Deciphering the role of polysialic acid in the macrophage response to Mycobacterium tuberculosis infection.

Mycobacterium tuberculosis (Mtb), the ethological agent of human tuberculosis, causes approximately 1.8 million deaths worldwide each year. During Mtb infection, Macrophages serve the dual role as the major host cell for Mtb replication, and as the cell that is primarily responsible for eliminating or containing the infection. In 2010, a genome-wide siRNA screen performed in Mtb-infected human macrophages has highlighted the potential involvement of the gene ST8SIA4 in regulating Mtb survival and intracellular multiplication. ST8SIA4 encodes a glycosyltransferase involved in the synthesis of the sugar polymer named polysialic acid (PolySia), but little is known about its role during immune response. Here, we showed that ST8SIA4 is highly expressed in pro-inflammatory human blood monocyte-derived macrophages polarized with IFNg or LPS/IFNg. Higher ST8SIA4 expression correlates with a strong expression of PolySia in the Golgi compartment and at the cell surface. In addition, our preliminary data suggest that PolySia can be released from the cell surface upon LPS stimulation or bacterial infection. In order to decipher the role of ST8SIA4 and PolySia in macrophage effector functions against bacteria, we are currently developing tools, including ST8SIA4-deficient mouse and human macrophages as well as ST8SIA4-deficient mice.

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