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Who is on guard for harmony?

On harmony, phagocytes and immunological identity

Jacek S. Podgórski[1]
Department of Philosophy of Science
Nicolaus Copernicus University
Torun, Poland
translation: Anna Węgrzyn

Abstract

The objective of this introduction is to outline certain historical and theoretical frames of modern immunology. Immunology as a discipline that has been shaped relatively recently attempts to explain all kinds of phenomena safeguarding the integrity of an organism. An organism is understood as a complex multi-system structure developed in the course of evolution. In the case of such a broad sense concept of immunity a penetrating discussion is required. Thus, biology philosophers as well as scientists – immunologists, for nearly 50. years have been analysing the basic definitions, which led them to interesting conclusions.

Keywords: immunological self, immunological selfhood, phagocytosis, immunological tolerance theory, Jerne's network theory

Introduction

In a standard way immunology is presented as a discipline looking into how living organisms defend themselves against infections, hazardous substances and foreign tissues. A classical paradigm assumes that an organism is capable of defending itself due to being equipped with highly specialised mechanisms classifying the encountered objects into 'self' and 'non-self' ones. The issue of organism peculiarity was also tackled by philosophers of biology. Together with immunologists they tried to provide answers to two kinds of questions. The first kind is of an ontological character and concerns the nature of immunological self: *What are the limits to*

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what may be seen as self?; *How to define what is self?*; *How does the immunological self of an organism change in time?,* etc. (Schaffner 1993: 8-19; Sarkar 1991: 125-138). The other kind of issues was related to the explanation procedures applied in immunology: *Do the terms and models used with regard to immunology explain the researched phenomena in a satisfactory manner?; Is the reductionist description of immunological phenomena expressed in molecular structure categories sufficient?* (Schaffner 1993: 64-89; Sarkar 1991: 138-163).

The perception of immunological phenomena in the *self/non-self* categories has prevailed since the 1950s. However, today this paradigm is more and more often contested. This results from the fact that modern research reveals the behaviours of immunological system that cannot be expressed in the category of mechanisms distinguishing the self and non-self objects (Janeway and others 2001).

In the following introductory text I am going to outline the basics of a standard immunological paradigm with its historical background, as well as point to its limitations and possible alternative conceptualisations.

However, before I do that I would like to introduce certain basic categories from the field of immunology.

Immune system

Immune system is a set of cells (including a gene-programmed network of lymphocytes), tissues and organism mechanisms, defending an organism against diseases through an identification and liquidation of pathogens and cancerous cells. These elements constantly seek various pathogenic conditions, and, by doing so, discern the healthy cells and tissues of an organism. Such activities aim at maintaining the biological balance – immunological homeostasis (Clark 2007: 3-14; Klein 1990).

In the course of evolution of species the mechanisms of pathogen detection evolved to such a degree that the defensive cells are now able to 'learn' and react adequately to the surroundings. As an example, each simple single-celled organism (e.g. bacteria) has a specified enzyme system protecting it from viral infections. Human immune system is composed of multiple protein types (e.g. cytokine), cells (e.g. lymphocytes T and B), tissues (e.g. mucous membrane tissues, nasopharynx) and organs (e.g. thymus, spleen) that interact in a complex and dynamic way, creating a complex system of structural interlocking (Janeway and others 2001; Howes 2008). The organs of immune system may be divided into central (primary) and peripheral (secondary) ones.

The immune system of mammals consists of two interrelated subsystems: innate and acquired immunity (Clark 2007: 3-7). Innate immunity is a system of primitive mechanisms and physical barriers – a sort of a first-line defence. Those barriers are constituted, among other things, by various tissue types that prevent pathogens from having access to an organism. If a pathogen manages to break through the said barriers, innate immune system will recognize it and remove it; however, it is not capable of remembering the pathogen pattern, nor prepare itself for a similar infection in the future. In other words, innate system is deprived of immunological memory.

In the situation when an ‘intruder’ manages to successfully avoid the response of non-specific (innate) immunity, mammals may make use of another protective barrier, i.e. an acquired or adaptive immune system. Such a subsystem is able to remember subsequent infections and improve its response to them in the future by recognising a previously eliminated pathogen. When an ‘intruder’ is destroyed, the subsystem ‘learns’ its response. This allows it to faster recognise and destroy this type of threats in the future (Clark 2007: 43-60).

As we may see on the example of the above description, immunology is dominated by the metaphor of a military conflict, where ‘enemy forces’ are clearly distinguishable from an organism’s ‘own army’ as if they were uniformed soldiers and marked vehicles. However, the problem rests in the fact that such a metaphor is more and more frequently subject to questioning. It is difficult to point to an object that could be an equivalent of a clear and always recognisable marking (Howes 2008: 280-284). An example is the host-friendly intestinal bacteria that are not fought by the immune system, although in their structure they remind of pathogens. Immune system ‘leaves’ its own cells ‘alone’, however starts to treat them as ‘hostile’ as soon as they die or become damaged. An interesting example is organ transplantation. Before the surgery doctors check the number of the so-called compatible tissue markers between the donor and the recipient, while chemically supressing the immune system of the recipient. Still, at times the markers fail – a seemingly compatible organ may be rejected by the recipient’s organism. This happens supposedly due to the fact that at the moment of operation the organism is ‘in distress’, which results in a strong immunological reaction (Wood 2006). Another mystery is found in numerous immunological diseases which – generally speaking – consist in the immune system’s attacking and destroying the cells of its own organism. Because of the above doubts, immune system is now commonly perceived as a network, a cognitive system or even an interlocutor maintaining a dialogue with the organism (Cohen 2001).

Let us now proceed to a historical reconstruction of the self/non-self paradigm development as well as modern attempts to move beyond its limitations.

The self/non-self paradigm and beyond it

The historical background of the paradigm should begin with works of Claude Bernard (1813-1878), a French doctor and physiologist (Silverstein 1989). It was him that posed the following question: *How do we define particular metabolic limitations necessary for a regular functioning of living organisms?* In his depiction, the body was composed of clearly divided modules, where the autonomy of the whole depended on the balance of 'internal elements'. This form of physical atomism radically changed the perception of the functions of an organism relying on an internal architecture of a limited environment (Tauber 1994: 51-53). Another of Bernard's innovations consisted in the introduction of a military metaphor when considering immunity. According to Bernard, in order to reach the state of homeostasis an organism uses its 'military forces' to attack and destroy the 'enemy' that is disturbing its balance.

Another important phase was the research carried out by Élie Metchnikoff (1845-1916) on phagocytes' behaviour and significance for the immunity. This is how he described immunity: for an organism to function properly it is required to be equipped with a regulatory system, i.e. a system providing an order to 'everything'; the 'harmony' of an organism is disturbed by foreign factors, and what is responsible for its restoration are specialized individuals shaped in the course of natural selection (Tauber 2003: 897). Such an individual was seen in a phagocyte researched by Metchnikoff, whose function rested in the absorption, and at the same time, neutralization of 'non-self' or damaged cells (Tauber 2003: 898-901). The phagocyte played the role of a 'guard' distinguishing and separating what was self (friendly, functional) from what was 'non-self' (toxic, damaged) (Tauber, Chernyak 1991: 135-175).

In the first half of the 20th c. immunology focused on an attempt to determine the chemical base of immunological reactions. After World War II the main research objects were transplantology and autoimmune reactions, as well as widely understood genetics. Also at that time, in one of his numerous publications, Sir Frank Macfarlane Burnet (1899-1985) introduced the term of 'immunological self'. This category, derived from psychology, gave rise to the theory of immunological tolerance (Burnet 1957: 67-69). Burnet described immunological reaction process in the following way: an organism has a certain biological identity acquired as early as in the prenatal period; such an identity has a genetic base. Each cell characterised by a proper pattern will be tolerated by immune system as friendly, whereas other objects, which do not have the said pattern, will trigger off an immunological reaction.

In that period immunology concentrated on the examination of lymphocyte structure and function. Burnet proposed a hypothesis according to which these cells were related to the mechanism of acquired immunity (Burnet 1959). This hypothesis was developed and tested by other researchers. Burnet spoke about immunity in the categories of immunological memory of cells that remember the intruder in order to be able to recognise it sooner in the future. Such a perception, in a way extending the previous concepts, became known as a clonal selection paradigm (Silverstein 2002: 793-796). It was to explain, among other things, the phenomenon of autoimmunization underlying autoimmune diseases.

A different approach was proposed by Niels Kaj Jerne (1911-1994). The central category of his explanatory model was an immunological network, i.e. a set of interrelated cells belonging to immune system, whose task was not to protect an organism against the non-self but rather to regulate – inhibit or strengthen – its own reactions (Jerne 1974: 373-389). We may say that Metchnikoff and Burnet focused on single cells, whereas Jerne pointed to interrelations between specialized agents. For instance, he pointed to the activity of antibodies (their production, formulation and adjustment). Following his idea, an antibody not only recognises a foreign antigen, but it is also capable of recognising particular antigens characteristic for its own structures. This means that depending on the situation, a 'recognising' element may at times prove to be the 'recognised' one. In simpler words, recognition of the self/non-self depends on the elements involved in the 'discussion' subject to particular 'grammatical' rules of constantly transforming immunological biology (Jerne 1984: 5-24).

Conclusions

It is necessary to point to three key moments in the history of immunology (Sarkar 1996: 125-170). First, Metchnikoff stated that immune system fulfils two functions: it defines an organism's identity and maintains its integrity – wholeness. The second important moment was formulating by Burnet the mechanism of differentiation of the self/non-self. The third moment was the description of the phenomenon of immunity by Jerne as 'flexible' and 'discursive' (Varela 1994: 31-40). In his proposal, the way of describing immunological phenomena may not be limited to the stiff logic of distinguishing the self/non-self. According to him, it should illustrate the system's cognitive capabilities that are subject to changes in a given biological environment (Jerne 1985: 439-451; Cohen 1992: 490-494).

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