Role of PTX3 in Cystic Fibrosis-associated infections

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Titre du colloque	Second Meeting of the ECMM/ISHAM Working Group Fungal respiratory infections in Cystic Fibrosis (Fri-CF)
Auteur	Hamon, Yveline [1], Person, Christine [2], Giniès, Jean-Louis [3], Bouchara, Jean-Philippe [4], Delneste, Yves [5]
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Résumé en anglais	PTX3, a soluble innate immunity receptor, binds to selected microbes and facilitates their clearance by phagocytes. PTX3 selectively binds to *Pseudomonas aeruginosa* and *Aspergillus fumigatus*, two microorganisms frequently colonizing the airways of patients with cystic fibrosis (CF), and sometimes causing true respiratory infections. PTX3 -/- mice are sensitive to *A. fumigatus* infection, highlighting the role of this protein in the protection against this pathogen. We thus hypothesized that PTX3 could be altered in CF patients and that this could be responsible, at least in part, to their susceptibility to some opportunistic pathogens. Serum and sputum samples from 30 CF patients (20 adults and 15 children) and 7 patients with chronic obstructive pulmonary disease (COPD) as the control group were analyzed for PTX3 expression and integrity by ELISA and Western-blotting, respectively. The role of endogenous or microbial proteases on recombinant human PTX3 was also analyzed. Results showed that PTX3 level was increased in CF and COPD serum, highlighting their infectious/inflammatory status, while, in contrast, PTX3 concentration was lower or undetectable in CF sputum than in COPD. Western-blotting showed that PTX3 is degraded in sputum samples from most of CF patients, but not in clinical specimens from COPD patients. The degradation of PTX3 was shown to be mediated by serine proteases. More precisely, both the neutrophil elastase and the alkaline proteinase from *A. fumigatus* have the ability to degrade *in vitro* PTX3. This study which shows that PTX3 is degraded in respiratory secretions from CF patients, provide new insights into the pathogenesis of microbial colonization of the airways and respiratory infections in CF patients, since degradation of PTX3 could be responsible, at least in part, for the sensitivity of CF patients to some opportunistic infections.
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