



Title	Neutrophil Extracellular Traps in Bronchial Aspirates : A Quantitative Analysis
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論文内容の要旨

Synopsis of Thesis

氏 名 Name	濱口 重人
論文題名 Title	Neutrophil Extracellular Traps in Bronchial Aspirates: A Quantitative Analysis (Neutrophil Extracellular Trapsの生体内動態に関する検討 - 痰中NETsの定量的評価)
論文内容の要旨 〔目的 (Purpose)〕 Neutrophil extracellular traps (NETs) are structures composed of DNA and granular proteins. NETs are thought to be a part of innate immunity and it rapidly traps and kills pathogen. Although the formation of NETs has been observed during infection, their role in vivo is still unclear. The purpose of this study is to quantified the NETs in sputum by measuring length of NETs, and to assess the association between NETs expression and various inflammatory cytokines. 〔方法 (Methods)〕 We examined the sputum collected from the intubated patients admitted to the ICU during the period from April to June 2011. Samples were collected at the onset of acute respiratory infection (= day0), day1, day3-5, and day6-8 thereafter. To identify NETs, DNA, histone H3, and citrullinated Histone H3 which are the components of NETs were simultaneously visualized by immunohistochemistry. The length of NETs was quantified using computed tracing software. 〔成績 (Results)〕 Nine patients met the criteria for this research. With all samples, the mean length of NETs was measured and compared at each time-point. There was significant difference between measure points by ANOVA for repeated measures ($p<0.001$). The lengths of NETs at day1 after the onset of infection were significantly longer than those at the onset day ($p<0.001$). The lengths of NETs at day 6-8 were significantly shorter than those at day1 ($p<0.05$). These results suggested that NETs in sputum are escalated in response to respiratory infection. Moreover, to evaluate the meaning of mean length of NETs, the time course of mean length of NETs was compared with the following clinical data (Body temperature, SOFA score, APACH II scare, WBC, Platelet, CRP, D-dimmer, lactate, procalcitonin, TNF-α, IL-6, IL-8, CXCL-2, HMGB-1, and E-selectin) with stepwise multiple regression analysis. As a result, four parameters (WBC, CXCL-2, lactate, IL-8) are selected as explaining variables. The time course of these four parameters had been correlated with the length of NETs. 〔総括 (Conclusion)〕 NETs reflect some part of disease progression in respiratory infections. Quantification of NETs in sputum might have a potential as a novel inflammatory biomarker.	

論文審査の結果の要旨及び担当者

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	論文審査の結果の要旨
	Neutrophil Extracellular Traps (NETs) は自然免疫の一つとして病原体を捕獲し排除する機能を持つとされるが、ヒトにおけるNETs と臨床病態との関連は未だ不明である。 本申請者は、急性呼吸器感染症における痰中NETsの動的変化を検討した。挿管患者を対象とし、急性呼吸器感染症と診断した患者の痰中NETsをグラム染色および免疫蛍光三重染色を用いて経時的に観察した。さらにNETsの定量的評価を用いて、NETs が急性呼吸器感染の発症に応答して吸引痰中に著明に発現し、病勢の改善とともに寸断化され徐々に減少することを明らかにした。 生体内でのNETsの定量的動態を明らかにした研究はこれまでになく、今後の臨床への応用にも期待できるものがあり、学位の授与に値すると思われる。