous- $As_2O_3$, QT prolongation has been found to be insignificant, and so far no cardiac arrhythmias have been observed after oral-$As_2O_3$ therapy. Arsenic trafficking into cells is tightly regulated. The water channel protein aquaglyceroporin 9 (AQP9) has recently been shown to control arsenic trafficking, with cell lines sensitive to $As_2O_3$ typically expressing high levels of AQP9, and resistant lines low levels. In addition to APL, $As_2O_3$ has been found to be active *in vitro* against a wide array of hematologic and solid tumors. Clinical trials of $As_2O_3$ in multiple myeloma and adult T cell lymphoma / leukemia have shown encouraging results. Current research efforts center on defining the molecular targets of $As_2O_3$ in other solid tumors.

## S4B-3. Potential of mesenchymal stem cells in cell-based therapy

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Stem cells are primitive multipotent cells which are capable of regenerating themselves and differentiating into more specialized cells for replacement purpose. In the bone marrow, at least 2 types of stem cells have been identified, the haemopoietic stem cells and mesenchymal stem cells (MSCs). MSCs were first isolated in 1974 by Friedenstein et al from the bone marrow, by virtue of their ability to adhere to tissue culture glass or plastic. They have generated much interest because of its plasticity i.e. not only they are able to differentiate into target cells of mesodermal lineage, but also target cells of endodermal and ectdodermal lineages such as liver cells and neuronal cells. Besides, they have low immunogenicity and suppress alloreactive T cell response. MSCs have been reported to be used as a carrier of transduced gene for correction of inherited genetic deficiency such as adenosine deaminase deficiency and Fabry's disease. MSCs were used to improve osteogenesis with fewer fractures in osteogenesis imperfecta. If used together with haemopoietic stem cells, they were shown to reduce incidence of graft versus host diseases. As transplanted allogeneic MSCs are not rejected by the recipient, they are increasingly being explored in the repair of damaged tissue such as spinal cord injury and infarcted myocardium. In addition, their ability to differentiate across lineage into target cells holds promise as an alternative to embryonic stem cells for generating target tissues or organs for repair. More recently, MSC are observed to migrate into tumour tissues. Genetically engineered MSC with transduced cytokine genes have been shown in animal model to cause tumour regression. These observations have defined a new role for MSCs as a carrier for cell-based gene therapy for cancers.