

## DEVELOPMENT OF THE T-CELL REPERTOIRE: CLONE SIZE DISTRIBUTION

STEPHEN J. MERRILL, ROB J. DEBOER AND ALAN S. PERELSON

Dedicated to Paul Waltman on the occasion of his 60th birthday

**ABSTRACT.** The development and maintenance of the T lymphocyte repertoire, which determines which antigens will elicit an immune response, involve a complicated learning process involving internal interactions and external (environmental) factors. The dynamics are not unlike that of thousands of nearly identical competing species. This paper examines the distribution of clone (species) populations, how it is created and how it is maintained.

**1. Introduction.** Diversity of the immune system repertoire is necessary to insure both that antigens are recognized and that specific challenges are met with precise (and proportional) responses. It is also necessary to insure that autoantigens do not elicit a strong response and that the system maintaining this diversity be adaptable to environmental conditions while holding a memory of the antigens encountered. And, this must be accomplished in both the B and T lymphocyte populations.

The establishment and maintenance of the T cell repertoire is studied here through the mechanisms which must be present in order that the system satisfy the demands of its required role. This study results in a novel picture of the dynamics of clonal selection [1].

T cells are produced in the bone marrow and mature and expand their population in the thymus before entering the circulation. While in the thymus, there is a “negative selection” which removes potentially autoreactive T cells and a “positive selection” for the ability of the T cell receptor (TCR) to bind one of the classes of the major histocompatibility complex (MHC). This positive selection provides the maturation signals for both the  $CD4^+$  and  $CD8^+$  populations depending on the class of MHC binding. The first selection process involves cellular proliferation and the second does not [10]. As a result, the output from

---

Received by the editors on March 9, 1993.