Pere H, Montier Y (co-first authors), Bayry J, Quintin-Colonna F, Merillon N, Dransart E, Badoual C, Gey A, Ravel P, Marcheteau E, Batteux F, Sandoval F, Adotevi O, Chiu C, Garcia S, Tanchot C, Lone YC, Ferreira LCS, Nelson BH, Hanahan D, Fridman WH, Johannes L, Tartour E. (2011). A CCR4 antagonist combined with vaccines induce antigen-specific $CD8^+$ T cells and tumor immunity against self antigens. *Blood 118*: 4853-4862.

Regulatory T cells (Tregs) may impede cancer vaccine efficacy in hematologic malignancies and cancer. CCR4 antagonists, an emergent class of Treg inhibitor, have been shown to block recruitment of Tregs mediated by CCL22 and CCL17. Our aim was to demonstrate the ability of a CCR4 antagonist (a small chemical molecule identified in silico) when combined with vaccines to break peripheral tolerance controlled by Tregs, a prerequisite for the induction of CD8(+) T cells against self Ags. Immunization of transgenic or normal mice expressing tumor-associated self Ags (Her2/neu, OVA, gp100) with a CCR4 antagonist combined with various vaccines led to the induction of effector CD8(+) T cells and partial inhibition of tumor growth expressing self Ags in both prophylactic and therapeutic settings. The CCR4 antagonist was more efficient than cyclophosphamide to elicit anti-self CD8(+) T cells. We also showed that the population of Tregs expressing CCR4 corresponded to memory (CD44(high)) and activated (ICOS(+)) Tregs, an important population to be targeted to modulate Treg activity. CCR4 antagonist represents a competitive class of Treg inhibitor able to induce functional anti-self CD8(+) T cells and tumor growth inhibition when combined with vaccines. High expression of CCR4 on human Tregs also supports the clinical development of this strategy.