

POSTER PRESENTATION

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Effect of Pile4 of *Francisella tularensis* subsp. holarctica (live vaccine strain) to brain endothelium

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From The 1st Conference on Neglected Vectors and Vector-Borne Diseases (EurNegVec): with Management Committee and Working Group Meetings of the COST Action TD1303 Cluj-Napoca, Romania. 8-11 April 2014

Francisella are rare, highly infectious vector-borne bacteria, which infect more than 250 host species, including humans. *Francisella* are able to invade multiple organs in the host body, such a skin, liver, lung and central nervous system. To invade various organs, *Francisella* have to cross the cell linings like endothelial barriers. Interaction with endothelial cells is multistage process, which includes adhesion and activation of signaling events. Our previous work has shown that *Francisella tularensis* subsp. *holarctica* Live Vaccine Strain (LVS) interacts and adhere to endothelial cells through Pile4 and Inter-cellular adhesion molecule 1(ICAM-1) interaction. To corroborate consequences of Pile4 adhesion to endothelial cells, we incubated brain microvascular endothelial cells with recombinant Pile4 protein and assessed the regulation of several genes with qRT-PCR. Results showed that Pile4 upregulated the expression of adhesion molecules (ICAM-1 and PECAM-1), matrix metalloproteases (MMP 1, MMP 3 and MMP 9) and molecules that are involved in pathogen recognition (TLR-6, MyD88, IRAK-1 and TRAF-6) in brain endothelium. On the other hand, we found down regulation of interleukins and NF-kB. Inhibition of NF-kB indicates that *Francisella* might use NF-kB subversion mechanism to evade immune response. This mechanism is described in other pathogens such as *Listeria* and *Yersinia*. Previous studies have showed that matrix-metalloproteases, mainly MMP-9, is crucial to disrupt cytoskeleton of brain endothelium to increase the permeability of BBB. In summary, work reveal hidden aspects of invasion and translocation of *Francisella* across the brain

endothelium, that offers new insight into the pathobiology of neuroinvasion of *Francisella*.

Acknowledgements

This work was supported by APVV-0036/10, VEGA-1/0054/12 and structural funds for centers of excellence-26220120002 (INFEKTZOON). E.B and L.B. are funding for post-doctoral studies from ITMS 26220220185.

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Published: 1 April 2014

doi:10.1186/1756-3305-7-S1-P10

Cite this article as: Bencurova et al.: Effect of Pile4 of *Francisella tularensis* subsp. *holarctica* (live vaccine strain) to brain endothelium. *Parasites & Vectors* 2014 **7**(Suppl 1):P10.

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