

Tumor necrosis factor- α /CD40 ligand-engineered mesenchymal stem cells greatly Enhanced the antitumor immune response and lifespan in mice.

Dr. Farid Mena,

Head CIC, San Diego, CA, USA

Abstract

The interaction between mesenchymal stem cells (MSCs) and dendritic cells (DCs) affects T cell development and function. Further, the chemotactic capacity of MSCs, their interaction with the tumor microenvironment, and the intervention of immune-stimulatory molecules suggest possible exploitation of tumor necrosis factor- α (TNF- α) and CD40 ligand (CD40L) to genetically modify MSCs for enhanced cancer therapy. Both DCs and MSCs were isolated from BALB/c mice. DCs were then cocultured with MSCs transduced with TNF- α and/or CD40L [(TNF- α /CD40L)-MSCs]. Major DCs' maturation markers, DC and T cell cytokines such as interleukin-4, -6, -10, -12, TNF- α , tumor growth factor- β , as well as T cell proliferation, were assessed. Meantime, a BALB/c mouse breast tumor model was induced by injecting 4T1 cells subcutaneously. Mice ($n = 10$) in each well-defined test groups ($n = 13$) were cotreated with DCs and/or (TNF- α /CD40L)-MSCs. The controls included untreated, empty vector-MSC, DC-lipopolysaccharide, and immature DC mouse groups. Eventually, cytokine levels from murine splenocytes, as well as tumor volume and survival of mice, were assessed. Compared with the corresponding controls, both in vitro and in vivo analyses showed induction of T helper 1 (Th1) as well as suppression of Th2 and Treg responses in test groups, which led to a valuable antitumor immune response. Further, the longest mouse survival was observed in mouse groups that were administered with DCs plus (TNF- α /CD40L)-MSCs. In our experimental setting, the present pioneered study demonstrates that concomitant genetic modification of MSCs with TNF- α and CD40L optimized the antitumor immunity response in the presence of DCs, meantime increasing the mouse lifespan.

Research Interests:

Dr. Farid Mena's research interest includes Preventive Medicine, Personalized Medicine, Translational Medicine, Integrative Medicine, Green Medicine, Nano medicine, Biotechnology, and Nanotechnology.

Biography

Farid Mena (Bsc. Eng., Bsc. Bio., Msc. Genetics Master Gerontology/Geriatry, PhD Radiation Oncology and Gerontology, EMBA Entrepreneurship and MD candidate), is an inter- and multi-disciplinary professional. Professor, Principal Investigator, Director, Consultant Editor, Reviewer, Event Organizer and Entrepreneur, Dr. Mena earned his degrees with highest distinctions from prestigious French universities and institutions. Dr. Mena followed a post-doctoral in Oncology as a NIH-fellow (San Diego, California, USA; 2004-2007). Subsequently, Dr. Mena pursued his career in Dermatology, and Stem Cells as a DFG-Fellow (Wuerzburg, Germany; 2007-2009). Then, Dr. Mena was promoted as Chief Scientific Officer and Vice-President R&D at Fluorotronics, Inc. (CA, USA; 2009-2010), a nanotechnology and fluorine chemical company.

Presenting author details

Full name: Farid Mena

Affiliation: Professor, Department of Nanomedicine San Diego, California, USA

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