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Author: Steven O'Reilly

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Toll Like Receptors in systemic sclerosis: an emerging target

Short title: TLRs scleroderma

Steven O'Reilly PhD*

Faculty of Health and Life Sciences,

Northumbria University,

Ellison Building,

Newcastle Upon Tyne,

United Kingdom

*Corresponding author email address: steven.o'reilly@northumbria.ac.uk

Highlights

- TLRs are critical in systemic sclerosis
- Activation of TLRs can be mediated by dangers signals from damaged cells
- DAMPs may mediate fibrosis via TLR-dependant release of TIMPs

Abstract

Pattern Recognition Receptors are critical receptors that elicit an immune response upon their activation that culminates in activation of NF-KB and cytokine secretion. Key among these receptors are the Toll-Like Receptors (TLRs). These evolutionary conserved receptors form a key part in the defence against various pathogens and comprise a key part of the innate immune system. Systemic sclerosis is an autoimmune disease in which a breach of tolerance has occurred and leads to fulminant autoimmunity, dysregulated cytokines, pro-fibrotic mediators and activation of fibroblasts leading to fibrosis via collagen deposition. It has become apparent in recent years that the innate immune system and specifically TLRs are important in disease pathogenesis; responding to internal ligands to initiate an innate immune response ultimately leading to release of a variety of factors that initiate and perpetuate fibrosis. This review will examine the recent evidence of TLR signalling in systemic sclerosis and the internal danger associated molecules that may mediate the fibrotic cascade. Evaluation of their contribution to disease in systemic sclerosis and possible therapeutic targeting will be discussed.

Introduction