Face to Face Interaction of Bacteria with Bio-surfaces

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INTRODUCTION: The interface between disease-causing bacteria and bio-surfaces are the microenvironment where bacterial virulence factors can be sensed by certain receptors on the host cells. Upon exposure to bacterial virulence factors including their surface antigens downstream inflammatory can be developed. In this presentation two dissimilar model bacteria, *Treponema denticola* and *Neisseria gonorrhoeae*, was used to discuss the consequences of exposure to their surface proteins.

METHODS: The major outer sheath protein (Msp) of the periodontal pathogen, *Treponema denticola* was enriched through a two-step isolation procedure using non-ionic detergents. Disassembly of actin cytoskeleton upon exposure to Msp was investigated with a barbed-end fluorescent labeling method. The functional impact of actin cytoskeleton disorganization was determined with an *in vitro* scratch wound migration assay in fibroblast monolayers and a videomicroscopy migration assay in neutrophils. The role of opacity protein (Opa) of *Neisseria gonorrhoeae*, the causative agent of gonorrhea was studied in a humanized mouse model. A vaginal infection model and an air pouch model were used to study the interaction between the surface protein Opa with the carcinoembryonic antigen-related cell adhesion molecules (CEACAMs) on the host cells.

RESULTS: Msp-treated fibroblasts became oval in shape and lost their actin cytoskeleton in the center while the control vehicle-treated cells maintained their stellate shape (Fig.1). Msp pretreatment had a significant inhibitory effect on the migration of the fibroblasts across a collagen substratum and inhibited the neutrophil chemotactic migration towards a chemoattractant. To test if CEACAM expression in transgenic mice can make a difference in terms of gonococcal colonization we conducted a vaginal infection with Opa-expressing *N. gonorrhoeae* strains. On day 3 post-infection, gonococci were able to colonized CEACAM transgenic mice to a higher degree compared to wild type mice. To assess the *in vivo* capacity of human CEACAM-expressing neutrophils to be recruited by *N. gonorrhoeae*, and consequent production of pro-inflammatory cytokines we took advantage of an air-pouch model of infection. When CEACAM-expressing mice were injected sub-dermally with *N. gonorrhoeae*, a substantially increased number of neutrophils and pro-inflammatory cytokines could be observed in the air pouch as compared to wild-type mice.

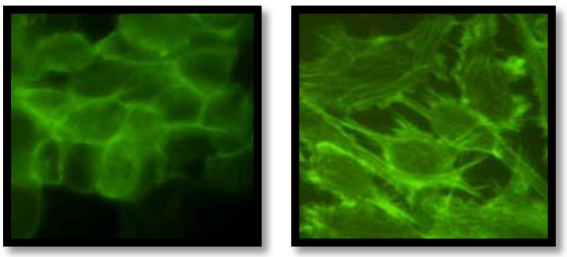

Fig. 1: Effect of major outer sheath protein (Msp) of T. denticola on fibroblasts: Stressed Msp-treated fibroblasts (left) vs. normal (happy) fibroblasts (right).

DISCUSSION & CONCLUSIONS: Both bacterial surface proteins, Msp and Opa can mediate mucosal damages through either disturbing fibroblast function[1] or recruiting neutrophils and productions of pro-inflammatory cytokines. CEACAMS are believed to be target molecules for various bacterial surface proteins including Opa[2].

REFERENCES: [1] M Amin, AC Ho, JY Lin et al. (2004). Induction of de novo subcortical actin filament assembly by Treponema denticola major outer sheath protein (Msp). *Infect Immun*. June; [2] E Klaile, TE Klassert, I Scheffralm et al. (2013) Carcinoembryonic antigen (CEA)-related cell adhesion molecules are co-expressed in the human lung and their expression can be modulated in bronchial epithelial cells by non-typable Haemophilus influenzae, Moraxella catarrhalis, TLR3, and type I and II interferons. *Respir Res*. 14(1).