Jun Li, Orthop Muscul Syst 2014, 3:2
http://dx.doi.org/10.4172/2161-0533.S1.016

OMICS Group Conferences
Accelerating Scientific Discovery

3rd International Conference and Exhibition on
Orthopedics & Rheumatology
July 28-30, 2014 DoubleTree by Hilton Hotel San Francisco Airport, USA

A novel epigenetic mark, Histone H1 fucosylation, regulates macrophage plasticity in Rheumatoid arthritis

Jun Li
University of Alabama at Birmingham, USA

Macrophages are the central players in the pathogenesis of Rheumatoid arthritis (RA) and are considered as important therapeutic targets in RA.They produce a number of inflammatory mediators and their professional antigen-presenting role has also been implicated in the pathogenesis of RA. High plasticity renders macrophagesan attractive tool for studying epigenetic reprogramming. A highly positive correlation between *TNFα* and fucosyltransferases *(FUTs) 1, 2, 3, 4, 5, 6, 7, 9, 10, 11* (p=0.0001) was observed in human RA synovial tissues. In sorted cells from RA synovial fluid, *FUTs* 1, 3, 5, 7, 9 (terminal and sub-terminal fucosylation) were highly expressed in M1 inflammatory macrophages, but not in M2 macrophages, synovial fibroblasts, and T cells ($p<0.01$), whereas *FUTs* 8 and 13 (core- and O-fucosylation) were predominately expressed in synovial fibroblasts. This highly indicated that terminal and sub-terminal FUTs are associated with the inflammatory M1 macrophagephenotypes.A fucosylation inhibitor, 2-Deoxy-D-galactose (2-D-gal) precluded the development of collagen II-induced arthritis in DBA/1J mice (scores 9.5±1.7 vs 0.5± 0.3, $p<0.01$) with reduced M1 macrophages in draining LN, decreased TNF-α and anti-CII in the serum ($p<0.05$). Ulex Europaeus Agglutinin I (UEA 1) pull down followed by mass spectrometry analysis indicated that the linker Histone H1 is the major protein that modified by a fucose-α-(1-2)-gal moiety in M1 macrophages. Disrupting this fucose modification by 2-D-galnot only altered the chromatin structure but also skewed the differentiation of M1 macrophages toward a M2 anti-inflammatory phenotype with a reprogrammed gene expression, including i)upregulated *Arg1, Megf8, Gsta1/2* and Hmox1 ($p<0.05$); ii) downregulated *Apol7c, Areg, Kynu, Fscn1, Ifnγ, Il6, Il12, Ly6c*, and *H2-Ab1*($p<0.05$). The studies identified that Histone 1 fucosylation is a novel epigenetic mark that orchestrates inflammatory macrophage plasticity andfucosylation inhibitor is a novel therapeutic strategy for RA.

Biography

Jun Li has received his MD from Sun Yat-sen University and his PhD (Physiology) and postdoctoral training (Immunology & Rheumatology) from University of Alabama at Birmingham (UAB). He is currently a faculty at the Division of Clinical Immunology and Rheumatology, UAB. He focuses on developing novel therapies for Rheumatoid arthritis (RA) and his major research interests include targeting M1 inflammatory macrophages in RA, regulation of macrophage plasticity by fucosylation in RA, and the bidirectional interaction between macrophages and T cells in RA. His research is funded by Arthritis Foundation. He has received multiple awards from The American Association of Immunologists (AAI). His research has also been recognized by Rheumatology Congress UK.He has served as a reviewer for *Arthritis and Rheumatism, Clinical Rheumatology* and other reputed journals.

junliuab@uab.edu