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Hyaluronan-binding T regulatory cells in human peripheral blood

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Regulatory T cells (Tregs) either natural or induced, play an important role in maintaining immune homeostasis. Alterations in the number and functions of Tregs have been involved in tumor growth, autoimmune disease and other immune pathologies. One of the possible mechanisms that contribute to the ability of Tregs to maintain peripheral tolerance involves interaction with extracellular matrix hyaluronan (HA). The ability of Tregs to bind HA is related to their activation state. Previous research showed highly enhanced suppressor function of HA-binding CD4+CD25+ Tregs after stimulation in mice. Considering the importance of HA-binding subset of Tregs we investigated their presence in human peripheral blood under normal physiological conditions. Freshly isolated CD4+ cells from peripheral blood of healthy donors (n=12) were incubated with HA immobilized on MACSi Beads. Then cell suspension was separated into HA-binding (HA+) and HA-nonbinding (HA-) fractions by immunomagnetic separation. Freshly obtained HA+ showed higher percentage of CD4+CD25+FOXP3+ natural Tregs compared with HA- (23.3±13.1, 10.4±7.8, p=0.03, Wilcoxon test). Elevated percentage of CD4+ CD25+FOXP3+ natural Tregs in HA+ was also observed after overnight incubation of the cells with polyclonal stimulus anti-CD3/anti-CD28/anti-CD2 (Treg Suppression Inspector, Miltenyi) (15.3±7.5, 2.9±0.5, p=0.02,Wilcoxon test). Moreover higher percentage of CD4+FOXP3+ Tregs was demonstrated in HA+ compared to HA- (15.6±2.4, 4.0±0.6, p=0.01, Wilcoxon test). CD4+FOXP3+ subset of HA+ showed increased expression of suppressive molecule CTLA4 compared to the subset of HA- (23.6±4.5, 11.8±4.8, p=0.04, Wilcoxon test). Other functional markers as GITR, IL-10, TGFβ, LAP were indistinguishable between HA+ and HA- CD4+CD25+FOXP3+ and CD4+FOXP3 Treg subsets. Thus we show that peripheral blood of healthy donors contains a small population of pre-activated Tregs that intensively bind immobilized high molecular HA and maintain their suppressive phenotype during stimulation. The results suggest that these cells can represent an important subpopulation of activated circulating Treg cells with CD4+FOXP3+CTLA4+HA+ phenotype that may have implications for the mechanisms of peripheral tolerance.

Biography

Yuliya Perfilyeva graduated five-year combined Bachelor's and Master's program in Biology from Al-Farabi Kazak National University, Almaty, Kazakhstan, in 2006. She is currently a PhD student at Al-Farabi Kazak National University and also a Scientific Researcher at the laboratory of Molecular Immunology and Immunobiotechnology of Aitkhozhin's Institute of Molecular Biology and Biochemistry, Almaty, Kazakhstan. Her current research interests include tumor immunology, innate immunity, T cell immunity.

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