

2nd International Conference on

AUTOIMMUNITY

November 06-07, 2017 | Frankfurt, Germany

Rab7b participation on the TLR4 endocytic pathway in hemolytic uremic syndrome

P Valles^{1,2}, A Gil Lorenzo^{1,2}, A Lafalla¹, V Bocanegra^{1,2}, V V Costantino^{1,2}, M E Benardon¹ and V Cacciamani^{1,2}¹University of Cuyo, Argentina²CONICET, Argentina

The inflammatory response of host endothelial cells to Shiga toxin and/or lipopolysaccharides (LPS) of *E. coli* is included in typical HUS. LPS stimulation of toll like receptor (TLR4) activates signal transduction pathways leading to proinflammatory cytokine secretion. The TLR4-LPS complex is rapidly internalized and TLR4-induced inflammatory signaling is stopped by targeting the complex for degradation. Rab7b, a small GTPase expressed in monocytes, regulates the later stages of the endocytic pathway. We studied the Rab7b participation on the TLR4 endocytic pathway and its effect on monocyte intracellular cytokine production along the acute course of HUS. The studies were performed in monocytes from HUS patients by flow cytometry and immunofluorescence confocal microscopy. Surface TLR4 expression determined by flow cytometry in CD14(+) monocytes from 16 HUS patients remains unchanged at onset and significantly increased by day four compared to 10 healthy children monocytes. Significant higher cytoplasmic TLR4 protein expression was accompanied by increased proinflammatory intracellular cytokines, tumor necrosis factor alpha (TNF- α), and interleukin 6 (IL-6) in HUS monocytes at days one and four vs. controls. On the contrary, monocytes display decreased surface TLR4 expression and significant reduction of intracellular TNF- α and IL6 levels released in a time-dependent manner after a disease follow up of 6 to 10 days. Furthermore, immunofluorescence confocal microscopy proved co-localization of increased intracellular TLR4/Rab7b determined by Pearson's coefficient in monocytes from HUS patients on day one. The highest co-localization of both proteins in monocytes was shown by day four, and then decreased TLR4/Rab7b co-localization was shown 10 days after HUS onset. The co-localization of TLR4 and Rab7b allows us to suggest that Rab7b participates in the control of the TLR4 endocytic pathways in HUS patient monocytes. A consequential fall in cytokine production throughout the early follow up of HUS is demonstrated.

pvalles@fcm.uncu.edu.ar

Notes: