MESENCHYMAL STEM CELLS FROM AMNIOTIC FLUID: DIFFERENTIATIVE AND PROLIFERATIVE POTENTIAL AND IMMUNO-MODULANT PROPRIETIES

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We investigated whether human amniotic fluid (AF) contains mesenchymal stem cells (MSCs) and evaluated their phenotypic characteristics, differentiation potential and immunomodulation proprieties in vitro compared to bone marrow (BM) MSCs.
AF was harvested during routine prenatal amniocentesis.
AF MSCs showed a high proliferative potential, were positive for CD90, CD105, CD29, CD44, CD73, CD166; showed Oct-4 and Nanog molecular and protein expression and differentiated into osteoblasts, adypocytes and chondrocytes. In Neural Progenitor Mantainance Medium AF-MSCs expressed neural markers and increased Na+ channel density. Inactivation of the TTX-sensitive channels accelerated and became more similar to native neuronal voltage-gated Na+ channels. CD4+CD25+ regulatory T cells significantly increased in presence of MSCs.
MSC co-cultures strongly inhibit the differentiation of monocytes to DCs. There was a significant reduction in the expression of CD83 mature DCs treated with MSCs, suggesting their skew to immature status. A decreased expression of presentation molecules (HAL-DR) and co-stimulatory molecules (CD80 and CD86) were also observed.
These data suggest that AF is an important multipotent stem cell source with a high proliferative potential able to originate potential precursors of functional neurons. These cells also showed a stronger immunosuppressive effect compared to BM-derived MSCs. This effect was mediated by inducing the generation of CD4+CD25+ regulatory cells and by suppressing monocyte differentiation into DCs, thus indicating the important role of AF-MSCs on immunoregulation.

WORKSHOP 3: IMMUNOTHERAPY

ALLOGENEIC CIK (CYTOKINE INDUCED KILLER) CELLS FOR TREATMENT OF LEUKEMIA RELAPSE

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Cytokine Induced Killer (CIK) cells are CD3/CD56 double positive T EMRA cells which have acquired also NK cells markers and functions. They show potent anti tumoral non specific cytotoxicity in vitro and in vivo as well as exquisite homing in tumor sites. Moreover allogeneic CIK cells show very little GVHD reactivity in several murine models. For these reasons, we obtained the authorization from Istituto Superiore di Sanità (Rome) to perform a phase I study with donor derived allogeneic CIK cells in patients who had been previously treated with hematopoietic stem cells transplantation but had relapsed of leukemia. This phase I study has shown lack of toxicity of allogeneic CIK cells and some positive indications of clinical activity. Therefore we subsequently obtained authorization from AIFA (Rome) to perform a phase II study of sequential administration of donor derived DLI and CIK cells into leukemia relapsed patients. The enrollment of the first three groups of patients (following an excalating design) and preliminary results will be shown. Additionally we will discuss more recent data on the functional dual T/NK nature of CIK cells and delineate the perspective of using CIK cells as a wide immunotherapy program in bone marrow transplanted patients.