GENOMICS AND PHENYLKETONURIA

By (Name)

Course

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Genomics

Not so long ago, biology was simply considered to be a pursuit of observations and experiments concerning living things. Years have now passed to reveal how the molecular revolution changed the entire perception of how the human body works. While molecular biology and genetics focus on the role and function of a single gene, genomics seeks to understand the entirety of the DNA. Genomic experts, therefore, strive to complete sequencing and analysis, particularly when understanding diseases. The contribution that genes have in the development of illnesses and diseases is momentous. Genes act as a deciding factor on whether disease would develop or not. Genetics identify how individual features are inherited and genomic determine how the correlation could be used to impact modern medicine. Improvement strategies such as health screening, change of lifestyle, understanding the causes of diseases, and modification of behaviors have been influenced by the contribution of genomics. In this regard, it is not true that genomics adds nothing new to what we already know. Instead, it adds to the existing knowledge of science and risk factors associated with the development of illnesses.

History of Genomics

Even though DNA was first isolated in 1869, it was until a nearly century after those genes were sequenced and thereby making genomics a new and relatable discipline. Therefore, genomics began in the 1970s and has had significant milestones that have shaped the field of medicine. The presence of nuclei was first identified in 1871 before Sutton and Boveri discovered that chromosomes occurred in matching pairs in 1904 (Pharm, 2019). Development in the knowledge of DNA further contributed to the knowledge of the current sequencing that began in 1977 when Sanger opened the way for the possibility of genomics to be recognized as critical in the field of medicine.

James Gusella identified the gene associated with Huntington's disease in 1983 and Mullis formed a technique that amplified DNA through the polymerase chain reaction in the same year. In 1985, Jeffreys developed a method of profiling DNA by counting the number of repeating DNA sequences at specific regions of the genome (Pharm, 2019). The addition of knowledge went further where in 1992 where techniques for testing embryos in the womb for genetic diseases such as cystic fibrosis and hemophilia were developed. The genome sequencing for the bacteria of Haemophilus influenza and yeast were completed in 1995 and 1996 respectively. The additional knowledge further paved the way for newborns to be screened for PKU while still in the womb.

The human genome projected had been launched in 1990 with the aim of sequencing 3 billion letters of the human genome but ended in 2003. Chromosome 22 was the first to be sequenced and added knowledge to the field of medicine that humans have 20,000 to 25,000 genes in their bodies (Pharm, 2019). In 2007, technology was developed to increase the sequencing process hereby leading to a 70-fold increase in DNA sequencing in a single year (Pharm, 2019). As scientists increase their desire to learn more about diseases, gene experts are continuously improving in their processes to add more knowledge to what already exists. Therefore, genomics adds a lot of information about what we already know.

Individualized Treatment

As one of the many inborn errors of amino-acid metabolism, phenylketonuria is known to be caused by gene variants that result in the accumulation of phenylalanine to neurotoxic levels. As a specific cause of mental retardation, PKU remains critical to be understood and treated. In this case, due to its genetic association, the condition reveals the dire need to use genomics in the field of medicine. In an era of extensive molecular pathology and diagnosis, gene sequencing

promises to provide better-personalized treatments to PKU patients (Blau, 2016, p 515) Gene therapy approaches to replace the defective PAH enzyme mutations seeks to cater for the deficiencies of amino acids. Genomic techniques are now comparing PAH and BH_4-regenerating proteins.

Information added from genomics science is more likely to influence the direction in which treatment options would take in people diagnosed with illnesses. Knowing and understanding individual genes and their susceptibilities to medicine as seen with adverse reactions would enable physicians to tailor specific treatment options to people. After all, people often react differently to medications not only due to exogenous factors but also due to their genetic makeup. In the same way, while certain people might appear to be healthier than others when placed in similar conditions, others are likely to weaker and susceptible to illnesses (Brown and Lichter-Konecki, 2016, p 8). Therefore, having prior knowledge on treatment options that suit individuals with certain characteristics would likely enable quick decision making, save on costs and time, as well as prevent diseases from aggravating.

Genomics can also influence treatment options by providing individuals with possible specific treatment. Stratifying PKU with specific gene traits would help in the early detection of the disease. Genes associated with PKU have enabled researchers to identify cancer in its early stages while providing the best treatment options suitable for the specific disease. Causes, diagnosis, and treatment of PKU have been significantly influenced by the advanced studies in genomics. The new information genomics adds refines the quality of life of people. In this regard, genomics it is incorrect to state that genomics adds nothing new to what we already know.

In the same regard, Shen 2017 reports that current PKU treatment techniques are using genetic repairs on the defect PAH variant. The process is done through a CRISPR/Cas9 system that was recently developed as a genome editing method that could be effectively used to correct site-specific mutations that have occurred on target genes. Despite precision problems affecting the homologous recombination repair, good protein expressions were notably rescued. This means that the technique has tremendous potential to correct and repair the condition.

According to Vockley & Niederhuber (2015), knowledge about cancer is constantly increasing due to the rapid improvements in techniques of identifying disease-causing factors. At the same time, discovering genes associated with cancer and analytical methods that integrate different types of data have significantly contributed to the advancements of cancer management. The recent advancements in genomics have helped in the identification of informative biomarkers. As the whole genome sequence data is generated and continues to be analyzed, the baseline on the variability of the human genome has shown the importance of understanding the ancestral genomic background. As a result, patients with a potential PKU causing variant would be able to be identified in the early stages of illness (Li et al., 2019, p 1390). Early identification of the diseases makes it easier and less costly to treat it while preventing further health complications. Development of disease could also be reduced or prevented in the promotion of health among people with high-risk factors. The authors also highlight that genomics and its advances in technology enabled the effect of variations on tumorigenesis and metastasis to be determined.

On the other hand, according to the National Human Genome Research Institute, genomic medicine is improving diagnostic and decision-making in healthcare. Currently, improvements are evident in oncology, infectious diseases, and pharmacology. There is the

possibility of there being personalized medicine (Brown and Lichter-Konecki, 2016). However, precision medicine would have to be achieved by incorporating environmental factors as well. genomics data would be used to guide individual diagnosis and treatment approaches for patients. In his regard, oncology provides a doorway that would allow genomics to be incorporated into medicine. Cancer screening is now looking for genetic markers that would identify the risks of the disease developing. Genomics has added new information that an individual patient's cancer has nearly 50 mutations that differ between individuals.

Genomic medicine makes discoveries that could be easily translated into practice. Pharmacogenomics allows individual genome of a person to determine the type of dosage or therapy one should be given for treatment to be effective. As a result, more than 100 FD-approve drugs have pharmacogenomics information on their labels in various types such as anti-cancer therapeutics and analgesics. DNA sequencing has also been used to diagnose bacterial meningoencephalitis that further helps in identifying the correct therapeutic treatment for a patient. Additionally, given that PKU is one of the less common genetic diseases, genomics has enabled more than 900 various gene variants to be recognized. Inherited deficiencies the metabolism of BH_4 closely associated with the condition. Fortunately, advanced genomics has also contributed to the identification of responsiveness and severity of PKU by analyzing gene variants. Protein-coded exomes that are inside genes are now being sequenced to identify extraordinary cases of illnesses (Li et al., 2019, p 1388). However, the relationship between genomics and PKU needs to be deeply understood.

More evidence of genomics adding more to medicine continues to reveal itself through the development of targeted therapies that target cancer. Ang, Yong, and Tan 2016 report that a multi-platform process of gene sequencing has allowed gastric cancers to be grouped under

molecular classifications. Promising agents against the mutations of tyrosine kinase targets appear to be helpful (Ang, Yong, and Tan, 2016, p 145) Given the fact that they are also associated with somatic mutations, gastric cancers make it ideal for genomic sequencing to provide treatment modules to affected individuals. The sequencing and development of classification systems, in turn, lead to personalized treatment to patients.

Phenylketonuria not only leads to mental health problems but also causes physiological and neurological problems if left untreated. According to Brown and Lichter-Konecki (2016), individuals with PKU require new treatments that would reduce their intake of natural proteins while reducing their risks of developing mental illnesses and reduce the Phe concentrations in the blood. The rare metabolic disorder is due to the failed conversion of Phe to tyrosine. Genomics sequencing has, therefore, provided ways of understanding the condition while working on individualized treatment plans for patients with PKU.

In the same regard, Thomas, James, and Ballinger 2015 state that the study of human genetics has provided a lot of insights into cancer. As sequencing processes continue to increase with advanced technologies and costs reduce, genomics is believed to transfer the world of cancer genetics. While people and scientists believe that hereditary factors influence disease development, very few genetic drivers have been identified. However, irrespective of ancestry and hereditary elements, genomics continues to penetrate into populations with the primary aim of understanding diseases (Thomas, James, and Ballinger, 2015, p 305) Genomics is vibrant in healthcare and growing at rapid rates to transform the way we think about human beings and the development of diseases. In this regard, it is not right to state that genomics adds nothing to what we already know.

Genomics has not only focused on PKU and cancer but also extended to other fields of medicine as well. The diagnosis of Charcot-Marie-Tooth neuropathy reveals that there are hereditary forms of the neuropathies (Elloumi, Pickersgill, McKnight, and Brandt, 2019). As genomics moves from exome sequencing and large scale sequencing, small panel testing may be easily undervalued. From the study, genetic testing for CMT through a carefully planned small panel testing showed that genomics has significant advantages for physicians. The diagnostic yield was high as opposed to other tests done in identifying CMT (Elloumi, Pickersgill, McKnight, and Brandt, 2019). The process also revealed that such genomic diagnosis reduces the burden of practices for physicians or hospitals which have limited resources in genetic services. Clinicians would better improve their decision-making with accuracy due to the availability of new information.

Challenges in Genomics

According to Hauden (2010), the more genomic experts look for more information, the more complicated things get. The development of genome sequencing that occurred ten years ago promises to even go further and help people trace back their ancestry and the evolution of diseases. Genome sequences have opened a door to numerous discoveries and raised a lot of questions that require further investigations. However, in many instances, the genome of human beings is far much complicated that we believe or think. The human network of DNA is made up of intricate elements that would take years to identify and understand them. Even though advancements in technology seeks to fasten the processes of getting outcomes, it would still take an enormous amount of time for the researched information to be translated into practice. The majority believe that it would be difficult to convince everyone that genomics is indeed helpful to medicine in treating illnesses such as cancer (Hauden, 2010, p 665). The more complicated

genomics get, the more likely it is for the progress not to end. After all, effectiveness would only be achieved once everything has been completed. Nonetheless, despite it being difficult, it is not impossible to accomplish the individual goals of genomics. At some point, the beauty of complication in genomics would be unraveled to solve diseases that appear challenging and difficult to understand and treat such as cancer.

On the other hand, even though genomics has revealed targets that would be aimed at during treatment therapies, not all of them have been successfully used in clinical testing. This is large because of the heterogeneity of mutations and tumors. Shared pathways would, therefore, have to be identified for successful targeting particularly when developing a personalized treatment (Pan et al., 2016). Additionally, there are still challenges in identifying the appropriate biomarkers to select patients with targeted gents during treatment. However, despite this setback, whole genome sequencing is believed to help widen the search for biomarkers in finding new targeting agents. WGS would further shed more light into the heterogeneity of PKU biomarkers (Li et al., 2019, p 1390). Despite the existence of challenges in the effective applications of genomics, every set of problems is provided with possible solutions. Therefore, the benefits of genomics in medicine and adding to what already exists outweigh the setback that is inevitable.

Next Steps in Genomic

Discovering how sequencing worked was the first step in understanding how instruction coded in the DNA influence body functioning in man. As technology advances and people get smarter, the next step of genomics is to derive meaningful knowledge from the sequencing processes. The objectives of the continued research in genomics is aimed at determining the functions of genes and the factors that influence them, the variations in sequencing and their significance particularly when predicting a person's risks of developing a disease, and

identifying the 3-D protein structures and their functions (U.S. National Library of Medicine, 2019. Genomics also seeks to understand how DNA interacts with both proteins and the environment in the formation of complex living systems, apply genome-based strategies for early detection, diagnosis, and treatment of diseases, use sequencing on other higher animals to compare the similarity between genetics and species, as well as study genomics on large scale. As more continues to be learned, genomics also highlights the importance of ethical, legal, and social issues that may arise in the field.

What is now remaining is for recent and successful research evidence to be integrated into practice especially when providing individualized treatment. Patients' genetic makeup would be analyzed to identify any risks of developing PKU particularly if one has a family history of diseases. For instance, a patient with a family history of PKU and mental illness would have tests done on him or her to establish whether they are at risk of developing similar diseases as well. at the same time, implementation would enable treatment interventions to be tailored to people sine individuals have different genetic compositions.

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