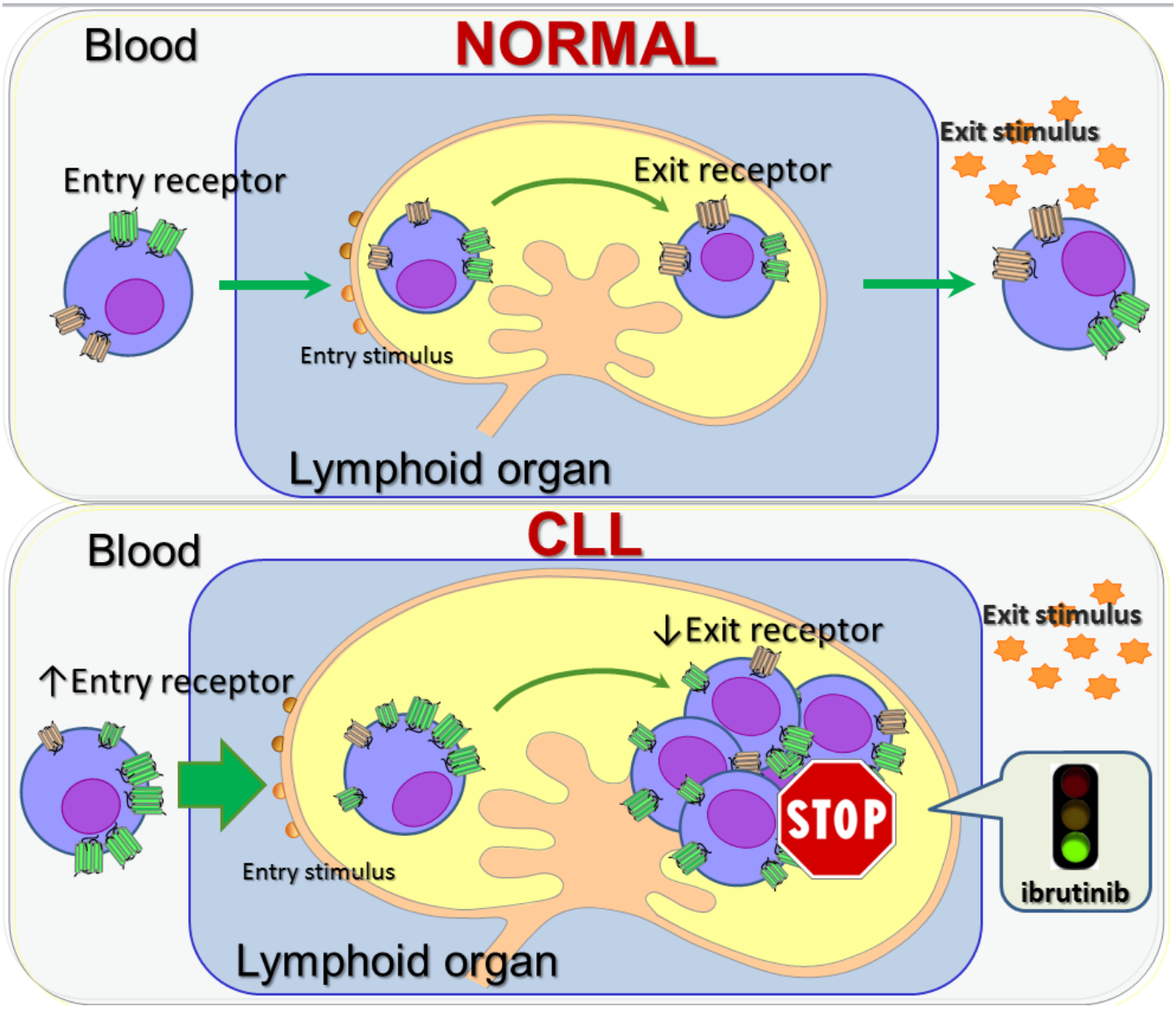
Unlocking trafficking impasse in life-and-death struggle of leukemic cells

Lymphocytes are immune system cells devoted to the defence against enemies coming from both outside (i.e. bacteria and viruses) and inside (tumours). Several times per day these cells escape from the blood and enter into the immune system headquarters, the lymphoid organs (such as tonsils and lymph nodes) searching for possible proofs of the presence of these enemies. When they find them, they immediately activate immune defenses and fight these enemies. Otherwise, they exit from lymphoid organs and reach again blood circulation. It is of great importance that, during their tour into the lymphoid organs, lymphocytes are subjected to stimuli that allow and favour their survival. It is striking that in leukemias the tumoral cells, which are lymphocytes gome awry, take advantage of their own cyclical trafficking throughout lymphoid organs to extend their life span. Unveiling the mechanisms that underly this essential process, especially concerning the molecules that act, like traffic lights, as regulators of traffic in and out of the lymphoid organs, can be useful to find new strategies to promote death of leukemic cells.



We recently published a study in the scientific journal Cancer Research that provides an explanation for the prolonged life span of tumoral lymphocytes in chronic lymphocytic leukemia (CLL), one of the most common types of adult B cell leukemia in Europe and USA. In this neoplasia lymphocytes fine-tune their molecular expression pattern to achieve a huge extension of their residency timeframe in the lymphoid organs, where they are subjected for prolonged time to the prosurvival stimuli provided therein. CLL cells increase indeed the receptors that recognize the signals which promote lymphocyte entry into lymphoid organs, while lowering the ones for signals which promote exit therefrom. This dysregulation results in a traffic impasse of tumoral cells, as they easily enter into lymphoid organs but find a red-light in the exit route such that they cannot escape therefrom. As a consequence, leukemic cells remain trapped into lymphoid organs where they receive survival signals and, importantly, are shielded against anti-cancer drugs. This

lymphocyte impasse can be unlocked by ibrutinib, a new drug which is currently used in combination with one of the conventional chemotherapeutic drugs for CLL. We found that ibrutinib is able to normalize the balance among the receptors responsible for lymphocyte trafficking. The red-light becomes then a green-light for these tumoral cells that are induced to exit from the shielded environment of the lymphoid organs to reach the blood circulation, where they become sensitive to antitumoral drugs.

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Publication

Enhanced Chemokine Receptor Recycling and Impaired S1P1 Expression Promote Leukemic Cell Infiltration of Lymph Nodes in Chronic Lymphocytic Leukemia.
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