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Title: ROG negatively regulating the expression of T cell cytokines through modulation on ICOS

Dr. Yuan-Sheng 27557 Zang doctorzangys@163.com MD , Dr. Yong-An 27558 Liu doctorliuya@163.com MD , Dr. Zheng 27559 Fang doctorfangz@163.com MD , Dr. Bing 27560 Li doctorlib@163.com MD and Dr. Qing-Yu 27561 Xiu doctorxiuqy@163.com MD . ¹ Department of Respiratory Medicine, Changzheng Hospital, Second Military Medical University, Shanghai, China, 200003 .

Body: Background. ROG, can simultaneously suppress expression of Th1 and Th2 cytokines. Since suppression of Th2 cytokines by ROG via suppression of GATA-3 is well understood, it is postulated that there are other molecular targets of ROG that can suppress expression of the Th1 cytokines. Based on the current theory, we hypothesized that ROG might suppress CD3, CD28, or ICOS, which can up-regulate the expression of T lymphocyte cytokines, or indirectly stimulate the expression of CTLA-4 or CD45, which can down-regulate the expression of T lymphocyte cytokines. Methods. Real-time quantitative PCR and Western Blot were performed to evaluate the mRNA and protein levels of CD3, CD28, ICOS, CTLA-4, and CD45 in Th1 and Th2 cells under various levels of ROG expression. ELISA was performed to measure the levels of IFN- γ and IL-4 in culture media of Th1 and Th2 cells. Results. The mRNA and protein levels of ROG were relatively low in Th1 and Th2 cells ($P < 0.01$). After ROG-pcDNA3.1 transfection, the mRNA and protein level of ROG was significantly elevated, while the expression of ICOS, IFN- γ , and IL-4 was markedly down-regulated ($P < 0.01$). Transfection of ROG-siRNA led to inhibition of ROG expression and up-regulation of ICOS, IFN- γ , and IL-4 ($P < 0.01$). The expression levels of CD3, CD28, CTLA-4, and CD45, however, did not change in both ROG-pcDNA3.1- and ROG-siRNA-transfected Th1 and Th2 cells ($P > 0.05$). Conclusions ROG can inhibit the expression of Th1 and Th2 cytokines by down-regulating the expression of ICOS, which could be a potential regulating target for asthma treatment.