First description of human innate response immunomodulation by Uropathogenic Escherichia coli (UPEC)

Escherichia coli, a gram-negative bacterium commensal to humans, is the most common agent isolated in 75-95% of acute urinary tract infections of bacterial origin. The one responsible for these urinary infections is called Uropathogenic Escherichia coli (UPEC). Once there is a lack of information in scientific literature regarding human innate immune response, especially DCs (dendritic cells) and UPEC interactions, we decided to perform experiments to reveal such data. Therefore, DCs were obtained from peripheral blood monocytes from healthy donors cultured with the V27 (isolated from human urosepsis) and J96 (isolated from a pyelonephritis case) strains of UPECs for 24 hours. After the DCs-UPECs interaction, we observed that both strains showed the same ability to infect DCs, with no significant difference concerning colony forming unit (CFU). In addition, both strains induce significant changes in DC morphology, causing cell death and reducing the number of recovered cells, especially for the V27 strain. In J96 recovered cells, we observed a significant presence of cells PI+ (from 1,87 +/-0,38% in control DCs to 6,07 +/-1,28%). Cells were also analyzed by flow cytometry to evaluate the expression of relevant surface molecules such as CD11c, CD1a, CD83, CD62L, CCR7, CD209, HLA-DR, CD86, CD80, CD40 and CD274. Among these molecules, J96 caused a significant decrease in CD11c expression (from 96,67 +/- 1,24% in negative control to 66,77 +/-10,44 %) and CD1a expression (from 42,28 ± 10,23% to 24,32 ± 5,66%). DC-SIGN (CD209) was significantly inhibited by UPEC (from 62,20+/-6,45% in control to 22,57 +/- 4,96%), CD86 (from 60,67+/-8,19% to 36,59+/-10,80%) and HLA-DR (from 86,56+/-5,58% to 36,59+/-10,80%). In conclusion, we observed that both UPECs strains were able to infect monocyte derived DCs, inducing morphologic alterations and cell death for some of those. In the surviving ones, UPECs seem to negatively regulate the expression of relevant DC markers and costimulatory molecules, including HLA-DR. In this way, these phenomena may reflect in a poor antigen presentation and T lymphocyte activation, favoring pathogen establishment and disease development.

Keywords : Acute urinary infection, dendritic cells, HLA-DR
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