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IL7 receptor signaling in T cells: A mathematical modeling perspective

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Abstract- Interleukin-7 (IL7) plays a nonredundant role in T cell survival and homeostasis, which is illustrated in the severe T cell lymphopenia of IL7-deficient mice, or demonstrated in animals or humans that lack expression of either the IL7R(alpha) or (gamma)c chain, the two subunits that constitute the functional IL7 receptor. Remarkably, IL7 is not expressed by T cells themselves, but produced in limited amounts by radio-resistant stromal cells. Thus, T cells need to constantly compete for IL7 to survive. How T cells maintain homeostasis and further maximize the size of the peripheral T cell pool in face of such competition are important questions that have fascinated both immunologists and mathematicians for a long time. Exceptionally, IL7 downregulates expression of its own receptor, so that IL7-signaled T cells do not consume extracellular IL7, and thus, the remaining extracellular IL7 can be shared among unsignaled T cells. Such an altruistic behavior of the IL7R(alpha) chain is quite unique among members of the (gamma)c cytokine receptor family. However, the consequences of this altruistic signaling behavior at the molecular, single cell and population levels are less well understood and require further investigation. In this regard, mathematical modeling of how a limited resource can be shared, while maintaining the clonal diversity of the T cell pool, can help decipher the molecular or cellular mechanisms that regulate T cell homeostasis. Thus, the current review aims to provide a mathematical modeling perspective of IL7-dependent T cell homeostasis at the molecular, cellular and population levels, in the context of recent advances in our understanding of the IL7 biology. This article is categorized under: Models of Systems Properties and Processes > Organ, Tissue, and Physiological Models Biological Mechanisms > Cell Signaling Models of Systems Properties and Processes > Mechanistic Models Analytical and Computational Methods > Computational Methods.

Index Terms- cytokine, immunology, mathematical model, receptor, signalling

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