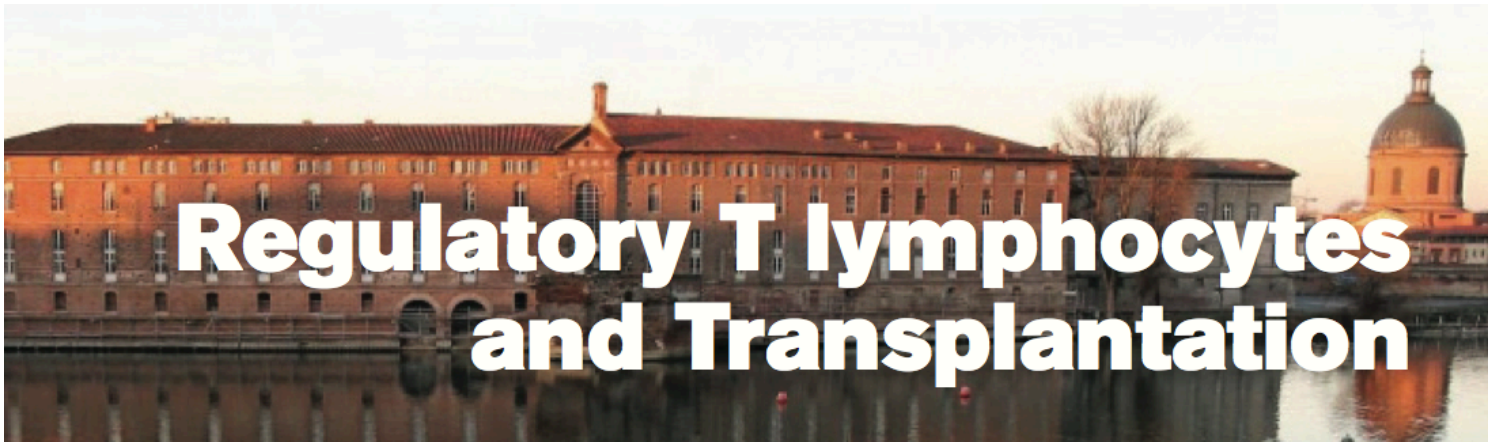

Homeostasis of the thymic pool of regulatory T lymphocytes

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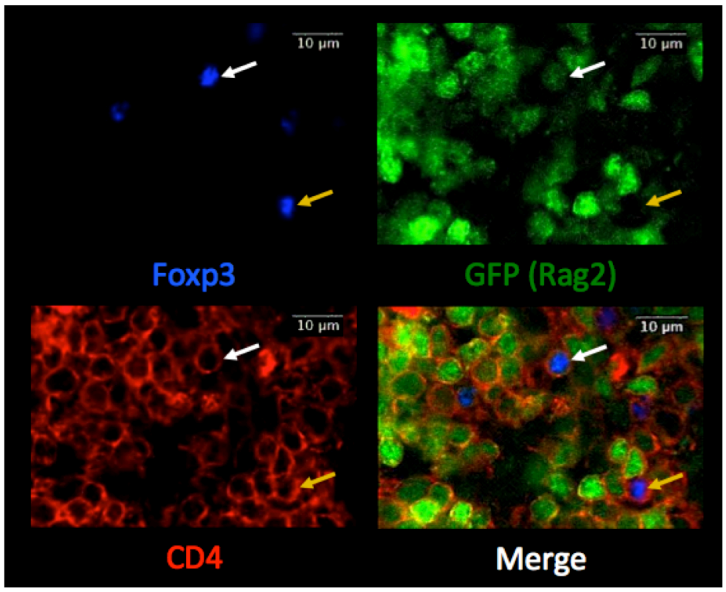
Regulatory T lymphocytes develop as a separate lineage in the thymus and they can also differentiate from conventional T cells during peripheral activation under specific conditions. The number of thymic Treg is very stable: Even in experimental systems in which "all" thymic precursors have the potential to develop into the Treg lineage, only limited numbers of cells appear to do so. We have investigated if the thymic niche limits the number of Treg developing in the thymus. When only very small numbers of precursors can develop into T cells, strongly increased proportions of Treg were observed. However, our data demonstrate that this phenomenon is due to delayed kinetics of development and thymic egress of Treg. It therefore appears that the thymic niche does not limit Treg development in the thymus in our experimental system. We also observed that mature peripheral Treg can recirculate back to the thymus. In adult animals, recirculating cells can represent more than half of the pool of thymic Treg. Peripheral modulation of the TCR repertoire of Treg is thus reflected in the thymus. Also the phenotype of thymic Treg is heavily influenced by peripheral events. Our data indicate the importance of clearly identifying recirculating cells when analyzing thymic Treg development. They also suggest a role for recirculating Treg in T cell development and/or differentiation.



Recirculating Treg are found in the thymic medulla. A thymus from a RAG2-GFP mouse was stained with antibody to Foxp3 and CD4. Note the presence of $CD4^{+}Foxp3^{+}$ cells that are green (upper arrow) or not (lower arrow). The green cells are newly developing thymocytes, the cells that have lost RAG2-GFP had recirculated back from the periphery (B. Binet)