Sima T. Tarzami, J Mol Biomark Diagn 2011, 2:4
doi: http://dx.doi.org/10.4172/2155-9929.S1.6

OMICS Group Conferences
Accelerating Scientific Discovery

2nd World Congress on
Biomarkers & Clinical Research

12-14 September 2011 Baltimore, USA

Myocardial CXCR4 interaction with β2-adrenergic receptor: a potential therapeutic approach for congestive heart failure

Sima T. Tarzami

Cardiovascular Research Center, Mount Sinai School of Medicine, USA

Chemokines are small secreted proteins with chemoattractant properties that play a key role in inflammation, metastasis, and embryonic development. We previously demonstrated a nonchemotactic role for one such chemokine pair, stromal cell-derived factor-1α and its G-protein coupled receptor, CXCR4. Stromal cell-derived factor-1/CXCR4 are expressed on cardiac myocytes and have direct consequences on cardiac myocyte physiology by inhibiting contractility in response to the nonselective β-adrenergic receptor (βAR) agonist, isoproterenol. As a result of the importance of β-adrenergic signaling in heart failure pathophysiology, we investigated the underlying mechanism involved in CXCR4 modulation of βAR signaling. Our studies demonstrate activation of CXCR4 by stromal cell-derived factor-1 leads to a decrease in βAR-induced PKA activity as assessed by cAMP accumulation and PKA-dependent phosphorylation of phospholamban, an inhibitor of SERCA2a. We determined CXCR4 regulation of βAR downstream targets is β2AR-dependent. We demonstrated a physical interaction between CXCR4 and β2AR as determined by coimmunoprecipitation, confocal microscopy, and BRET techniques. We assessed the effect of cardiac overexpression of CXCR4 during TAC using a cardiotropic adeno-associated viral vector (AAV9) carrying the wildtype CXCR4 gene (AAV9.CXCR4^{WT}). Cardiac overexpression of CXCR4^{WT} in mice with pressure overload prevented ventricular remodeling and maintained function as determined by echocardiography and in vivo hemodynamics. The CXCR4 interaction with β2AR will provide further insight into how CXCR4 modulates calcium homeostasis and chronic pressure overload responses in the cardiac myocyte. Together these results suggest that AAV9.CXCR4 gene therapy is a potential therapeutic approach for congestive heart failure.

Biography

Dr. Sima Tarzami received her B.Sc. and M.Sc. degrees from Hofstra University, New York, and her Ph.D. from Albert Einstein School of Medicine, New York, all in USA from 1992-2002. She has been a faculty in Mount Sinai School of Medicine since 2007, first as a Research Instructor and then promoted to an Assistant Professor of Medicine. Her major area of research is related to myocardial expression, signaling and function of chemokine receptor-4 in the animal models of heart disease. She currently holds a Grant in Aid from the American Heart Association, and KO2 from the NIH. She is an author of 14 peer reviewed papers and 10 published abstracts. She is a member of editorial board of international journal of clinical and experimental medicine (IJCEM) and also a manuscript reviewer of number of major journals including AHA.