

Therapeutic role of mesenchymal stem cells combined with nanoparticles in controlling prognosis of hepatocellular carcinoma in murine model

Mansour WA ¹, Kamel M ¹, Attia S ¹, Hussein TA ³, Abdel Fattah H ³, Mohsen R ¹

Theodor Bilharz Research Institute(TBRI), Egypt

³National Organization for Drug Control & Research, Egypt

Abstract

Mesenchymal stem cells (MSCs), represent an attractive tool for the establishment of a successful stem-cell-based therapy of liver diseases. Also, nanoparticles allow early detection and delivery of chemotherapeutic drugs to tumor site. The present study was conducted to evaluate the tumor suppressive effects of bone marrow derived mesenchymal stem cells (MSCs) with or without monoclonal antibodies conjugated nanoparticles against VEGF and CD90 in an experimental hepatocellular carcinoma (HCC) model. Serum samples were collected and analyzed for AFP, caspases-3, VEGF-A, ALT and AST. Liver sections of sacrificed animals were analyzed.

The results of the study demonstrated that BMSCs treatment caused a delayed tumor growth and a prolonged survival in mice tumor models. Histopathological examination of liver tissues of mice which received DEN showed the presence of anaplastic carcinoma cells and macro-regenerative nodules type II with foci of large and small cell dysplasia. Administration of MSCs into mice after induction of experimental HCC improved the histopathological picture which showed minimal liver cell

damage, reversible changes, areas of cell drop out filled with stem cells. Amelioration of the liver status after administration of MSCs showed a significant decrease of ALT, AST, caspase-3 enzyme and Alpha fetoprotein serum levels. The group injected with monoclonal antibodies conjugated nanoparticles against VEGF and CD90 showed significant differences in comparison to pathological control; both achieved significant decrease in all serum parameters, containing AFP, caspases-3, VEGF-A, ALT and AST. MAb-conjugated nanoparticles group showed the best improvement in liver architecture. In conclusion, Administration of MSCs in chemically induced HCC has tumor suppressive effects on tumor and is feasible to be applied in cancer treatment as evidenced by subsequent amelioration of liver histopathological pictures and functions. Also, dumbbell-like nanoparticles conjugated to CD90 and Avastin is a novel therapeutic tool for HCC totarget cancer stem cells and endothelial cells in the niche of the tumor.