Innovative immunotherapy for prevention and treatment of relapse following conventional chemotherapy or stem cell transplantation

Immunotherapy represents the treatment of choice against chemo-radio resistant malignant cells and cancer stem cells that are priorly resistant to anti-cancer modalities. The documented therapeutic effects of donor lymphocyte infusion (DLI) following maximally tolerated myeloablative chemoradiotherapy following allogeneic stem cell transplantation (SCT) suggests that cell-mediated immunotherapy may represent the treatment of choice for elimination of otherwise resistant malignant cells. Accordingly, we have developed a new approach for induction of graft versus malignancy (GVM) effects by intentionally mismatched IL-2 activated killers (IMAK) while avoiding GVHD following conventional chemotherapy or haploidentical SCT using reduced intensity conditioning (RIC) followed by post transplant elimination of host and donor's alloreactive T-cells for prevention of rejection and GVHD. Long term GVM effect was induced post-SCT by IL-2 activated donor NK cells prepared by negative selection of CD3+ T cells or positive selection of CD56+ NK cells. Mismatched NK cells induced most effective GVM while avoiding GVHD in patients with resistant relapsed leukemia. Short-term GVM effects with no prior SCT was accomplished by haploidentical or unrelated IMAK activated in vitro and in vivo following infusion with low dose IL-2 for 5 days. More effective and more selective GVM effects against residual cancer cells could be accomplished using monoclonal or bi-specific antibodies bound to Fc receptors on killer cells targeting killer cells against antigens over-expressed on malignant cells (e.g., Rituximab or Pinatumomab against B-cell malignancies). Using IMAK against MRD following conventional chemotherapy or SCT can result in cure of otherwise resistant hematological malignancies while avoiding GVHD.

Biography
Shimon Slavin is a Professor of Medicine, pioneered the use of personalized anti-cancer immunotherapy mediated by donor lymphocytes and innovative methods for stem cell transplantation for malignant and non-malignant disorders including treatment of autoimmune diseases and induction of transplantation tolerance to bone marrow and organ allografts. More recently, he has pioneered the use of multi-potent mesenchymal stromal cell for regenerative medicine. He has authored 4 books, 660 scientific publications and serves on many Editorial Boards and many national and international Advisory Boards. He has received many international awards in recognition of his contributions for treatment of malignant and non-malignant disorders.

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