EXPRESSION OF THE ANG II TYPE 1 RECEPTOR ON HUMAN $CD4^{+}CD25^{+hi}$ REGULATORY T CELLS

Rasini Emanuela, Marino F., Guasti L., Ferrari M., Legnaro M. Schembri L., Venco A., Lecchini S., Cosentino M.

Department of Clinical Medicine, University of Insubria, Varese, Italy

The immune system is a key modulator in atherosclerosis (ATH). Increasing body of evidence suggests that T helper type 1 (Th1)-driven responses are detrimental to the atherosclerotic process, and that the Th1/Th2 balance controls ATH progression. $CD4^{+}CD25^{+hi}$ regulatory T (Treg) cells are key regulators of immune homeostasis, and it has been recently hypothesized that these cells may have a role in the control of ATH. Since it is well known that angiotensin II (ang II) through the activation of its type 1 receptor (AT_1R) is involved in the modulation of inflammatory processes in the vascular wall and that AT_1Rs are expressed on human leukocytes with subset-specific patterns [1], the aim of the present study was to investigate the expression of AT_1R on human Tregs.
The expression of AT_1Rs was evaluated as both mRNA (by real-time PCR, results expressed as AT_1R mRNA Ct / 18 S rRNA Ct) and cell surface protein (by flow cytometry, results expressed as either frequency [% of total] of AT_1R positive cells or AT_1R density on positive cells [mean fluorescence intensity - MFI]). To this end, venous blood was obtained from 5 healthy donors, and $CD4^{+}CD25^{+}$ and $CD4^{+}CD25^{-}$ T cell subsets were either isolated by immnunomagnetic cell sorting or identified on purified $CD4^{+}$ T cells using flow cytometry.
The AT_1R mRNA levels were significantly higher in $CD4^{+}CD25^{+hi}$ with respect to $CD4^{+}CD25^{-}$ cell subsets (1.96±0.15 vs 0.88±0.26, $P<0.001$). Two-color flow cytometric analysis revealed that $CD4^{+}$ T cells extensively expressed AT_1Rs (frequency = 92.4±1.8, MFI = 5.03±1.75). Among CD4+ T cells, AT_1R density was lowest in $CD25^{-}$ (MFI = 4.38±1.58), intermediate in $CD25^{+}$ (7.48±2.02, $P<0.05$ vs CD25-), and highest in $CD25^{hi}$ (11.16±2.58, $P<0.001$ vs CD25- and $P<0.05$ vs CD25+).
In view of the relevance of immune-mediated mechanisms and of AT_1R-operated pathways in ATH, the presence of AT_1Rs on $CD4^{+}CD25^{+}$ T cells warrants further studies to assess their functional relevance as well as their possible contribution in the response to pharmacotherapy.

[1] Rasini E, Cosentino M, Marino F, Legnaro M, Ferrari M, Guasti L, Venco A, Lecchini S. (2006) Angiotensin II type 1 receptor expression on human leukocyte subsets: a flow cytometric and RT-PCR study. Regulatory Peptides 134:69-74.