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Infections in cystic fibrosis patients: effect of PTX3 genetic variants on endogenous PTX3 production and function

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Background. PTX3 is a component of innate immunity involved in resistance to infections. In previous research projects funded by Fondazione Ricerca Fibrosi Cistica, our group demonstrated the therapeutic potential of PTX3 in Pseudomonas aeruginosa and Aspergillus fumigatus infections and showed that specific PTX3 genetic variants are associated to P. aeruginosa infection in cystic fibrosis patients and in A. fumigatus infection. Both in infectious and inflammatory conditions, PTX3 behaves as a potential diagnostic and prognostic biomarker. PTX3 is under development for the transfer to the clinic as therapeutic tool for opportunistic infections and as diagnostic/prognostic marker in inflammatory conditions.

Hypothesis and objectives. The main objectives were to investigate whether PTX3 plasma levels and PTX3 production by leukocytes could represent a novel diagnostic and prognostic marker of inflammation and infection in CF patients and/or a marker of defective functional activity of leukocytes.

Essential Methods. PTX3 levels were analysed in plasma and breath samples of CF patients and in monocytes in response to LPS stimulation.

Results. PTX3 plasma levels were analysed in P. aeruginosa infected CF patients at admission to the hospital for revaluation and antibiotic treatment, and end of hospitalization. Results obtained indicate that PTX3 levels were increased in all patients, in comparison to the value considered normal in healthy donors, however, the analysis did not reveal statistical significant associations between PTX3 levels and clinical parameters. In only one patient PTX3 levels were below the normal value (2 ng/ml) both at admission and discharge, suggesting defective PTX3 production. PTX3 levels were not detectable in breath samples. The analysis of the production of PTX3 and IL-8 by monocytes collected from CF patients showed that most patients (7/9) poorly responded to LPS and did not produce increased levels of PTX3 upon stimulation. Unresponsiveness to LPS also included the production of IL-8 in 4 out of 9 patients. These results are in agreement with previous studies suggesting a state of tolerance to LPS of CF monocytes.

Spin-off for research & clinical purposes. The analysis of PTX3 plasma levels is potentially useful in identifying defective production of PTX3 in CF patients and improving the transfer to the clinic of PTX3 as therapeutic molecule.

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