

Autoimmune diseases: backfiring of an otherwise unerring defense

Editorial

Autoimmunity, a condition where host immune system turns against self-molecules and cells, and resulting diseases from such turmoil are called autoimmune diseases (ADs). The main cause behind targeting self-molecules is anomalies in the immune tolerance to auto-reactive immune cells due to genetic, infectious agents or environmental influences.¹ In a well-regulated immune system, immune competent cells like T and B lymphocytes distinguishes between self and non-self antigens based on their surface receptor expressions, and immune tolerance is maintained by the network of immune cells and soluble mediators. Prime tolerance occurs during lymphocyte development in thymus and bone marrow. At these sites, T and B lymphocytes that recognize self-antigens are deleted before they develop into fully immunocompetent cells, keeping autoimmune responses in check.² Amongst the others, there are some common sites for development of ADs such as thyroid gland, stomach, adrenal glands, and pancreas. Additionally, there are systemic ADs occurring in skin, joints and muscle tissues.¹ It is a general belief that autoimmunity is the cumulative result of multiple factors like the occurrence of autoimmunity-prone genes, infections with certain bacteria and viruses, and environmental influences.³ To make matter worse, there are over 80 currently known ADs, which have sometimes overlapping symptoms and are hard to diagnose. Furthermore, most of these diseases also have cycles of flare-ups, when patients' condition deteriorates to greater extents and then recede.²

Human immune response to foreign agents incorporates involvement of various organs and cell types in its two branches, innate and adaptive immune responses. One of the crucial cell types of immune system are lymphocytes that constitute about 20% of entire white blood cells. Lymphocytes include small granular cells namely T and B cells and large granular cells called natural killer cells, which act against cancerous or virus-infected cells. Both T and B lymphocytes are developed from progenitor stem cells in bone marrow, followed by maturation of T cells in thymus where host-specific cells are destroyed by apoptosis, generating a state of self-tolerance. Once matured, T cells reside in secondary lymphoid organs and also circulate in the bloodstream. However, B lymphocytes mature in bone marrow itself and come to circulation. Once stimulated they develop into plasma cells which act as factories for antibody production.⁴ T cells actions include cytotoxic killing and secretion of lymphocytes, which regulate the migration and activation of other immune cells. One the other hand, B, and plasma cells produce antibodies which result in the formation of antigen-antibody complexes that are engulfed by phagocyte cells and activate the humeral complement system.⁵

Other crucial cells of the immune system involve antigen-presenting cells such as dendrite cells and macrophages, that are known to take up complex macromolecular antigens, process them, and present fragmented peptides along with major histocompatibility complex molecules to T cells. T cells post antigen presentation either act by directly damaging foreign agents or by releasing cytokines to regulate other immune cells like macrophages, monocytes and B cells.⁵ Anomalies in such intricate networking between immune cells and molecules, due to genetic or environmental influences

Special Issue - 2018

Sachin Kumar Samuchiwal

Department of Medicine, Harvard Medical School, USA

Correspondence: Sachin Kumar Samuchiwal, Department of Medicine, Harvard Medical School, Boston, MA; Division of Rheumatology, Immunology and Allergy, Brigham and Women's Hospital, Boston, USA, Tel 6177357874, Email sachinsamuchiwal@gmail.com

Received: April 26, 2017 | **Published:** November 26, 2018

lead to recognition of host antigens as foreign, that triggers an immune response against host own cells and organs, and lead to the development of ADs.

There are various mechanisms that have been identified behind development of ADs and to mention a few, generation of autoantibodies to double stranded DNA in Systemic Lupus Erythematosus (SLE), association with HLA-B27 in Acute Anterior Uveitis, misrepresentation of human leukocyte antigen (HLA) class II on hepatocytes in Autoimmune Hepatitis, autoimmune destruction of insulin-producing beta pancreatic cells in Diabetes Mellitus Type 1, inflammation elicited damage to myelin sheath in Multiple Sclerosis, or abnormal immune response against thyroid gland to cause hyperthyroidism or Graves' Disease.⁶ Some of these conditions could arise from genetic abnormalities, that render them incurable for life, and only symptomatic relief can be provided through pharmaceuticals. But in the majority of cases in spite of presence or absence of genetic predisposition, an environmental factor is needed to trigger the immune system falsely.

Environmental factors can be crucial in promoting, causing or modifying ADs. Most common AD linked environmental factors include toxic metal exposure; exposure to toxic metals such as mercury, cadmium, lead, arsenic, aluminum, nickel and other may stimulate generation of autoantibodies, and toxic chemical exposure; toxic chemicals such as pesticides, solvents, industrial chemicals, household cleaning agents and hair dyes can be associated with certain ADs. Some ADs have also been linked to certain vaccinations. Tobacco smoking is also a prominent factor that could promote ADs. Other inducers of ADs include stress, UV irradiation, silica dust, pesticides, and infections. Host infections, particularly viral infections could initiate or flare the disease in some conditions e.g. Epstein-Barr virus is a major risk factor for SLE.⁷ More and more studies favor that among genetically susceptible people, the ones who had encountered some infectious agents are at higher risk of developing ADs. In addition to these factors, there are other parameters that make some people at larger risk of developing an AD. Such parameters include.

- Gender; as due to causes still unknown women are at higher risk of developing Ads.
- Age; as young and middle- age group is more prone to develop an AD.

- c) Race; studies suggest that people from African American, American Indian, or Latino ethnic groups are more susceptible to developing ADs in comparison to Caucasians.

The host system has several lines of defense; from non-specific to specific immune responses that involves complex and finely regulated networking of immune cells and molecules like lymphokines, cytokines, immunoglobulin's and complements proteins. In a well-regulated immune system, every mediator works together with a great deal of synergy that is needed for host defense against infections and cancers. Defects in this fine balance due to genetic aberrations, pathogenic infections or environmental factors lead to misfiring of host's own immune system to self-tissues and cells. In order to develop treatments and relieving agents for ADs, profound understanding of immune system regulations and association with environmental factors is needed.

Acknowledgments

None.

Conflicts of interest

Author declares that there is no conflicts of interest.

References

1. Smith DA, Germolec DR. Introduction to immunology and autoimmunity. *Environ Health Perspect.* 1999;107(5):661–665.
2. Pan PY, Ozao J, Zhou Z, et al. Advancements in immune tolerance. *Adv Drug Deliv Rev.* 2008;60(2):91–105.
3. Invernizzi P, Gershwin ME. The genetics of human autoimmune disease. *J Autoimmun.* 2009;33(3–4):290–299.
4. Janeway CJ, Travers P, Walport M. Chapter 7: The Development and Survival of Lymphocytes. 5th ed. *Immunobiology: The Immune System in Health and Disease.* USA: Garland Science; 2001. p. 600.
5. Warrington R, Watson W, Kim HL, et al. An introduction to immunology and immunopathology. *Allergy Asthma Clin Immunol* 2011;7(Suppl 1):S1.
6. Marrack P, Kappler J, Kotzin BL. Autoimmune disease: why and where it occurs. *Nat Med.* 2001;7(8):899–905.
7. Javierre BM, Hernando H, Ballestar E. Environmental triggers and epigenetic deregulation in autoimmune disease. *Discov Med.* 2011;12(67):535–545.