Stability analysis of a model of local immune responses with regulatory T cells

B. M. P. M. Oliveira (Faculdade de Ciências da Nutrição e Alimentação da Universidade do
N. J. Burroughs (Mathematics Institute, University of Warwick, UK)
A. A. Pinto (Departamento de Matemática da Escola de Ciências da Universidade do Minho
M. Ferreira (Departamento de Matemática da Escola de Ciências da Universidade do Minho

June 1, 2008

Abstract

The primary function of the immune system is the protection of the host from pathogen invasion. During such an invasion, T cells under exposure to their specific antigen are activated leading to secretion of growth cytokines (predominantly interleukine 2, denoted IL2), and expression of the IL2 receptor which triggers cytokine driven proliferation. Under most circumstances, the immune system is able to successfully remove the pathogen. However, the immune system may also target self antigens (autoimmunity) and cause tissue damage and death. Regulatory T cells (Tregs) limit such autoimmune responses by growth inhibition of T cells. Therefore, the immune system has to achieve a delicate balance between appropriate immune activation and immune response suppression. How such a balance is established and controlled is studied in this presentation. Our motivation is the observation that T cell proliferation through cytokines already has such a control structure; cytokine driven growth exhibits a quorum population size threshold. We propose that Tregs locally adjust these thresholds by inhibiting IL2 secretion. The immune response-suppression axis is then a balance between the local numbers of activated T cells and activated Tregs. We study the effects in the quorum T cell population thresholds by the parameters of the model and we describe the equilibria manifold in a neighbourhood of the default values for the parameters and variables.

Keywords: Immunology, Tregs, cytokines, secretion inhibition, growth model, quorum threshold, ODE model.

References

[1] R. J. de Boer and P. Hogeweg. Immunological discrimination between self and non-self by precursor depletion and memory accumulation. *Journal of Theoretical Biology* **124** 343 (1987).

[2] N.J. Burroughs, B. M. P. M. Oliveira and A. A. Pinto, Regulatory T cell adjustment of quorum growth thresholds and the control of local immune responses. *Journal of Theoretical Biology* **41** 134–141 (2006).

[3] S. Sakaguchi. Naturally arising CD4+ regulatory T cells for immunological selftolerance and negative control of immune responses. *Annual Review of Immunology* **22**, 531 (2004).

[4] A. M. Thornton and E. M. Shevach CD4+CD25+ immunoregulatory T cells suppress polyclonal T cell activation in vitro by inhibiting interleukine 2 production. *Journal of Experimental Medicine* **188**, 287 (1998).