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## Tumor necrosis factor- $\alpha$ /CD40 ligand-engineered mesenchymal stem cells: Towards the development of a new anti-cancer vaccine

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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- $\alpha$  (TNF- $\alpha$ ) 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 co-cultured with MSCs transduced with TNF- $\alpha$  and/or CD40L [(TNF- $\alpha$ /CD40L)-MSCs]. Major DCs' maturation markers, DC and T cell cytokines such as interleukin-4, -6, -10, -12, TNF- $\alpha$ , tumor growth factor- $\beta$ , 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 co-treated with DCs and/or (TNF- $\alpha$ /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- $\alpha$ /CD40L)-MSCs. In our experimental setting, the present pioneered study demonstrates that concomitant genetic modification of MSCs with TNF- $\alpha$  and CD40L optimized the antitumor immunity response in the presence of DCs, meantime increasing the mouse lifespan.

### Biography

Farid Menaa is the Head of the Oncology, Stem Cells and Nanomedicine Department, Fluorotronics USA, Inc. and Global Innovation & Trade, Inc., San Diego, CA, USA. He got his BSc in Biomedicine and Biochemistry, BSc in Cell Biology and Physiology, Master in Genetics, National Master in Gerontology, Doctorate in Radiation Oncology and Gerontology from prestigious French Universities. He pursued his career as a Post-doc fellow and Principal Investigator in Oncology (La Jolla, CA, USA), Dermatology (Wuerzburg, Germany) and Hematology (São Paulo, Brazil). He is member of prestigious scientific and medical associations, and was the recipient of several awards. His R&D interests include the integration of innovative green techniques, technologies, methods and applications for personalized and translational medicine, in particular to improve the outcomes of cancer patients, stroke patients and to delay the anti-aging process while improving the life quality of the human beings.

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