T cell is reduced in bone marrow of ARHGAP21 heterozygous mice which might be related to reduction of CXCR7 recycling to the membrane resulting in lower migration

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ARHGAP21 protein is a RhoGAP family member that interacts with PKCζ and FAK, which are downstream proteins of the CXCL12/CXCR4 pathway. This pathway is critical for migration, retention and development of hematopoietic cells. Our group developed a mouse model with reduced expression of ARHGAP21 (Arhgap21⁺⁻ mice) and this model showed that this protein has a role in migration, adhesion and homing of hematopoietic stem cells suggesting that ARHGAP21 may be a strong candidate for CXCL12/CXCR4 axis regulation. Recently, CXCR7 was identified as GPCRs, another CXCL12 ligand receptor, but its contribution to hematopoiesis is still unknown. Given the lack of information, the aim of our study was to verify the relationship of ARHGAP21 with CXCR4 and CXCR7. Then, we immunophenotyped hematopoietic cell populations in the bone marrow of Arhgap21⁺⁻ mice by flow cytometry and compared with the wild-type littermates. The analysis showed a reduction of T lymphocytes (CD4⁺ and CD8⁺; p=0.02, Mann-Whitney test), erythroblasts (Ter119⁺, p=0.01) and myeloid cells (Gr1⁺Mac⁺, p=0.02). There was no difference in B lymphocytes (B220⁺). Regarding the receptors, CXCR7 was significantly lower expressed in T lymphocytes membrane (p = 0.002). No difference in CXCR4 expression was observed in any cell type. Moreover, peripheral blood showed a significant reduction in CD8⁺ cells (p=0.04) but similar amounts of CD4⁺ cells in Arhgap21⁺⁻ animals compared to the wild-type mice. Thymus did not show difference in CD4⁺ and CD8⁺ populations. Based on these results, we hypothesized that the reduction of T cell migration to the bone marrow, in Arhgap21⁺⁻ mice, may be related to a reduction in CXCR7 in the membrane of the cells and therefore, lower attraction to the CXCL12 ligant. Therefore, since GPCRs recycling to the membrane needs β–arrestin association, experiments aiming to analyze the relationship of β–arrestin and ARHGAP21 is currently underway.

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References


