Fucosylation, a key player and a novel therapeutic target in Rheumatoid Arthritis
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Inflammatory macrophages (MΦ) play key roles in the pathogenesis of rheumatoid arthritis (RA). We have observed an upregulation of Fucosyltransferases (FUTs) expression in RA synovial tissues compared to that of osteoarthritis (OA). There is a highly positive correlation between TNFα with FUTs 1, 2, 3, 4, 5, 6, 7, 9, 10, 11, 12 (p=0.0001), but not FUTs 8 and 13 in human RA synovial tissues. In sorted cells from human RA synovial fluid, FUTs 1, 3, 5, 7, 9 were highly expressed in M1 inflammatory MΦ, but not in M2MΦ, synovial fibroblasts, and T cells (p<0.01), whereas FUTs 8 and 13 were predominately expressed in synovial fibroblasts. This highly indicated that expression of subsets of FUTs might associate with the inflammatory M1 MΦ characteristics and that inhibition of these FUTs might result in the resolution of inflammation. Indeed, a FUT1/2 inhibitor, 2-Deoxy-D-galactose (2-D-gal), precluded the differentiation of M1 MΦ derived by GM-CSF from mouse bone marrow or human PBMC monocytes. Additionally, 2-D-gal treatment of fully differentiated M1 MΦ for 2 days significantly reduced their uptake, processing and presentation of GFP-Ea(from I-Edα)and FITC-Collagen II (CII) antigens (p<0.01). In vivo, 2-D-gal treatment dramatically blocked bovine CII-induced arthritis (scores 9.5±1.7 vs 0.5±0.3, p<0.01) with reduced inflammatory MΦ in draining LN (1.3±0.3% vs 0.5±0.1%, p<0.05), decreased TNF-α (130 vs 39 pg/ml, p<0.05), and anti-CII in the serum. Together, our study indicated that fucosylation orchestrates M1 MΦ differentiation and function, and is a novel therapeutic target in RA.

Biography
Jun Li received his M.D. from Sun Yat-sen University and his Ph.D. and postdoctoral training from University of Alabama at Birmingham (UAB). He focuses on developing novel therapies for autoimmune diseases including rheumatoid arthritis. He is currently an Instructor of Medicine at UAB. His major research interests include targeting M1 inflammatory macrophages in RA, determining the pathogenic roles of fucosylation in RA, and identifying the bidirectional interaction between macrophages and T cells in RA. His work is supported by an Arthritis Foundation Post-doctoral Fellowship Award.

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