AUTOLOGOUS VS. ALLOGENEIC MESENCHYMAL STEM CELLS IN NEONATAL BRONCHOPULMONARY DYSPLASIA

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BACKGROUND

• Bronchopulmonary dysplasia (BPD) - a chronic lung disease affecting primarily premature infants
• Defined as: Need for supplemental oxygen at 36 weeks post menstrual age
• Significance:
  • Mortality ~ 30%
  • Morbidity: Poor growth, Poor neurodevelopmental outcomes, and cardiovascular dysfunction.
  • Pathophysiology: Arrested alveolar development and vascular remodeling.
• Current Management:
  • All supportive
  • No known cure

• Bone-Marrow Derived Mesenchymal stem cells (MSCs) and their conditioned-media (MSC-CM) have been shown to have protective effects against the development of BPD in mouse models.
  • Act in a paracrine manner: release of immunomodulatory and vaso-protective factors.
  • MSC-CM media: has factors involved in lung development, injury, and repair possible key mediator to BPD.

• Study Question: Does human umbilical cord MSCs from BPD and non-BPD infants have similar growth and differentiation potential and secretion of biomarkers as human term umbilical cord and mouse bone-marrow derived MSCs?

OBJECTIVES

1. To isolate, culture, immunodeplete and differentiate human preterm (BPD & non-BPD) MSCs into their conditioned media relevant to neonatal BPD, utilizing advanced proteomic analysis.

METHODOLOGY

A) Specimen Collection:
  • 10 cm Segment of preterm umbilical cord in sterile PBS and/or NS collected.
B) Cell Isolation and Culture:
  • Wharton’s jelly chopped into 15mm pieces and placed in in vitro cultures.
  • D-MEM media with FBS and penicillin/streptomycin supplement used.
  • Media changed every 2-3 days, growth checked at 5 days.
  • Three different clones from three different umbilical cords generated.
  • Cells maintained in tissues culture with splitting performed at 75% confluence.

C) FACS Analysis for Immunodepletion using ISCT guidelines

1. To identify the biomarkers secreted by these MSCs into their conditioned media relevant to neonatal BPD, utilizing advanced proteomic analysis.

D) Cell Differentiation:
  • Induction of adipogenesis by culturing cells in adipogenic media.
  • Induction of osteogenesis by culturing cells in osteogenic media
E) Confluent Cultures of MSCs were incubated in serum free media x24hrs
  • Conditioned media from equal number of cells in each culture was concentrated 10-fold using a centrifugal Filter device (MW cut off of 10kD, 10-50 kD, and > 50kD)

F) Western immunoblot performed to quantify peptides present in highest concentration.

RESULTS

1. Compared to BPD UC-MSC, non-BPD MSCs has a significantly
   • Increase in function:
     o Proliferation and apoptosis
     o Cell interaction and motility
     o Immune response and inflammation
     • Decrease respiratory disease

CONCLUSION

• The human preterm BPD umbilical cord MSCs lack growth and differentiation potential compared to preterm non-BPD and term MSCs
• Human preterm BPD umbilical cord MSC may lack potential therapeutic efficacy making allogenic MSC treatment a challenge in BPD.
• Human preterm BPD and non-BPD MSC media to be tested in experimental BPD
• Understand pathways of lung injury and repair which are modulated by MSCs

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