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Role of citokynes and growth factors in affecting P. aeruginosa infection in murine cell models

Pseudomonas aeruginosa is a Gram negative bacteria associated with chronic lung infections. P. aeruginosa is able to: i) control complement; ii) produce proteases, toxins, and lipases, which inhibit the function of the cells of the immune system (phagocytes, NK cells, T cells), inactivate several cytokines (IL-1, IL-2, IFN-gamma, TNF), cleave immunoglobulins and inactivate complement; iii) resist to phagocytosis by biofilm formation. Interestingly, P. aeruginosa establish an immune modulation in the host shifting immune responses away from host protective Th1 responses to pathogen protective Th2 responses[1]. In fact, C3H/HeN and BALB/c, generally known as Th1 and Th2 responders, were challenged with P. aeruginosa and C3H/HeN presented a lower mortality in comparison with BALB/c mice. P. aeruginosa was cleared more efficiently in C3H/HeN mice and significantly more C3H/HeN mice showed normal lung histopathology[2].

Interestingly, Qa2 molecules, the murine homolog of human HLA-G[3], are characterized by an immune inhibitory function and are up-regulated during pathogen infections[4]. Our preliminary results obtained from the analysis of bronchoalveolar lavage fluids (BALs) from P. aeruginosa challenged mice showed an increased expression of Qa2 in presence of P.aeruginosa infection. Since Qa2 acts as a tolerogenic and anti-inflammatory molecule, we hypothesized that P. aeruginosa is able to induce Qa2 expression inducing an immune-inhibited environment that in turn protects bacteria from host immune system through a mechanism of immuno-escape.

The purpose of this project is to test the effect of different cytokines and growth factors from the ImmunoTools IT-Box-Cy55M on the P. aeruginosa virulence. We are mostly interested in analysing the different effect of rm EGF in LL/2 murine lung epithelial cell line and rm IL-10, rm IL-6, rm IL-17A, rm IFN-gamma in IC-21 murine macrophage cell line.

We will evaluate the effect of these molecules on P. aeruginosa growth and virulence and on cell activation and Qa2 expression.
The results obtained will represent an important start point to improve our knowledge on the role of environmental cytokines on P. aeruginosa infection in lungs and the effect on host immune cells during chronic infection. These data could allow the identification of new therapeutic strategies to reduce and prevent P. aeruginosa and biofilm forming bacteria chronic lung infection.

References
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3. Lau P, Amadou C et al. Characterization of RT1-E2, a multigenic family of higly conserved rat non-classical MHC class I molecules initially identidief in cells from immunoprivileged sites. BMC Immonol 2003; 4:7.

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ImmunoTools IT-Box-Cy55M for Daria Bortolotti
includes 55 recombinant mouse cytokines

rm EGF, rm Eotaxin / CCL11, rm FGF-a / FGF-1, rm FGF-b / FGF-2, rm FGF-8, rm Flt3L / CD135, rm G-CSF, rm GM-CSF, rm GRO-a / CXCL1, rm GRO-b / CXCL2, rm IFNgamma, rm IL-1alpha, rm IL-1beta, rm IL-2, rmIL-3, rm IL-4, rm IL-5, rm IL-6, rm IL-7, rm IL-9, rm IL-10, rm IL-11, rm IL-13, rm IL-15, rm IL-16, rm IL-17A, rm IL-17C, rm IL-17F, rm IL-19, rm IL-20, rm IL-21, rm IL-22, rm IL-25 / IL-17E, rm IL-27, rm IL-31, rm IL-33, rm IP-10 / CXCL10, rm LIF, rm MCP1 / CCL2, rm M-CSF, rm MIP-1α/ CCL3, rm MIP-1β / CCL4, rm MIP3α / CCL20, rm MIP3β / CCL19, rm NGF-beta, rm PDGF-AA, rm PDGF-BB, rm RANTES / CCL5, rm sCD40L / CD154, rm SCF, rm SDF-1α / CXCL12a, rm SDF-1β / CXCL12b, rm TNFα, rm TPO, rm VEGF DETAILS