



THE IMPORTANCE OF GENETICS AS A SCIENCE IN RELATION TO THE COVID-19 PANDEMIC

IMPORTANCIA DE LA GENÉTICA COMO CIENCIA EN RELACIÓN A LA PANDEMIA DE COVID-19

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ABSTRACT

The current COVID-19 pandemic has become a serious global public health problem, with more than 6 million cases and hundreds of thousands of deaths to date. Genetics plays a leading role in the identification, management, and treatment of diseases. This article details the importance of genetics as a science to face the global threat of COVID-19, from different approaches. These actions focus on the contributions that genetics has had and will continue to have in the identification of the new SARS-CoV-2 virus, the development of new diagnostic techniques, the prevention of infections, and the development of serious symptoms. As well as, the design of vaccines and the proposal and evaluation of treatments for COVID-19.

Key words: COVID-19; SARS-CoV-2; Genetics; Pandemic (source: MeSH NLM).

RESUMEN

La actual pandemia de COVID-19 se ha convertido en un grave problema de salud pública mundial, contándose más de 6 millones de casos y centenas de miles de muertes a la fecha. La genética por su parte está teniendo un papel protagónico en la identificación, manejo y tratamiento de enfermedades. En el presente artículo se detalla sobre la importancia de la genética como ciencia para afrontar la amenaza global de la COVID-19, desde diferentes enfoques. Se resaltan los aportes que ha tenido y seguirá teniendo la genética en la identificación del nuevo virus SARS-CoV-2, en el desarrollo de nuevas técnicas diagnósticas, en la prevención de contagios y del desarrollo de cuadros graves, así como en el diseño de vacunas y en la propuesta y evaluación de tratamientos para la COVID-19.

Palabras clave: COVID-19; SARS-CoV-2; Genética; Pandemia (fuente: DeCS BIREME).

INTRODUCTION

The COVID-19 pandemic is one of the biggest global public health problems in recent times. It is caused by the SARS-CoV-2 virus that has a high basic reproduction number (2-2.5), which translates into large numbers of infections around the world. These characteristics add to a crude mortality rate of 3 to 4%⁽¹⁾. In June 2020, with daily reports by the WHO, the global risk level is classified as "very high", counting more than 6,000,000 confirmed cases and more than 375,000 deaths from COVID-19 in

the world⁽²⁾. In Peru, the figures amount to more than 178,000 confirmed cases and more than 4,800 deaths, with an increasing trend⁽³⁾, despite the measures taken by the government. It should be noted that COVID-19 still lacks specific drugs approved by the Food and Drug Administration (FDA) to treat the disease⁽⁴⁾ and that the hope of a vaccine is still months away, at best. cases⁽⁵⁾.

Genetics is the science that studies biological inheritance, and it has come a long way from Mendel to the present day. Today, the

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understanding of genes, population genetics, molecular biology, epigenetics, and gene editing is at its peak^(6,7). The potential of genetics as a science is not limited to a specific area, being a transversal science that enters into the different biotechnologies and is involved in fields as disparate as medical, environmental, or industrial, among many others⁽⁸⁾. Precisely, with respect to the current pandemic, genetics as science has had and will continue to have a leading role in terms of the identification of the disease, the development of diagnostic techniques, the prevention of contagions, and the manifestation of severe cases. As well as the preparation of vaccines, the proposal and potential improvement of future treatments. Recognizing the value of this field of science in this specific context allows us to understand with clear examples of the process and investment in basic and applied research. Due to situations such as the present (as well as in many others), the contribution of genetics to humanity is indisputable. This article will detail the importance of genetics, from different perspectives, with respect to COVID-19, and highlight its key role in facing this global threat.

IDENTIFICATION OF A NEW CORONAVIRUS

Coronaviruses are a group of viruses that generally affect a wide spectrum of mammals and other animal groups. However, the possibility of a spillover infection, in which a virus that affected only animals starts to affect humans, is a well-known phenomenon that leads to zoonotic diseases. Although most illnesses caused by coronaviruses are usually mild, examples of serious illnesses have been seen in the latest epidemics of 2002 and 2012, with severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS), respectively⁽⁹⁾. Genetics plays a fundamental role in the identification of these types of diseases. Once the specific symptoms of these are manifested and the health authorities of the outbreak sites are alerted, it is through genetics that diseases are identified as such. The product of specific viruses⁽¹⁰⁾, was the case of SARS-CoV-2 for the current COVID-19 pandemic^(11,12). In this sense, genetics is not only essential for the declaration that there is a new zoonotic disease but also allows us to understand its origin and direction. Through phylogenetic studies, a 96% similarity has been identified between SARS-CoV-2 and bat coronavirus, which strongly suggests its natural origin. On the other hand, 2 main types of SARS-CoV-2 have been identified, the L and the

S, having presented a selection towards the type with the most aggressive manifestation, the L, which indicates the direction in which the virus currently is evolving⁽¹³⁾. In fact, the ability of genetics to determine the origin of these diseases is also helpful in discarding conspiracy theories⁽¹⁴⁾ that are spread by the concern and fear that accompany pandemics and government actions to control them⁽¹⁵⁾. With this contribution, genetics helps reduce the problems that these beliefs generate for the community, such as disrespect for mitigation measures. On the other hand, phylogenetics effectively helps the surveillance of these emerging diseases from the earliest stages of these public health crises. For example, estimating the value of the virus's reproduction number⁽¹⁶⁾, thereby at the same time, predicting the contagion rate, and planning the actions required to control the disease. Regarding disease prevention issues, the understanding of the genetics of this type of virus and the nature of spillover infections determined risk factors that could facilitate the spread of coronavirus to humans. This prevents the possibility of diseases such as COVID -19 emerged, specifically in places like Wuhan-China, the place of the outbreak of this disease^(17,18). Paying attention to the suggestions that arise from multidisciplinary studies based on genetic knowledge may help to avoid such great health crises as the one we are experiencing now. In conclusion, genetics is necessary for the identification of a new coronavirus, such as SARS-CoV-2. Understanding is a key step in being able to start taking adequate measures against diseases, such as COVID-19. However, this branch of biology also provides valuable information on the origin and evolution of the disease, helps to monitor it from the early stages of the outbreak, and provides us with information to prevent future emerging diseases of this type.

DIAGNOSTIC TECHNIQUES

Once a new disease has been confirmed and especially when a pandemic is declared, diagnostic techniques are of vital importance to estimate contagion and mortality rates, to evaluate the situation of each patient, and to make medical decisions. As well as to execute plans at the government level and predict the infected curve in each region, country, and locality⁽¹⁹⁾. The development, implementation, and optimization of diagnostic techniques for COVID-19 was and continues to be an active area of research since April 2020. Various strategies have been approached to diagnose COVID-19, ranging from the support of medical images by computed



tomography (CT), through tests that look for proteins of both the virus and human antibodies against it, to the techniques that seek the viral genetic material⁽²⁰⁾. For diagnosis, tests based on the detection of nucleic acids using the RT-qPCR technique have been the most weighted for this type of viral disease due to their high sensitivity⁽²¹⁾; however, it is worth noting that its great diagnostic power benefits from the combination of other techniques^(22,23). These contributions are especially valued when asymptomatic patients are actively infecting the population⁽²⁴⁾, so accurate diagnoses are even more necessary. On the other hand, genetics regarding the diagnosis of COVID-19 has not been limited to one technique (based on RT-qPCR), but it remains at the forefront, facilitating the proposal of new rapid diagnostic techniques, such as those based on CRISPR that are already being tested⁽²⁵⁾. With regard to diagnosis, genetics plays without a doubt a fundamental role due to its sensitivity, not being exclusive, but additive with respect to other techniques. In any case, it is a science that allows the application of variants and innovations that undoubtedly benefit humanity in terms of COVID-19 diagnosis.

INFORMATION TO PREVENT

As already mentioned, COVID-19 is generated by the SARS-CoV-2 virus. This virus enters human cells taking advantage of the fact that its protein S is recognized by the angiotensin-converting enzyme 2 (ACE2) and activated by the transmembrane serine protease 2 (TMPRSS2)⁽²⁶⁾. Since COVID-19 is a respiratory disease, the specific cell type of the respiratory system that this virus is targeting was searched for and identified, being type 2 pneumocytes precisely because of their high co-expression of ACE2 and TMPRSS2⁽²⁷⁾; however, these proteins are also known to be expressed in a wide range of human tissues⁽²⁸⁾. In the face of the current pandemic, knowing the distribution, quantity, and variety of the proteins that allow viral infection helps us to determine and understand the risk groups and to propose protection plans for them, seeking to prevent the manifestation of serious COVID-19. Through transcriptomic analysis, it has been determined that the ACE2 and TMPRSS2 proteins are expressed mainly in the epithelial cells of the lung, kidney, intestine, and blood vessels⁽²⁹⁾, but their increased expression has also been reported in the brain and in the heart, which could explain cases with serious failures in the nervous system and

cardiac injuries, beyond lung damage^(30,31). Likewise, it has been seen that, in patients with hypertension, diabetes, obesity or smoking, ACE2 is overexpressed, which could partly explain why these people have been found to be more susceptible to developing severe COVID-19^(29,32,33). Another group vulnerable to COVID-19 are the elderly, and the increased level of ACE2 expression in this group probably explains at least partially the reason for its correlation with severe and even fatal cases⁽³⁴⁾. On the other hand, it has been proposed that it is necessary to study the genetic predisposition to COVID-19 according to populations, having as a precedent the existence of polymorphisms in the ACE2 gene and which, in turn, have already been related to other diseases⁽³⁵⁾. Immunological genetics regarding the severity of COVID-19 cases is another area to exploit in our fight against the disease. The effectiveness of the immune response is mainly due to the recognition of antigens by T cell receptors, which is mediated by major histocompatibility complexes (MHC). The MHC alleles being variable between individuals and being under constant selection pressure are the main candidates to relate them to genetic susceptibility in infectious diseases⁽³⁶⁾. That is, different MHC haplotypes would be related to the response of patients to COVID-19, which could help determine the severity with which the disease would present if contracted. By defining which individuals have a lower predisposition to develop severe disease, it can be proposed from the development of detection kits that help in a strategic clinical management and an evaluation of the efficacy of vaccination according to individuals, to the election of the personnel of health that interacts with patients⁽³⁷⁾. Genetic information offers us alternatives to prevent infections and to be able to protect the vulnerable population from suffering severe COVID-19 conditions. Different strategies may be adopted with the understanding of who and why they are most susceptible.

ASSISTANCE WITH VACCINE PRODUCTION

In recent months, much of the research around the world on COVID-19 has focused on developing an effective vaccine for the current pandemic. The WHO announced in February that it is expected to have a vaccine with marketing authorization and application within the next 18 months⁽⁵⁾, which, although it may seem still far away, would be a record in terms of how soon an approved vaccine will be launched. Currently, vaccines for COVID-19



are being designed based on attenuated viruses, RNA, viral proteins, and multi-epitope proteins^(38,39), using different methodologies and technologies such as recombinant DNA. Countries such as the United States, China, France, among others, have developed specific vaccines for COVID-19 that are currently being tested in humans within approved clinical trials⁽⁴⁰⁾. In addition, it is worth mentioning that Peru is also beginning to develop a vaccine, at the hands of the Cayetano Heredia University (UPCH) and the private company Farvet⁽⁴¹⁾. While, for years, vaccine design has been an extremely laborious, expensive, and time-consuming process, currently with the help of immuno-bioinformatics and protein modeling, based on information from genetic sequences, the identification of highly immunogenic epitopes it is carried out in considerably less time and costs⁽⁴²⁾. An example of these advances is that the candidate peptides were discovered and designed in the context of the current pandemic in approximately 2 months since the first sequence of the virus genome was released⁽⁴³⁾. The use of reverse vaccinology, by analyzing the genomic sequences of the virus with the help of bioinformatics tools. It has managed to determine the proteins most likely to induce high protective immunogenicity like protein S, non-structural protein 3 (nsp3), and protein non-structural 8 (nsp8) which are currently being tested in different vaccines for COVID-19⁽⁴⁴⁾. Regarding the development of vaccines for COVID-19, genetics has become an essential tool that greatly reduces design times and costs. This improvement in the process of generating efficient vaccines brings us closer to obtaining one in the coming months that will translate into the definitive brake on the current pandemic.

GENETICS AND PROSPECTIVE TREATMENTS

Genetics can contribute considerably in the design of effective treatments for COVID-19, according to specific populations and individuals, with the focus of precision medicine. To do this, pharmacogenetics studies the relationship between genetic variability and the effectiveness of a drug, while pharmacogenomics studies the genetic and molecular bases of a disease to find new treatment routes⁽⁴⁵⁾. In the current context, they have already begun to study these branches of genetics and pharmacology, concluding that it is necessary to

consider a strategy according to populations to evaluate the effectiveness and toxicity of drugs proposed to treat COVID-19 (such as ribavirin, α -interferon or captopril) since interethnic variations have been identified in involved pharmacogenes⁽⁴⁶⁾. On the other hand, genetics supports the promotion and development of therapies against COVID-19. An example of this is the use of genetic editing of mesenchymal stem cells (MSC) to enhance their anti-inflammatory therapeutic qualities in so-called fourth-generation cells⁽⁴⁷⁾, recalling that different therapies based on MSCs are currently proposed and in clinical trials to treat COVID-19. An example of these fourth-generation cells is LIFnano cells, an alternative ready to be produced at scale under Good Manufacturing Practice (GMP) conditions⁽⁴⁸⁾. In addition, another strategy proposed for the development of treatments for COVID-19 is based on microRNAs as regulators of protein synthesis at the translational level, and potential microRNAs for this type of therapy has already been identified by bioinformatics methods, which are planned to be incorporated. in exosomes and administered intravenously or by inhalation to inhibit virus reproduction in patients⁽⁴⁹⁾. Genetics is a key tool for the development of precision medicine in COVID-19 treatments, although many challenges remain to be solved (such as the identification of specific pharmacogenes for new drugs), it remains a branch of science that provides us with a range of options and potential to optimize and develop new therapies in turn.

CONCLUSION

In conclusion, genetics is a science that has proven essential to control and combat the current COVID-19 pandemic. Genetics is involved from the identification of the disease, the development of diagnostic methodologies, preventive techniques, and vaccine design, to the design and evaluation of drugs and therapies for COVID-19. Recognizing its value both in Peru and in the world serves to understand and promote investment in this area of knowledge, in order to be better prepared to face crises such as the current and future ones that may come. It is necessary to identify the scientific and technological gap that exists in Peru and in the region within this area to consider the importance that governments and private companies make to decrease it.



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