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TUMOR NECROSIS FACTOR-α/CD40 LIGAND-ENGINEERED MESENCHYMAL STEM CELLS GREATLY ENHANCED THE ANTITUMOR IMMUNE RESPONSE AND LIFESPAN IN MICE

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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-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 inducted by injecting 4T1 cells subcutaneously. Mice (n =10) in each well-defined test groups (n=13) were co-treated 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 anti-tumor 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.

Biography

Farid Menaa is a Professor, Director and Independent Consultant of Department of Internal Medicine and Nanomedicine California Innovations Corporation, CA, USA. He is an inter- and multi-disciplinary professional with worldwide reputation. He has three international post-doctoral terms in Oncology, Dermatology, and Hematology, MBA Entrepreneurship and MD candidate. During his ongoing career, he has mainly contributed to the identification and functions of new human disease-causing genes and variants, formulated natural products for anti-aging and developed innovative theranostic strategies against cancers, cardiovascular diseases, diabetes, obesity and infectious diseases. He has more than 10 years' of experience either in the academic, hospitals or industrial sectors. As Chief Scientific Officer and Vice-President R&D at Fluorotronics, Inc. he actively participated in the development of the disruptive "Carbon-Fluorine Spectroscopy". He collaborates with various organizations worldwide. He is a Member of several prestigious medical and scientific organizations and Editorial Boards in the field of medicine, science, technology and business, including in the nano-segment. He has authored more than 100 articles including research and review articles, books, book chapters, textbooks, proceedings, and has participated to over 200 scientific international events including as co-organizer, keynote speaker, chairman. His worldwide collaborations, holistic point of view and strong expertise in various fields led him to prevent, implement early diagnosis, and develop efficient and safer therapy. His research interest includes preventive medicine, personalized medicine, translational medicine, integrative medicine, green medicine, nanomedicine, biotechnology, and nanotechnology.

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