

AP Capstone

AP Research

Research Report:

Evaluating the Lack of Knowledge On the Causes of Autoimmune Diseases That Could Possibly
Be Hindering the Advancement of Effective Treatments and Cures

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Abstract

Autoimmune disease is a chronic illness in which an individual's immune system mistakenly attacks their own healthy cells causing tissue and organ damage, eventually leading to overall bodily malfunction. However, with autoimmune diseases on the rise and the advanced technologies that are present in today's society, the causes behind these diseases are relatively undefined. As a result, researchers have redirected their resources towards identifying the causes that fall under the category of these chronic diseases, narrowing down the main causes towards genetics and environmental factors. However, there continues to be other underlying factors that may play a part in why the etiology, or the causes, of autoimmunity is still unknown, such as how these researchers are conducting these academic experiments, their chosen methodology, and other setbacks in terms of protocols for both researchers and physicians. However, through systematic review, it is prevalent that there is a disparity between what researchers know about autoimmune diseases and how they approach this type of research, hindering advancements towards potential treatments and cures. It is important to evaluate to what extent the lack of knowledge on the causes of autoimmune diseases has hindered the advancement towards effective treatments and cures.

Introduction

In today's society, there are many diseases that are affecting a large amount of people worldwide. However, there is a problem with how little society knows about the causes of autoimmune diseases and their treatments or cures. Autoimmune disease is a disease in which one's immune system attacks healthy cells, causing bodily malfunction. Autoimmune diseases are widely known across the United States and the rate in which people are developing this

disease is slowly increasing. Through extensive research, researchers have come to a consensus that there are two crucial factors that can cause an individual to develop an autoimmune disease: their genetic components and environmental factors. This has been distinguished by the foundational texts used in my literature review such as “Autoimmune disease and their environmental triggers” by Manole Cojocaru, Inimioara Mihaela Cojocaru, and Isabela Silosi and “Human autoimmune diseases: a comprehensive update” by Lifeng Wang, Fu-Sheng Wang, and Eric Gershwin. Within these foundational texts, both studies stressed the importance of the relationship between autoimmunity and these two factors. When trying to gather more information about the topic and causes of autoimmunity, most of the studies discussed either the genetic component of individuals or the environmental factors acting as a triggering effect in relation to autoimmunity. However, with the causes narrowed down to these factors, due to the diversity of humans, pinpointing a set cause to an autoimmune disease becomes additionally difficult, expanding the pool of possibility. In addition, researchers are faced with issues such as different experimental results between animal and human models and the methodology in which researchers take when approaching their research on the etiology of autoimmune diseases. For experimental models, it is possible for autoimmunity to be tested positive on an animal model, but may not hold up the same results on a human model. Moreover, the methodology researchers may decide to use when approaching certain breakthroughs may hinder their advancements towards potential treatments or cures. For instance, despite discovering the direct causes for these autoimmune diseases or any possible treatments or cures with advanced technologies we have in the scientific field, those affected by this chronic disease are unable to be cured. Overall, I hypothesize that the reason for the lack of certainty on the causes of autoimmunity is due to the

idea that many factors must be taken into consideration, both within and outside the field of science, inevitably creating a larger pool of possible causes for this chronic disease. And a result, this has ultimately led me to evaluate to what extent the lack of knowledge on the causes of autoimmune diseases has hindered the advancement towards effective treatments and cures.

Prominence in autoimmune disease

Over the years, cases of autoimmune diseases have steadily increased worldwide, pushing for extensive research to be done about the causes towards autoimmunity. As a result, ever since 1997, published studies about the environmental factors in terms of these autoimmune diseases and how the human body reacts with these diseases has gradually increased about 7% every year (3). Autoimmune diseases affect approximately 10% of the human population worldwide, according to the American Autoimmune Related Disease Association whose only goal is to eliminate the effects of autoimmune diseases on human individuals through channels of public awareness and research (3,6). As time has passed, the amount of people affected by autoimmune diseases has slowly increased, specifically in females and monozygotic twins. Firstly, between genders, the ratio between males to females with autoimmune diseases is one to ten, respectively (2). This emphasizes on the more likely rate in which females are to development an autoimmune disease than males. A potential reason for this may be that females primarily have more estrogen hormones¹ within their body while males have more testosterone hormones², showing how the differences between the sexes may contribute to the rate of receiving an autoimmune disease (4). Secondly, in monozygotic twins, where the twins

¹ Estrogen hormone - hormones found predominantly found in females and is responsible for the development and growth of females (17).

² Testosterone hormone - hormones found predominantly found in males and is responsible for the development and growth of males (18).

originate and develop from the same zygote but later splits into their own embryo, the chances of receiving an autoimmune diseases ranges from 12-67% (2). This can be connected to the relationship of developing an autoimmune disease with the idea of an individual's genetic structure. Furthermore, this relationship can be seen particularly with multiple sclerosis³, where individuals who have a family medical history of this disease is most likely to develop it some time in their life, strengthening the correlation between genetics and autoimmune diseases (12). While this only highlights the cruciality of the genetic components of autoimmune diseases, the environmental factors that triggers these diseases also plays an important part. However, according to Aristo Vojdani, a researcher who has a Ph.D. in microbiology and clinical immunology, he stresses that the genetic components in humans takes generations to change, leading researchers to focus more on the environmental factors than the genetic components (3). All in all, the two main factors to an individual receiving an autoimmune disease has been narrowed down to their genetic components and environmental factors, however, researchers are still faced with issues that may hinder their advancement towards potential treatments or cures. These issues consist of the diversity of humans with one another, how every human reacts uniquely to their environment, the diversity of humans in relation to experimental animal models, how the anatomy of an animal differs completely from a human's, and how researchers may approach breakthroughs in a direction that steer away from further advancements, contributing to the hinderance of developed effective treatments and cures.

³ Multiple sclerosis - an autoimmune disease that targets the central nervous system, or more specifically, the barrier that surrounds a body's nerve cells (19).

Methodology

The most effective research methodology that aligns best with my research question is systematic review. Systematic review is the process of analyzing and interpreting qualitative data from multiple studies and drawing your own conclusions from these findings. In relation to my research, systematic review was chosen because experimentation and analysis of statistical data is strictly limited. This is partly due to the requirement that the researcher must have the credentials and credibility to conduct said research and that quantitative data must be ample. Showing that analyzing multiple studies based off their qualitative data is the most effective methodology. Moreover, public databases that consist of various scientific journals and publications, such as PubMed, would use either systematic review, meta-analysis, or evidence-based research depending on the availability of resources in terms of quantitative data or the ability to conduct experiments. Limited to the process of analyzing my sources, I evaluated my studies based on their overall discipline, any evidence that would either support or counter my original assertion, any presented critical or theoretical concepts that may play an influential role in the conclusion, and the overall discussion of the study as a whole. In addition to my methodology, I also reached out to two expert advisors. The first was Dr. Trevor Marshall, a former biomedical scientist and currently the Director of the Autoimmunity Research Foundation. The second is the National Institute of Allergy and Infectious Diseases, an organization whose sole goal is to comprehend, treat, and inevitably prevent infectious, immunologic, and allergic diseases. These expert advisors helped guide me on my research topic and presented new ideas that would further the progression of my research project. With systematic review, it has both its strengths and its limitations. Some strengths include the ability

for a researcher to combine their analysis of qualitative data within a single source and combine their findings from other studies to draw a conclusion that may either support, or oppose, a given assertion. More strength to this methodology is that sources are easily accessible, capable of reaching a larger audience, and allows for replication of the research to be relatively easy. However, for limitations, this research methodology is only effective if qualitative data is readily available. Moreover, systematic review does not completely reflect quantitative data, which is when meta-analysis would be the preferred methodology. Lastly, systematic review is fairly a descriptive methodology that only focuses on keywords in given studies, narrowing the finding of studies that may or may not be used within a research report. For instance, within the presented literature review, most of the chosen studies consisted of keywords such as genetics, environmental factors, causes of autoimmune diseases, and autoimmune research. Concludingly, systematic review is the most appropriate methodology for my research report because it allows me as the researcher to draw conclusions that either support or refutes my original hypothesis by collaborating the findings of the research studies being used.

Diagnostics of Autoimmune Disease

Firstly, for an individual to receive an autoimmune disease, they must have the genetic component for a disease, however, the autoimmune gene stays dormant until it is triggered by an environmental factor, making an individual's body target healthy cells. Normally the human immune system produces antibodies⁴ and T cells⁵ in order to target and neutralize any signs of infections in the body (1). As for these infections, pathogens play the biggest role in terms of environmental factors when triggering someone with an autoimmune gene. These infections may

⁴ Antibodies - a protein found in the body whose function is to fight off pathogens such as viruses and bacteria (20).

⁵ T cells - a type of white blood cell or lymphocyte that seek out foreign substances through that body like viruses and bacteria (21).

then enter the body, causing various immune responses to occur, possibly triggering the genetic components towards autoimmunity (5). Overall, for an individual to be diagnosed with an autoimmune disease, that individual must consist of both the genetic component that codes for the disease as well as being affected from surrounding environmental factors. Correspondingly, systematic review was the selected methodology for this specific research project due to its limitations towards experimentations and quantitative data and its alignment with worldwide databases, where the same methodology is used with studies under the same field.

Genetics and Heterogeneity

Alongside the wide ranges of genes in the human body, and the unique ways in which someone can react to different environmental factors, genetics and heterogeneity contributes to the issue of why pinpointing the causes of an autoimmune diseases is so difficult. While genetics play a significant role in the etiology of autoimmunity, genetics only shows great prevalence in a minority of cases. Within these cases, monozygotic twins are the ones who are seen to develop autoimmunity in relation to genetics due to their analogous genetic structure (3). For instance, there has been some genetic correlation with type 1 diabetes⁶ and monozygotic twins, where it is seen that these individuals develop this autoimmune disease approximately 40% of the time (5). While this may show some correlation between autoimmune diseases and genetics, there is still some uncertainty between defining certain genetic factors with direct causes to autoimmunity. In addition to the concept of genetics, an individual's genetic structure takes various generations for them to alter, showing how difficult it is for researchers to define the genetic causes to

⁶ Type 1 diabetes - an autoimmune disease focused on the yield of insulin in relation to the body's pancreas (22).

autoimmunity. (3). In general, the human genome alone contributes to the pool of possibilities towards the causes for autoimmune diseases, resulting in the reason why defining the etiology of autoimmunity is challenging for researchers.

Another one of the most important concepts behind defining the causes to autoimmune diseases is to understand the human bodily function and heterogeneity. Within an individual's bodily function, there are various immune responses the body can undergo that can potentially initiate autoimmunity. One of the mechanisms in which the body may activate a dormant autoimmune gene is through a microorganism's ability to initiate what is called bystander activation. Bystander activation is an immune mechanism where "T cells are activated in absence of specific T-cell receptor stimulation⁷, which allows T cells to bypass certain immune regulatory checkpoints." Since T cells are being activated unnecessarily, these cells are causing the body to initiate an immune response, that the body does not need to go through (16). More specifically, involving the presence of antigens, the body can undergo bystander activation which can "cause the release of previously sequestered self-antigens⁸ or stimulates the innate immune response, resulting in activation of self antigen-expressing antigen presenting cells." As a result, cross-reactions occur where these microorganisms eventually trigger the autoimmunity gene laid dormant within certain individuals (6,13). Similar to bystander activation, another mechanism called molecular mimicry includes the acts of cross-reaction. Molecular mimicry starts when a pathogen mirrors the protein structure of healthy cells in an individual's body. Then, the body begins to produce T cells that are misled to cross-react with what they believe to be healthy cells,

⁷ T cell receptor stimulation - a molecule found on the surface of T cells that is responsible for recognizing fragments of antigens (23).

⁸ Self-antigen - any molecule or chemical group of an organism which acts as an antigen in inducing antibody formation in another organism but to which the healthy immune system of the parent organism is tolerant (24).

or autoantibodies⁹, but instead react with the foreign organisms, triggering the dormant autoimmunity gene to then become active (5). For example, occurrences have been seen in cases with autoimmune hepatitis¹⁰, where autoimmune hepatitis autoantigens¹¹ cross-reacted with a pathogen, causing autoimmunity. However, it must be taken into consideration that individuals react with various pathogens throughout their lifetime, where some have the unique ability to show no physical symptoms within an individual's body. Correspondingly, this means that some pathogens may not be detected during diagnoses broadening the undefined causes of autoimmune diseases (8). To conclude, humans can undergo various types of immune responses that can possibly induce autoimmunity, but there continues to be uncertainty because the idea of environmental factors triggering these bodily reactions still remains undefined.

Between heterogeneity and genetics, there is a link between the two that may hinder the process of defining the causes of distinct autoimmune diseases. To recapitulate, in order for an individual to receive an autoimmune disease they must have the gene that codes for that specific autoimmunity. However, even if two individuals had the specific autoimmunity gene, the “genotypic¹²-phenotypic¹³ correlation” of the individuals may differ completely. As a result, pinpointing the direct correlation between autoimmune diseases and their causes becomes very difficult. For instance, it is believed that a mutated gene found on the human chromosome 21 called the autoimmune regulator¹⁴ (AIRE) is the cause for autoimmune polyglandular syndrome

9 Autoantibodies - antibodies, or immune proteins, that mistakenly target and react with a person's own tissues or organs (25).

10 Autoimmune hepatitis - an autoimmune disease that targets an individual's liver, causing inflammation (26).

11 Autoantigen - an antigen that is a normal bodily constituent and against which the immune system produces autoantibodies (27).

12 Genotypic - all or parts of the genetic constitution of an individual or group (28).

13 Phenotypic - the observable properties of an organism that are produced by the interaction of the genotype and the environment (29).

14 Autoimmune regulator - a protein that in humans is encoded by the AIRE gene (30).

type 1¹⁵. However, the two patients that were tested for this specific gene expressed different reactions to the mutation proving the relevance heterogeneity has in discovering the causes to autoimmune diseases (10). In all, genetics and heterogeneity plays a significant part in the development of autoimmunity but as humans differ in genetic structures and immune responses, the causes for autoimmune disease continues to be unknown.

Environmental Factors

Complementary with the diagnosing of autoimmunity, an individual must be around environmental factors in order to trigger the dormant gene leading to the development of a specific autoimmune disease. The main environmental factors that are seen in most autoimmune cases consist of pathogens, such as viruses and bacteria, and exposure to xenobiotics, a more general term that consist of all other environmental factors besides pathogens. However, as a result to the increased pool of possibilities, this proves to pose the same challenge towards defining the causes of autoimmune diseases since humans are exposed to an unlimited amount of these unknown substances.

Pathogens such as Viruses and Bacteria

Every individual in the world has a unique environmental setting that surrounds them, in which they are exposed to an unknown amount of pathogens that may or may not present any noticeable side effects. Likewise to these environmental factors, pathogenic infections can initiate autoimmunity in an individual through cross-reactions mechanisms such as bystander activation and molecular mimicry (1). Taking into consideration the effects of heterogeneity and the unlimited amount of pathogens that

¹⁵ Autoimmune polyglandular syndrome type 1 - a rare and complex inherited disorder of immune-cell dysfunction with multiple autoimmunities such as potentially life-threatening endocrine gland and gastrointestinal dysfunctions (31).

exists in the world, this contributes to the difficulties in defining the causes of autoimmunity. However, there have been cases where signs of pathogenic infections have had some relationship with specific autoimmune diseases. In Guillain-Barré syndrome¹⁶ a test was done with an individual's serums and other bodily fluids, where there was a 30% occurrence of an individual's genetic component being triggered when exposed to *C jejuni*¹⁷. However, the odds of an individual having the genetic components for Guillain-Barré syndrome as well as being exposed to *C jejuni* is less than a third of a chance (4). While there has been some correlation between *C jejuni* and Guillain-Barré syndrome, cases where a single pathogen may explain the etiology of the corresponding autoimmune disease is not always recurrent. Moreover, autoimmune diseases such as type 1 diabetes and multiple sclerosis may be caused by an unknown amount of pathogens. This concept contributes to the difficulty of the idea that an autoimmune disease can be caused by a single pathogen or a combination of pathogens (5). Similarly between the tests done with Guillain-Barré syndrome, there has been some correlation between mycobacterium infections and primary biliary cirrhosis where multiple tests were done by researchers showed a relationship between the two while others experiments were inconclusive. This enhances the idea that the connections between environmental factors, such as pathogens, and autoimmune disease are not always completely accurate, contributing to the discrepancy between autoimmunity and its etiology (9). To contribute to the complexity of the issue, it is possible for an individual to already be exposed to a pathogen where it lies dormant within the body's system showing no visible symptoms.

¹⁶ Guillain-Barré syndrome - a condition that attacks an individual's nerve cells in their central nervous system (32).

¹⁷ *C jejuni* - a species of bacteria that is one of the most common cause of food poisoning in the United States (33).

For instance, Epstein-Barr Virus¹⁸ can remain dormant and undetected in an individual for an exceptional amount of time, but then can be reactivate later in one's life under the correct conditions. As a result, the virus undergoes the same process like most pathogens in initiating autoimmunity in an individual (8). Even though pathogens consist of only a fraction of the environmental factors that surround humans on a daily basis, the numerous ways humans may react with these pathogens contributes to the reasons why the etiology of autoimmune diseases remains undefined.

In addition to pathogens prompting autoimmunity in an individual through their genetic component and bodily function, pathogenic infections can instead accelerate the development of the disease. For example, an individual may have a gene that specifically codes for an autoimmune disease and is then exposed to a pathogen, but it is possible that the pathogen does not necessarily trigger autoimmunity. However, the pathogen can then potentially accelerate the body's reactions and responses towards the gene allowing other pathogens that do react with the autoimmune-specific gene to initiate the disease in the individual (8). In conclusion, defining the etiology of the different autoimmune diseases becomes more complex to the extent that certain pathogens may either initiate autoimmunity in an individual or accelerate the process, expanding the pool of possible causes for autoimmune diseases.

Other environmental factors

Furthermore, there has also been correlations between other environmental factors and autoimmune diseases. For example, in systemic sclerosis and certain renal

¹⁸ Epstein-Barr virus - a member of the herpes virus family and is one of the most common human viruses that most commonly spreads through bodily fluids, primarily saliva (34).

autoimmune diseases, there has been a connection between silica dust exposure and the increase development of these autoantibodies that target an individual's own cells (4). In addition to silica dust, other xenobiotic substances can be exposed to an individual causing their autoimmunity. Xenobiotics covers the general spectrum of molecules foreign to an individual's body that, similarly, has the ability to react with an individual's protein structure and eventually initiating immune responses towards autoimmunity (9,11). Overall, xenobiotics introduces the idea of the various amount of other environmental factors that could potentially induce autoimmunity, showing how distinguishing the correlation between diseases and their causes are difficult. As a result, even though there have been cases where specific environmental factors have correlated with certain autoimmune diseases, due to heterogeneity and the multiple factors that play a significant role in the causes of autoimmunity, it is difficult for researchers to pinpoint precise causes to these autoimmune diseases.

Autoimmune Research in Terms of Experimenting and Testing

As autoimmune diseases have become more prominent in today's society, affecting 10% of the total population, efforts towards researching the causes of these diseases have increased (3). According to researchers, understanding the reactions environmental and genetic factors have on different individuals are essential on narrowing down the etiology of autoimmune diseases (2). Taking this into account, most researchers have completed experiments based off animal models, such as mice, since these test subjects are more accessible than human models. However, there are three key differences between mice and humans: metabolism, immune response, the genomes of the respective species, showing that these experiments do not provide a

direct relationship between the autoimmune disease being tested and how that would affect humans (15). For example, while an animal-based test may have the possibility to show positive result of the correlation between a pathogen and the development of an autoimmune disease, the relationship still remains ambiguous in human models. Disregarding the presented uncertainty, these animal models do have the ability to highlight the possible correlations between autoimmune diseases and environmental factors showing how potential causes and side effects on animals may occur in human models (5). Overall, researchers have been able to further their knowledge about potential causes of autoimmune diseases, but not to the extent where the causes of autoimmunity are known to create effective treatments or cures.

Mischosen Methodology and Setbacks

Outside the realm of science, there are factors such as the methodology of researchers that can play a crucial part in why defining the causes of autoimmune disease and developing effective treatments and cures is difficult. With the current knowledge that has been obtained about autoimmune diseases, it is believed that these pieces of information is “based on observational and circumstantial evidence” (11). Moreover, this idea can be pointed towards the chosen methodology researchers use when conducting research particularly with autoimmune diseases. These methodologies consist of mostly meta-analysis research or evidence-based research, but these choices can potentially hinder the advancements towards effective treatments and cures. Meta-analysis relatively focuses on the statistical data of multiple studies in order to come up with a specific solution. However, instead of directing these statistics towards the development of potential treatment and cures, these numbers are used as evidence for briefings and conferences. Overall, it is believed that researchers are not taking advantage of the statistical

data being gathered from autoimmune disease research and are not focusing on the medicinal concept of the research. This delays the development of treatments and cures showing that the mischosen methodology researchers have been using to conduct autoimmunity research adds to the reason why developing treatment and cures is a difficult process.

While defining the etiology of autoimmune diseases is the first step towards developing treatments and cures for autoimmune patients, there are certain scientific and medical guidelines that may hinder these kinds of advancements. Generally, in order for a drug to be admitted for the public to use, it must undergo approximately three to four clinical trials through the Food and Drug Administration that could take about twelve years (15). Meaning that even if a potential treatment or cure is developed, it must take the time to pass all the clinical trials and must avoid failing these tests to avoid restarting the process. In addition to these federal guidelines, physicians must follow similar protocols in terms of their treatments and their practice.

Science is a dynamic realm of constant discoveries and advancements, however, the protocols researchers and physicians must follow do not change with the progression of the scientific field. From the very beginning of a future physician's education, they are taught to "apply the 19th century Postulates of Robert Koch¹⁹ when looking for infectious disease causation." After two centuries of advancements and discoveries, prospective physicians are taught old applications of medicine rather than modernized applications. As a result, physicians are persistent in practicing the old applications of medicine rather than advancing towards more effective types of treatments or cures for autoimmune diseases. After years of schooling,

¹⁹ 19th Century Postulate of Robert Koch - the four criterias designed to establish a causative relationship between a microbe and a disease (35).

physicians and their practice are constantly being observed by their corresponding medical boards. As a result, physicians are discouraged from diverging from their standard practice towards experimentation with their patients in fear of losing their medical license for “accusation of unprofessional conduct, incompetence, or even gross negligence.” Furthermore, this means that the physicians who are dealing with the autoimmune patients the most are deterred in expressing their ideas which could potentially lead towards medical breakthroughs for these certain diseases. However, in order for a physician to safely diverge from their practice, or standard of care, they must receive consent from their patient after being fully informed about the experimentation taking place (15). Overall, physicians who have first-hand experience with autoimmunity after dealing with patients that suffer through these diseases are discouraged from expressing potentially innovative ideas under most circumstances.

Nevertheless, there still proves to be some potential delay in the application of medicine. This can be taken to the extent that even if there were some development of these treatments and cures for autoimmune diseases, the time for these appliances to be effective towards autoimmune patients is extensive. Generally, the time for successful research about practices of treatment or cures to influence a physician’s practice takes approximately seventeen years, but the difficulty and specification of these procedures continues to play a role on the time disparity, fluctuating the amount of years it may take (15). In order to maintain the safety of medicine in society, various tests must be conducted in order to be safely distributed to the public, however, the time it would possibly take to move towards more effective treatments and cures for autoimmune diseases is hindered.

Current Solutions

While the causes of autoimmune diseases are still undefined, there are some temporary treatments that have been developed in order to reduce the effects this chronic disease may have on patients. For example, there has been development of a treatment dealing with biological agents that can alter specific pathways affected by the autoimmune disease to minimize the negative effects on an individual. However, this type of treatment only works effectively with certain autoimmune diseases such as multiple sclerosis, rheumatoid arthritis²⁰, systemic lupus erythematosus²¹ and a few others (2). Other than this type of treatment there are not many other ways to treat autoimmune diseases, however, researchers have proposed potential ways to reduce an individual's development of an autoimmune disease as well as to attempt in defining the causes of this illness. One of the ways includes the removal of a majority of environmental factors in an individual's environment in order to test which factor can possibly trigger the autoimmunity that is coded in their genome (3). While the process is time consuming, researchers will inevitably be able to receive answers to their questions which could ultimately lead to further breakthroughs. Another way includes the method of how researchers may approach the broad causes of autoimmune diseases. Some argue that "epigenetic²² or stochastic²³ events may become a critical bridge" towards understanding the connection between the causes of autoimmune diseases and the initiation of the disease in an individual. With these two categories, additional research will be required to produce conclusive results since these topics touch on different aspects of the scientific field (2). While the definition of the causes of

20 Rheumatoid arthritis - an autoimmune disease that targets many joints including those in hands and feet (36).

21 Systemic lupus erythematosus - an autoimmune disease in which the body's immune system mistakenly attacks healthy tissues in many parts of the body (37).

22 Epigenetic - functionally relevant changes to the genome that do not involve a change in the nucleotide sequence (38).

23 Stochastic - an adjective in English that describes something that was randomly determined (39).

autoimmune diseases remain unknown throughout society, with the current knowledge that has been obtained through research, there has been theoretical developments that could minimize the initiation of autoimmune in an individual.

Conclusion

Autoimmune diseases have grown to become more relevant within society which has pushed researchers to find the etiology of autoimmune diseases as well as potential treatments and cures to assist those affected by this chronic disease. However, it has come to a crucial realization that this lack of knowledge about the causes of autoimmune diseases, whether it be from within or outside the realm of science, plays a significant role towards the development of these treatments and cures. With an increase in research being done about this illness, it has been narrowed down that in order for an individual to develop an autoimmune disease they must have both the genetic components that contains the specific autoimmune disease along with a specific environmental factors that offsets the disease. However, the possible correlation between the genetic components and environmental factors and a specific autoimmune disease is so vast that defining theses causes is difficult for researchers. In addition to the specific causes of autoimmune diseases, the discrepancy between animal models being used in research experiments and human models complicates the understanding of the etiology of autoimmune diseases. Outside the realm of science, the methodology researchers have chosen to use to conduct their research studies may also play a part in the hindered advancements towards these treatments and cures. Nevertheless, while the causes of these autoimmune diseases are still unknown, very few effective treatments exist in order to assist those affected by this malady. With everything considered, my original hypothesis was correct to the extent that multiple

factors other than the genetic and environmental components of individuals plays a significant role in the reasons why the causes of autoimmune diseases are still undefined. Moreover, researchers must continue to approach their studies in different directions in order to move towards the answers to their questions about the causes of autoimmune disease.

Since the discovery of autoimmune diseases, researchers have been able to define the distinct effects this illness has on humans. However, in order to treat or even eradicate the negative effects of autoimmune diseases, defining the pathogenesis must be a researcher's top priority. Yet researchers themselves face issues that are outside the realm of their research. One of these issues includes the need for funding for such a prominent disease such as autoimmunity since this type of resource is limited for a researcher. In order to address or even solve this issue, a worldwide fundraiser towards autoimmune disease research should rise to possibly reach the same potential as the amyotrophic lateral sclerosis, or ALS, Ice Bucket Challenge which was able to raise enough money to fund the research needed to be done. Another issue that researchers face is that they are unable to have easy access to information that may be necessary in a their study. In order to address this issue, it should be recommended that for the case of autoimmune diseases, a program should be created that is similar to the National Cancer Institute's Surveillance, Epidemiology, and End Results Program, which act as a pool for information that is relevant to the field of cancer. As a result, researchers will be able to have easy access to information that is necessary for the advancement of treatments and cures for autoimmune diseases (7). Everything considered, the first thing researchers must do in order to make the essential steps toward the development of treatments and cures for autoimmune

diseases is to recognize the gap between their research and the causes of autoimmune diseases to create effective applications of medicine for patients to use.

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