Delivery of extracellular vesicles-encapsulated microRNA-125b produced in genetically modified mesenchymal stromal cells inhibits hepatocellular carcinoma cell growth

Silvia Baldari¹, Alessandra Magenta², Giuliana Di Rocco³, Maurizio Muraca⁴, Gabriele Toietta¹

¹ Unit of Immunology and Immunotherapy and ³ Unit of Cellular Networks and Molecular Therapeutic Targets, IRCCS Regina Elena National Cancer Institute, Rome, Italy.
² Vascular Pathology Laboratory, IRCCS Istituto Dermopatico dell’Immacolata, Rome, Italy.
⁴ Department of Women’s and Children’s Health, University of Padova, Padova, Italy.

BACKGROUND

- Extracellular vesicles (EVs) are membranous vesicles originating from several cells and released in body fluids.
- Delivery of therapeutic molecules such as miRNAs, through EVs may be an innovative avenue for cancer therapy.
- Over-expression of miRNA-125b in hepatocellular carcinoma cells (HCC) induces cell cycle arrest, inhibits proliferation, migration and invasion.
- We are currently evaluating a miRNA-125b replacement strategy for the treatment of HCC via delivery of EVs-containing miR-125b produced in engineered human stromal cells isolated from adipose tissue (ASCs).

RESULTS

Adipose tissue-derived cells is a proficient source of extracellular vesicles-encapsulated microRNA-125b (miR-125b)

(A-D) Cell proliferation and (E-H) clonogenic assays performed on human non tumorigenic (NT) adipose tissue derived stromal cells (hASC), human hepatocellular carcinoma (HCC), and colorectal cancer (CRC) cells overexpressing EVmiR125b.

EVmiR-125b overexpression in HCC cells modulates MCL-1

EVmiR-125b gene transfer into HCC cells. (A) Fluorescence analysis. (B) Immunoblot analysis of the miR-125b target MCL1, an anti-apoptotic member of the Bcl-2 family.

EV-mediated delivery of miR-125b reduces hepatocarcinoma and melanoma cells growth

Clonogenic assay quantification performed on HCC, melanoma (Mel) and CRC cells exposed to EV-containing miR-125b purified from genetically-modified hASC.

Preliminary Conclusion & Future Direction

- It is possible to produce and purify EVs containing selected tumor suppressor miRNAs from engineered ASC.
- Future studied will focus on the possibility to exploit the tumor-homing capacity of ASC genetically-modified to secrete EVs containing miR-125b in 3D and in vivo models of HCC.

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