MODULATION OF TREM1 SIGNALING IN MACROPHAGES INFECTED WITH Aspergillus fumigatus

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INTRODUCTION

Pattern recognition receptors (PRR) play a central role recognizing Aspergillus fumigatus components and initiating immune responses in the lungs1. In the last few years, a new family of PRRs, called TREM, has been identified, of which TREM1 was the first to be characterized2. TREM1 is constitutively expressed in myeloid cells such as neutrophils and macrophages3. TREM1 potently synergizes with Toll-like receptors (TLRs) for a substantial amplification of the immune response and production of pro-inflammatory mediators such as TNFα, IL1β, IL6 and CXCL14. TREM1 has both activator and inhibitory isoforms. For this reason the blockade of TREM1 with small molecules and peptides is being studied as a possible therapy target4.

OBJECTIVES

1. To investigate the functional effect of TREM1 deletion on the TLRs mediated signaling pathway against A. fumigatus.
2. To study the immunomodulation of the TREM1 response during antifungal therapy.
3. To study the pharmacological inhibition of TREM1 with blocking peptides and the effects on the immune response.

CONCLUSIONS

1. TREM1 modulates the TLR signaling in macrophages by altering the expression of both receptor and effector proteins that are critical to the response against A. fumigatus.
2. The possibility of modulating the inflammatory response in a favorable direction through the TREM1 pathway may represent a new approach for the development of novel immunotherapeutic antifungals to treat patients with invasive Aspergillosis.

REFERENCES


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