MECHANISMS OF IMMUNE RESPONSES TO INFECTIONS BY ARBOVIRUSES

ORIGINAL ARTICLE

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ABSTRACT

Arboviruses and arboviruses represent an ancient threat to a large part of humanity. This threat consists mainly in the ease that viruses and their vectors have to adapt, also in the fact that their RNA allows many mutations and genetic recombinations. There are still no effective vaccines for arboviruses such as Dengue, Chikungunya and Zika virus, therefore, it is extremely important for the scientific community to produce work on our body's defenses against these arboviruses. The present research, which has a qualitative, descriptive and exploratory character, has as its main objective to investigate how immunological responses to arboviruses occur, with specific objectives to explore the various aspects related to the epidemiology of arboviruses and aspects related to the microbiology and cell biology of the processes immune responses of arbovirus hosts. The work consisted of a bibliographic review covering scientific works such as articles, monographs, dissertations and theses related to the investigated theme. After the aforementioned data collection, it was possible to describe how immune responses occur in their various forms, which are shown to be the main immunological mechanisms performed by our organism.

Keywords: Arboviruses, Immune responses, Infections.

ARBOVIRUS EPIDEMIOLOGY AND PATHOGENESIS

Arboviruses are viruses that cause arboviruses, diseases transmitted to humans through arthropod animals, such as hematophagous insects, which suck human blood. Arboviruses have a wide geographic distribution, mainly affecting subtropical, temperate and tropical countries, such as Brazil (OLIVEIRA, 2011; LOPES, NOZAWA, LINHARES, 2014 CASSEB, *et al.*, 2013; FIGUEIREDO, 2007).

The term arbovirus is derived from the phrase arthropod-borne, adding the term virus if you have arthropod-borne viruses. Arboviruses constitute the largest group of existing viruses, totaling about 537 viruses distributed in 63 antigenic groups. They are usually composed of one- or two-stranded RNA (CRUZ; VASCONCELOS, 2008; OLIVEIRA, 2011; FERREIRA, 2015;).

It is estimated that there are about 545 species of arbovirus divided into 5 families, more than 150 of which are associated with diseases transmitted to humans. Diseases from arboviruses are transmitted to humans and domestic and wild animals through the bites of hematophagous insects (LOPES; NOZAWA; LINHARES, 2014; CARVALHO, 2013; BURGUENO, 2012).

Diseases caused by arboviruses are among the most important today, a fact that is relevant not only for Brazil, but also for the whole world, as contamination by arboviral diseases represents about 30% of all types of contamination in the last decade (FERREIRA, 2015; LOPES; NOZAWA; LINHARES, 2014; CRUZ; VASCONCELOS, 2008).

Dengue is the most prevalent arbovirus disease in Brazil, it has been causing problems for decades, while Oropouche fever is the second most prevalent arbovirus in Brazil. However, other arboviruses have been shown to be potential emerging threats to our country and to other countries, such as the Chikungunya virus and the Zika virus. These three diseases are mainly transmitted by the Aedes aegypti mosquito (FERREIRA, 2015; OLIVEIRA, 2011; FIGUEIREDO, 2007).

About 95% of cases of contamination by arboviruses in Brazil concern Dengue, Oropouche and Yellow Fever. The remaining 5% refer to circulating arboviruses, such as Cacipacoré, Iguape, Caraparu, Saint Louis Encephalitis, Eastern Equine Encephalitis, Equine Encephalitis, among others (HENRIQUES, 2008; LOPES, 2014; FIGUEIREDO, 2007).

Mosquitoes are insects of worldwide distribution, these animals are important for public health because they can be transmitters of several viruses. When a mosquito bites a host infected by a virus, it becomes a vector of this virus and can transmit it to people and animals until the end of its life (OMETTO, 2013; CASSEB, *et al.*, 2013; LAVEZZO, 2010).

The World Health Organization (WHO) estimates that about 40% of the world's population, nearly 3 billion people, are at risk of being infected by arboviruses, mainly Dengue. This fact occurs because this population comes from regions where transmitters and the virus adapt easily, such as tropical countries (LAVEZZO, 2010; LOPES, 2014; VASCONCELOS, 2013).

In addition to the ease that arboviruses have to adapt to the environment where they are, as well as their vectors, other elements such as social aspects are decisive with regard to the prevalence of arboviruses. Most countries that are very affected by arboviruses are poor countries, because of this many of them do not have adequate infrastructure. As a result, arthropod vectors find it even easier to adapt and spread arboviruses more (VASCONCELOS, 2013; LOPES, 2014; CASSEB, *et al*., 2013).

Another factor that contributes to the dengue virus being so adaptable to different environments is that the virus has a high mutation rate. RNA viruses in general have a greater tendency to mutate, but in the Dengue virus the mutation is amplified with the occurrence of genetic recombinations, which increases the diversity and variability of the virus, thus making it more difficult to be fought (LEANDRO, 2011; GUY, 2011; SILVA, 2013).

IMMUNE RESPONSES

The immune system consists, in general, of all the mechanisms by which the body defends itself against invaders. In addition, this system is responsible for removing dead cells, renewing cellular structures and also for immunological memory. For the immunity system to function properly, the action of many structural, cellular and molecular components is necessary. Because of this, the immune response process is quite complex (VIEIRA, 2012; CRUVINEL; *et al*., 2010; MARTINEZ, ALVAREZ-MON, 1999).

Knowledge about this system and the processes of parasite-host interactions help to understand the immune mechanisms developed by the host in an attempt to control an infection. Chief among these mechanisms are immune responses. Immune responses are important both for protection against infection and also for the elimination of infection, and also for balancing the immune system, thus avoiding the configuration of immune mechanisms that may be harmful and worsen the clinical condition of the host (DETTOGNI, 2015; COELHO-CASTELO; *et al*., 2009; MACHADO; *et al*., 2004).

The immunity or resistance of the host organism against virus infection depends, among other things, on the integrated action of the innate immune response and the acquired immune response. These mechanisms of our immune system act immediately after contact with the viral antigen, in an attempt to prevent the proliferation of the virus (COELHO-CASTELO; *et al.*, 2009; MACHADO; *et al.*, 2004; CRUVINEL; *et al*., 2010).

The immune response plays a key role in defending our body against infectious agents, constituting the main means of preventing the occurrence of generalized infections. In almost all infectious diseases, the number of people exposed to infectious agents is greater than the number of people actually infected who have the disease (MACHADO; *et al.*, 2004; VIEIRA, 2012; CRUVINEL; *et al*., 2010).

Immune responses are divided into two groups, innate and adaptive immunity. The first concerns the occurrence of physical, chemical and biological barriers that happen quickly, without the need for prior contact with viral agents. The main mechanisms of innate immunity are phagocytosis, the release of inflammatory mediators, the activation of complementary proteins, cytokines, chemokines and the synthesis of acute phase proteins (CRUVINEL; *et al.*, 2010; FERRAZ, *et al.*, 2011; MACHADO; *et al.*, 2004).

As previously mentioned, the innate immune response occurs without the need to detect a viral agent in the body, this type of immune response can happen in two ways, absolutely, completely protecting the individual from the disease. The second is the relative form, where the response does not prevent infection by the disease, but prevents the disease from spreading (MIOTO; GALHARDI; AMARANTE, 2012; FERRAZ, *et al.*, 2011; MACHADO; *et al*., 2004).

The adaptive immune response, different from the innate one, depends on the activation of specific cells, these specific cells are the so-called lymphocytes and the molecules they produce. The main characteristics of this type of immune response are the specificity and diversity of recognition, its immunological memory, the specialization of its response, self-limitation and tolerance to the components of the organism itself (CRUVINEL; *et al.*, 2010; MIOTO; GALHARDI; AMARANTE, 2012; FERRAZ, *et al*., 2011).

Although lymphocytes are the main cells involved in the adaptive immune response, there are other cells that help in this process, such as dendritic cells.

These cells act in both types of immune responses, in the case of the adaptive immune response, they have the function of capturing and presenting antigens to lymphocytes (CRUVINEL; *et al*., 2010; MESQUITA JÚNIOR, *et al*., 2010; COELHO-CASTELO; *et al.*, 2009).

Lymphocytes have three main groups, T and B lymphocytes, and receive help from NK cells. T lymphocytes act both in the identification of antigens and also in the formation of specific antibodies to combat the identified antigen. B lymphocytes, on the other hand, act in the production and release of antibodies necessary for the immune response (MESQUITA JÚNIOR; *et al.*, 2010; COELHO-CASTELO; *et al*., 2009; LORENZI, LORENZI, ZANETTE, 2012).

It can be seen from this that our body, when it has an adequate immune system, and personal care is taken, our body manages to destroy these infectious micro-organisms by itself and prevent the progression of the disease (MACHADO; *et al*., 2004; CRUVINEL; *et al*., 2010; MESQUITA JÚNIOR; *et al.*, 2010).

However, not much is known about the immune responses resulting from arbovirus infection. It is known that as a result of Dengue infection, thrombocytopenia occurs, among other things, that is, a decrease in the number of platelets in the body. Platelets are fundamental for the action of our immune system (ROLIM, 2005; OLIVEIRA, 2011; POLONI, 2013).

The decrease in platelets is mainly related to the suppression of the bone marrow affected by the infection, they can also be destroyed by antiplatelet antibodies and by the formation of immune complexes on the surface through the direct binding of the virus to them. Thus, platelets are cleared by macrophages and activation of complementary antiplatelet cells (DORNAS, 2012; GUY; *et al.*, 2011; MESQUITA JÚNIOR; *et al*., 2010).

Much has been researched in academic laboratories and linked to the pharmaceutical industry, a way to obtain a vaccine against Dengue, because, it is known that it cannot be counted only with the natural defenses of our organism, and also not enough is known about the immunological responses, however the expected result has not yet been reached, thus not obtaining the vaccine (GUY; *et al*., 2011; MESQUITA JÚNIOR; *et al*., 2010; CRUVINEL; *et al.*, 2010).

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