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FasL Pleiotropic Role on Bone Marrow Stromal Cells and its Potential Regulation by Micro RNAs

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Several lines of evidence suggest a pleiotropic role of FasL/CD95 on BM-MSC function. Although FasL was initially described as a T-cell-associated protein capable of inducing apoptosis by binding to its receptor Fas, a pleiotropic role in other cell populations has also been described. Fas engagement in resting T lymphocytes transduces inhibitory or costimulatory signals in a FasL dose-dependent manner, and in hematopoietic progenitors FasL receptor transduces dual apoptotic and trophic signals. Fas and FasL are expressed in freshly isolated BM–MSCs. However, cell death induction does not seem to be the Fas/FasL system's main role in bone homeostasis. Fetal BM have functional extrinsic apoptotic pathways, whereas adult BM–MSCs are resistant to Fas-mediated apoptosis. FasL has a limited role in osteoblast and osteoclast apoptosis, but inhibits osteoblast differentiation in mice. We investigated the effect of FasL on BM–MSC apoptosis, proliferation, and differentiation into adipocytes to clarify the role of the Fas/FasL system in BM–MSC biology. FasL exerts a pleiotropic action on BM–MSCs depending on its concentration: low doses induce proliferation, whereas higher doses have a slight but significant apoptotic effect and, more importantly, inhibit adipogenesis; all such effects are exerted without affecting BM–MSC stemness, irrespective of dosage. Our findings show a FasL-dependent regulation of BM– MSC biology and adipogenesis, and suggest a role for FasL in conditions involving altered BM adipogenesis, such as osteoporosis in the elderly. Furthermore, our unpublished data show a modulation of several miRNAs during BM-MSC adipogenesis, Several of those regulating Fas/FasL expression, are cellular and circulating markers of aging and inflamm-aging (miR-21, miR-146a, miR-98 and miR-181a), Interestingly, plasma soluble Fas ligand concentration decrease whereas miR-21 miR-146a increase in elderly humans. Altogether these data suggest a functional axis involving miRNAs, Fas/Fasl system, bone marrow adipose tissue and aging.

Biography:

Dr. Maria Rita Rippo was a student at the Department of Experimental Medicine, Policlinico Umberto I, of the University of Rome "La Sapienza 1993 –1994. She obtained her Degree in Biological Sciences from the University of Rome "La Sapienza", in 1995. She has done her PhD from 1994-2001 Department of Experimental Medicine and Biochemical Sciences, Laboratory of Signal Transduction, including a 4 months collaboration and training period at the laboratory of "Apoptose, Cancer et Immunologie", CNRS, Villejuif, Paris, France, directed by Guido Kroemer M.D. for Immunological Sciences & In 2000 she got the Fondazione Adriano BuzzatiTraverso post-doctoral fellowship, Department of Experimental Medicine and Biochemical Sciences, University of Rome "Tor Vergata" Laboratory of Signal Transduction. She was research fellow from 2001-2002 at Polytechnic University of Marche. Worked as a Researcher and consultant (2009- 2010) at the Center of Clinical Pathology and Innovative Therapies, Italian National Research Center on Aging (INRCA-IRCCS). Obtained her Specialization in Clinical Pathology (2015) University G.d'Annunzio, Chieti, 70/70 cum laude. Since 2002-2016 she is a Researcher in Experimental Medicine, Pathophysiology and Clinical Pathology Department of Molecular Pathology and Innovative Therapies, Polytechnic University of Marche. And is presently an Associate Professor in Applied Medical Technologies, Department of Molecular Pathology and Innovative Therapies, Polytechnic University of Marche.