TITLE: PIC FROM *Escherichia coli* INDUCES AN INTENSE INFLAMMATORY RESPONSE BY MACROPHAGES

AUTHORS: LIMA, Y.A.[1]; DUTRA, I.L.[1,2]; NASCIMENTO, J.R.[1,2]; VALE, A.A.M.[1,2]; SOUSA, E.M.[3]; SILVA, R.M.[4]; ELIAS, W.P.[5]; NASCIMENTO, F.R.F.[1,2]; ABREU, A.G.[2,3]

[1]*Laboratory of Immunophysiology, Federal University of Maranhão, São Luís, Brazil;*
[2]*Programa de Pós-Graduação em Ciências da Saúde, Federal University of Maranhão, São Luís, Brazil;*
[3]*Programa de Pós-Graduação em Biologia Parasitária, UNICEUMA, São Luís, Brazil;*
[4]*Departamento de Microbiologia, Imunologia e Parasitologia, Escola Paulista de Medicina, Universidade Federal de São Paulo, São Paulo, Brazil;*
[5]*Laboratório de Bacteriologia, Instituto Butantan, São Paulo, Brazil.*

Escherichia coli strains are important pathogens responsible for a variety disease, and albeit using distinct mechanisms of pathogenesis, some have in common the production of Pic, a serinoprotease involved in colonization. The aim of this study was to investigate the action of Pic on macrophages. The ability of bacteria to induce macrophage polarization to M1 or M2 (pro-inflammatory and anti-inflammatory profile, respectively), as well as the cytokines and nitric oxide (NO) production were evaluated after infection of RAW264.7 macrophages. Macrophages were incubated with Pic-producing *E. coli* (F5), F5Δ*pic* mutant or purified Pic for 6, 12 and 24 h. Immunophenotyping was performed using specific antibodies and analyzed by flow cytometry. Six hours after infection, an increase in NO production was observed in all groups infected with bacteria, being statistically significant in the cells infected with *E. coli* F5. Interestingly, purified Pic induced an intense NO production, as well as the cytokines IL-6, MCP-1 and TNF-α. On the other hand, there was no statistically significant IL-10 production among groups. In addition, the immunophenotyping also showed a high expression of pro-inflammatory markers (IaIe and LyC6) on the cells infected by Pic or Pic-producing bacteria. Trerefore, this work showed that Pic has a high potential to induce M1 macrophage polarization with intense inflammatory response.

Keywords: Pic, Macrophages, Cytokines, Nitric oxide, Inflammation.

Development Agency: Fundação de Amparo à Pesquisa e ao Desenvolvimento Científico e Tecnológico do Maranhão (FAPEMA).