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Abstract

The pathogenic role of mesenchymal stem cells during Systemic Sclerosis

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Abstract:
Systemic Sclerosis (SSc) is autoimmune disease, characterised by microangiopathy and fibrosis. Due to the heterogeneity, in terms of extent, severity, and rate of progression, the optimal therapeutic interventions for SSc is still lacking. One future therapeutic option may be the regenerative therapies, by using mesenchymal stem cells (MSCs), displaying immunomodulatory, angiogenic and antifibrotic capabilities and counteracting the three main pathogenic axes of SSc. Considering the therapeutic potential of these cells, we largely studied MSCs isolated from SSc patients (SSc-MSCs), reporting the evidence that SSc-MSCs may be primed toward a profibrotic profile, playing a pathogenetic role during SSc. In vitro results show that SSc-MSCs, although senescent, may display immunosuppressive and regulatory properties, such as the ability to induce functional Tregs as well as to inhibit the proliferation of peripheral blood mononuclear cells [1]. Conflicting results have been reported concerning their angiogenic properties. Although SSc-MSCs overexpress bioactive mediators and pro-angiogenic growth factors in vitro, these cells, in presence of endothelial cells from patients with SSc, switch from architectural and metabolic supporting cells to migratory and profibrotic cells [2], probably involved in the pathogenic steps that from the endothelial damage may lead to fibrosis. Furthermore, perivascular SSc-MSCs may be committed to trans-differentiate toward activated myofibroblasts [3], expressing high levels of CD248, modulating the molecular target responsible to fibrosis [4]. Additionally, we reported an in silico comparative analysis of miRs profile of MSCs isolated from different sources (bone marrow and adipose tissue) of SSc patients, showing that, independent from the source, SSc-MSCs display disease inherent abnormalities [5], suggesting that these cells might contribute to the disease progression.

From a translational point of view, a better knowledge of pathogenic role of SSc-MSCs, might allow us, in the future, to better select and potentially manipulate the MSCs to improve the development of MSC-based therapy for SSc.

Biography:
Roberto Giacomelli is Professor of Rheumatology, Director of the Rheumatology Clinical Unit and Director of Department of Biotechnological and Applied Clinical Sciences, at University of L'Aquila, L'Aquila, Italy. He was recipient of grants supported by PRIN, Ministry of Health and Ministry

of Research, for his research in the field of Scleroderma. He is also recipient of competitive grants in other inflammatory diseases (HORIZON 2020 and ASPIRE 2016). He participates in numerous international scientific groups including European Scleroderma Study Group (EU), Scleroderma Clinical Trial Consortium (USA), Eular Scleroderma Trial And Research group (EUSTAR) (EU), Autologous Stem cell Transplantation International Scleroderma Trial (ASTIS TRIAL) (EU). He is a referee for several Journals in the fields of Rheumatology and Clinical Immunology and is the author of over 200 published scientific articles, reviews and book chapters. He has been involved in phase II, III, IV clinical studies according to GCP.

Publication of speakers:

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