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IDO与Treg在支气管哮喘小鼠中的相互作用及其意义

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Title: Interaction of indoleamine 2, 3-dioxygenase and $CD4^+CD25^+Foxp3^+$ regulatory T cell in asthmatic mice

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关键词: 吲哚胺2; 3双加氧酶; 调节性T细胞; 支气管哮喘; 实时荧光定量PCR; 流式细胞术

Keywords: indoleamine 2; 3-dioxygenase; regulatory T cell; asthma; real-time fluorescence-based quantitative PCR; flow cytometric analysis

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摘要: 目的 探讨吲哚胺2，3双加氧酶(indoleamine 2,3-dioxygense，IDO) 与$CD4^+CD25^+Foxp3^+$调节性T细胞（Treg）之间的相关性及在支气管哮喘发病机制中的作用。 方法 BALB/c小鼠用随机数字表法分成对照组和哮喘组，每组8只。哮喘组以鸡卵清蛋白（ovalbumin ,OVA）致敏，激发小鼠建立哮喘模型，无创肺功能仪检测气道反应性，支气管肺泡灌洗液(BALF)进行细胞学分析，ELISA检测BALF中INF-γ、IL-4、IL-10浓度，实时荧光定量PCR检测肺组织IDO和Foxp3 mRNA表达，免疫组织化学方法检测IDO蛋白表达，流式细胞仪检测Treg占$CD4^+$细胞的百分率。 结果 哮喘组小鼠气道反应性、BALF中细胞总数、嗜酸性粒细胞比例及IL-4浓度明显高于对照组($P<0.01$)；而INF-γ与IL-10浓度、IDO和Foxp3的mRNA表达、IDO蛋白表达、Treg占$CD4^+$细胞的百分率明显低于对照组($P<0.01$)；对照组与哮喘组IDO与Foxp3的mRNA表达呈正相关（$r=0.819$，$r=0.807$,$P<0.05$），对照组与哮喘组IDO蛋白表达与Treg占$CD4^+$细胞的百分率呈正相关（$r=0.783$,$r=0.765$,$P<0.05$）。 结论 哮喘小鼠IDO和Foxp3表达降低，Treg数量减少，且IDO蛋白表达与Treg占$CD4^+$细胞的百分率呈正相关，表明IDO与Treg相互调节，打破免疫耐受，诱导哮喘发生。

Abstract: Objective To explore the interaction and the role of indoleamine 2,3-dioxygenase (IDO) and $CD4^+CD25^+Foxp3^+$ regulatory T cell (Treg) in a mice model of allergic bronchial asthma. Methods BALB/c mice were sensitized and

challenged by ovalbumin (OVA). Penh were measured to evaluate the airway responsiveness by noninvasive lung functional instrument. Bronchoalveolar lavage cytology was analyzed. IFN-γ, IL-4 and IL-10 in BALF were detected by enzyme-linked immunosorbent assay (ELISA). The mRNA expression of IDO and Foxp3 was measured by real-time fluorescence-based quantitative PCR. The protein expression of IDO was detected by immunohistochemistry. The percentage of Treg in $CD4^+$ cells was assessed by flow cytometry. Results The airway responsiveness, the total cell number, the eosinophils and IL-4 in BALF of the asthmatic group significantly increased as compared with the control group (P<0.01). The levels of IFN-γ and IL-10 in BALF, the mRNA expression of IDO and Foxp3, the protein expression of IDO, and the percentage of Treg in $CD4^+$ cells in the asthmatic group were significantly lower than those in the control group (P<0.01). The mRNA expression of IDO and Foxp3 was positively correlated with each other (r=0.819, 0.807, P<0.05). The protein expression of IDO was positively correlated with the percentage of Treg in $CD4^+$cells (r=0.783, 0.765, P<0.05). Conclusions IDO and Treg reciprocally regulate each other, which surmounts immune tolerance and induces asthma. Therefore, IDO and Treg may play important roles in asthma.

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