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Direct LPS recognition and activation of CD8⁺ T cells via TLR4 in patients with rheumatoid arthritis

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Toll-like receptors (TLRs) have been established to recognize specific patterns of microbial components and lead to systemic immune responses in rheumatoid arthritis (RA). TLRs are expressed by cells in inflamed joints of RA patients and variety of endogenous TLR ligands is present within those joints. This study suggests that the over expression of TLR4 in CD8⁺ T cells from RA patients may contribute to the abnormal immune activation of pro inflammatory cytokines and enhance the acute inflammation. We analyzed the expression of TLR4 in transcript level by real-time PCR and protein level by flow cytometry in CD8⁺ T cells of RA patients. Different cytokines level was checked after stimulation of CD8⁺ T cells in TLR4 agonist and TLR4 inhibitor. A significant increase of TLR4 in both transcript level and protein level in patients with RA compared to healthy donors ($p < 0.001$). We found that the surface expression of TLR4 on CD8⁺ T cells directly correlates with disease severity ($r_s = 0.96$). Moreover, these CD8⁺ T cells respond to the TLR4 ligand lipopolysaccharide (LPS) and express robust amounts of cytolytic and inflammatory molecules including TNF α and IFN γ . After inhibiting TLR4 we found a normal level expression of inflammatory cytokines in CD8⁺ T cells of patient. An increased expression of TLR4 on peripheral CD8⁺ T cells of RA patients and its role in skewing CD8⁺ T cells towards activated and inflammatory phenotype; thereby playing a significant role in pathogenesis and progression of RA.

Biography

Tripathy Archana is a PhD Scholar of KIIT University, Bhubaneswar, India. Her research interests focus around the improvement of physical function and quality of life of rheumatoid arthritis patients. In particular she is interested in the mechanisms that drive inflammation which is common in rheumatoid arthritis, but are under researched.

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