

**PIC PRODUCED BY *Escherichia coli* BINDS TO EXTRACELLULAR MATRIX
AND COAGULATION CASCADE COMPONENTS**

GOMES, J. V.¹; SILVA, L. B.¹; SOUZA, M. C. L.²; GONÇALVES, M. B. S.³; ELIAS,
W. P.²; BARBOSA, A. S.² and ABREU, A. G.^{1,3*}

¹*Programa de Pós-Graduação em Ciências da Saúde, Federal University of Maranhão,
São Luís, Brazil;*

²*Laboratory of Bacteriology, Butantan Institute, São Paulo, Brazil;*

³*CEUMA University, São Luís, Brazil.*

The serinoprotease Pic (protein involved in colonization) is an autotransporter protein produced by Enteroaggregative *E. coli* (EAEC), *Shigella flexneri* and *Citrobacter rodentium*. Pic has several biological roles such as hemagglutination, mucinolytic activity, degradation of factor V of the coagulation cascade and cleavage of leukocyte surface glycoproteins, which are involved in trafficking, migration and inflammation. Our group has demonstrated its ability to act on the human complement system thus conferring the bacterium the ability to circumvent the host's innate defense mechanisms, favoring the development and maintenance of sepsis. Thus, the aim of this study was to investigate the action of Pic on the components of the extracellular matrix and the blood coagulation cascade. For this purpose, Pic (HB101/Pic) and non-Pic (HB101) - producing *E. coli* culture supernatants, as well as BSA were incubated at different times with several coagulation cascade molecules (plasminogen, fibrinogen and fibrin) and extracellular matrix (type I collagen, type IV collagen, decorin, laminin and plasma fibronectin) to evaluate binding and/or degradation of these components. In addition, a plasminogen activation assay was also performed, since its activation product, plasmin, is a key molecule in the formation of clots and the activation of other pathways of the immune system. According to our results, the culture supernatant of HB101/Pic was capable of significantly binding to collagens type I and IV, laminin and fibronectin, as well as plasminogen. Furthermore, Pic-bound plasminogen was converted to its active form, plasmin, in the presence of the exogenous activator urokinase (uPA). We believe that the serine protease Pic produced by the bacterium binds to the extracellular matrix through various components, thus facilitating the infectious process in the host. Plasmin generated in the presence of Pic may also contribute to a synergistic effect on the degradation of complement system molecules, as well as to deregulated and increased activation of the blood coagulation cascade.

Keywords: Pic; extracellular matrix, coagulation cascade, plasmin, plasminogen.