On the principles of immune system adaptation

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1. Abstract

To describe normal state of the immune system, a theoretical approach is considered based on the assumption about the availability of the immune system goal-seeking behavior – physiological adaptation. To characterize immune defense effectiveness, energy cost of host-pathogen interactions is estimated. To study the influence of environmental changes on the immune defense parameters, the stationary model of the immune system adaptation is proposed. The dependence of optimal resource allocation from the parameters of antigen load is studied. The results are used for the explanation of the immunostimulation protective effect in chronic infections. It is suggested that the impaired immune control due to anergy development as an adaptive trait aimed at diminishing energy cost of the immune system-antigen interactions, could be a principal mechanism of positive feedback responsible for an observed age-related increase of cancer incidence.

Keywords: immune defense, energy cost, antigen load, adaptation, immunostimulation , anergy, cancer

2. Problem formulation

Basic principles which govern the immune system *long-term* adaptation, possible implications for aging and cancer research.

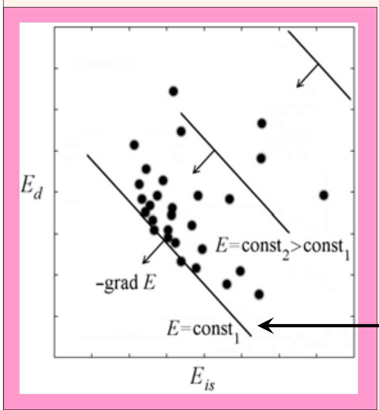


Figure 1. Energy allocation into the immune defense (E_{is}) and associated metabolic cost of infectious and other immune-controlled pathologic states (E_d) – various traits for different hosts

3. Treatment

The concept of immune defense energy cost and the principle of minimal energy dissipation (Romanyukha, 1996; Romanyukha et al., 2006):

$$E = E_{is} + E_d \to \min \quad (1)$$

Energy cost of the immune system maintenance (E_{is}); Energy cost of infections and other immune-controlled diseases (E_d)

Equipotential lines = a fragments of circles of the 1st Holder norm in $\mathbb{R}^2=(E_{is},E_d)$

3.1. Stationary model of the immune system adaptation

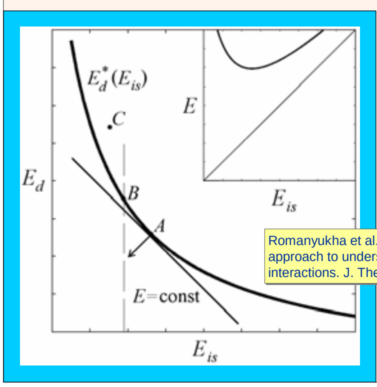
Let the model of immune system-antigen interactions has the form

$$\begin{cases} \frac{dx}{dt} = f(x,t,\alpha,\beta) \\ x(0)=x_0, \end{cases} \quad (2)$$

where x is the vector of time- or age-dependent variables, α – the parameters of immune defense, β – the parameters of antigen load, and x_0 is the initial state of the system. Let the vector of the parameters of antigen load β is fixed: $\beta=\overline{\beta}$. Then, we can determine α as the solution to the minimization problem (1):

$$\alpha^* = \arg\min E(\alpha,\overline{\beta}). \quad (3)$$

Let us call the model system (2) with the vector α determined from the condition (3) the stationary model of the immune system adaptation. The value α^* here corresponds to the normal state of the immune system at given β.

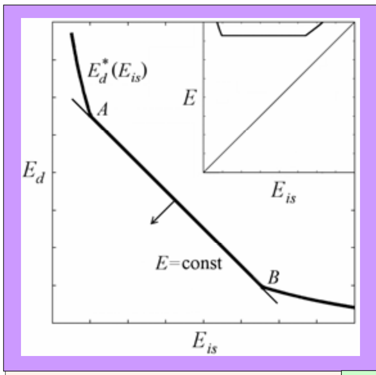


3.2. Simple case (continuous and strictly convex 'energy surface'): a unique solution to the minimization problem (1)

State A corresponds to 'normal' immunity
B – secondary immunodeficiency
C – primary immunodeficiency

Romanyukha et al., 2006. Energy cost of infection burden: an approach to understanding the dynamics of host-pathogen interactions. J. Theor. Biol. 241, 1-13.

Figure 2. Illustration of the concept of normal immune status and immune deficiencies



3.3. 'Complex' case 1 (non-strictly convex 'energy surface'): an infinite set of solutions to (1) – the whole segment *AB*

Physician's view: **1D**
(rate and severity of infections only!)

Biologist's view: **2D**
(fitness traits)

Figure 3. The concept of spurious immunodeficiency (illustration)

3.3. 'Complex' case 2 (non-convex 'energy surface'): a (possibly, finite) set of local minima

Interpretation: the necessary condition for successful immunostimulation in chronic infections

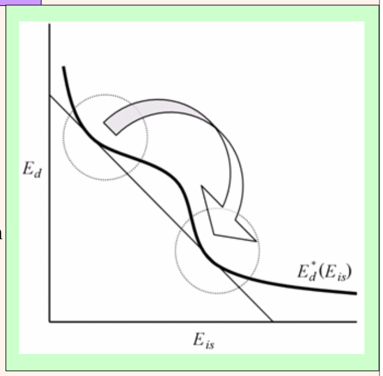


Figure 4. Illustration of immunostimulation protective effect in chronic infections

3.4. A rising effect of the increase in antigen load on body mass and metabolism with age

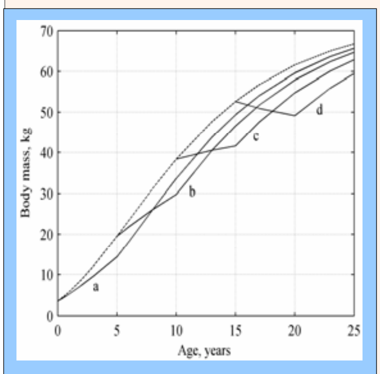


Figure 5. An increasing effect of temporal 2-fold increase in antigen load on body mass with age

3.5. Numerical result:

Inverse relationship between the value of antigen load and the rate constant of T cells division.
Interpretation: infection anergy development with an increase in total antigen load.

Rudnev S.G., Romanyukha A.A., Yashin A.I. Modeling of immune life history and body growth: The role of antigen burden. MPIDR Working Paper WP-2006-042, November 2006, Max Planck Institute for Demographic Research, Rostock, Germany. 34p.

Compare: As the frequency of infections increases it becomes more profitable to the immune system to tolerate pathogens in the body rather than attempt to eliminate them (Romanyukha et al., 2006)

4. Relation to cancer and aging?

4.1. Main assumption

Cancer incidence and the rate of aging are both proportional to total antigen load

4.2. Suggested scheme of positive feedback leading to the increase of cancer incidence with age (*metabolic hypothesis*):

Increase in total antigen load → Progressive negative effect on energy stores → 'Malnourished'-type immunodeficiency (energy deficit) → Development of infection anergy (adaptive trait!) → Lack of immune control (variety of factors) → Increase in total antigen load

Increase in total antigen load ↔ Cancer incidence

Aging → Lack of immune control (variety of factors)

For further information

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