

ABOUT GENOMICS

• Heredity is transmitted from your parents through DNA. A gene is a region of DNA that contains instructions to make RNA molecules that code for other proteins. When genes are transmitted through the process of reproduction, they govern inheritance of genetic traits like hair color or blood type.

• The Human Genome Project (HGP) was an international research effort to sequence and map all human genes, which are together known as the genome. The HGP's completion in 2003 gave scientists the ability, for the first time, to read nature's complete genetic blueprint for the human organism.

• HGP has estimated that every human has between 20,000 and 25,000 genes.

• The completion of the genome map has created the emerging field of "precision medicine" (also known as "personalized medicine"), which will allow health care providers to better optimize therapies for each individual patient in the future.

VA RESEARCH ON GENOMICS: OVERVIEW

• VA researchers are working to develop personalized treatments, based on patients' genes and other individual factors. • VA is well-equipped to study genomics. The department has a large and diverse patient population; an integrated network of basic research and clinical programs; and an electronic medical record system that offers a rich source of health and clinical data.

Genomic medicine is the application of our rapidly

expanding knowledge of the human genome to medical practice. VA uses genomic medical research to find new

health care solutions and move those into Veterans' care.

VA research on

GENOMICS

• A Genomic Medicine Program Advisory Committee, which advises the Secretary of Veterans Affairs, lays the groundwork for the VA Research Genomic Medicine Program. Members include leaders in the public and private sectors and academia in the fields of genetic research and medical genetics; genomic technology; health information technology; and health care delivery, policy, and program administration. The committee also includes a Veterans Service Organization representative.

• One such large-scale <u>effort</u> is PRIME Care (Precision Medicine in Mental Health Care), performing genomic drug metabolism testing (pharmacogenomics) to help reduce adverse events in patients medically treated for major depression.

• VA's <u>Million Veteran Program</u> (MVP) was conceived and implemented to foster discoveries and bring precision medicine to the forefront of VA care. MVP is now well more than halfway past its enrollment goal of 1 million Veterans, whose coded DNA samples and health information will provide an unprecedented resource for researchers.

SELECTED MILESTONES AND MAJOR EVENTS

2006 – Launched a <u>genomic medicine</u> <u>initiative</u> to advance knowledge of how genes affect health and to promote personalized medicine for Veterans

2007 – Established a <u>laboratory</u> in Little Rock, Arkansas, to conduct diagnostic or treatment-related genetic tests for Veterans

2011 – Launched the <u>Million Veteran</u> <u>Program</u> (MVP) to establish one of the world's largest databases of health and genetic information

2014 – Found that an alteration in a common gene could help predict how well patients with lung cancer respond to chemotherapy

2016 – Developed a <u>test</u> to determine whether a respiratory illness is caused by an infection from a virus or bacteria

2016 – <u>Announced</u> a collaboration with the Department of Energy (DoE) to apply the powerful computing assets available at DoE National Labs to the MVP program

2016 – Began the <u>APOLLO Network</u>, a new tri-agency coalition with the Department of Defense (DoD) and the National Cancer Institute (NCI) that will enable oncologists to more rapidly and accurately identify effective drugs to treat cancer based on their patients' unique genomic profiles

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2016 – <u>Announced</u> a collaboration with IBM to expand and scale access to precision medicine for Veterans with cancer

2018 – Found that a risk score can identify people with a precursor to Alzheimer's disease who are still in their 50s

RECENT STUDIES: SELECTED HIGHLIGHTS

Researchers have identified genetic changes to a pathogen that causes problems in patients with chronic obstructive pulmonary disease. The study by VA Western New York Healthcare System researchers and their colleagues identified changes to Haemophilus influenzae—bacteria that cause various infections—that allow it to survive in the human respiratory system. Understanding these genetic changes is key to determining where the pathogen's vulnerabilities are and what the best strategy might be to eradicate it. (Proceedings of the National Academy of Sciences USA, April 3, 2018)

A study identified specific variants on chromosomes that may trigger the development of sleep problems and demonstrated a genetic link between insomnia and both psychiatric disorders and physical conditions. VA San Diego Healthcare System researchers confirmed that insomnia has a partially heritable basis and also found a strong genetic link between insomnia and type 2 diabetes. Among participants of European descent, the team also found a genetic tie between sleeplessness and major depression. (*Molecular Psychiatry*, March 8, 2018) A large international study involving several VA researchers examined the risk factors for PTSD. The study included some 200 billion pieces of genetic information from more than 20,000 adults throughout the world. The results demonstrate genetic influences on the developments of PTSD, identify shared genetic risks between PTSD and other psychiatric disorders, and highlight the importance of multiethnic and multiracial samples. (*Molecular Psychiatry*, March 2018)

A polygenic risk score can identify Alzheimer's disease risk in younger populations, found a study led by a VA Boston Healthcare System researcher. Polygenic risk scores summarize genome-wide genotype data into a single variable that predicts disease risk. The study found that an Alzheimer's disease polygenic risk score can be used to correctly identify adults with mild cognitive impairment who were only in their 50s. Previously, polygenic risk scores were only used to predict the likelihood of Alzheimer's for people in their 70s. (*Molecular Psychiatry*, Feb. 27, 2018)

Gene variations may explain why some patients with bipolar disorder do not respond to lithium, found an international consortium including several VA researchers. Lithium is the standard mood stabilizer used to treat bipolar disorder, but up to 30 percent of patients do not respond to the drug. Results showed that most patients who had gene variations previously shown to predict schizophrenia also did not respond to lithium. The results can be used to predict how effective lithium treatment will be for individual patients.

(JAMA Psychiatry, Jan. 1, 2018)

Researchers from the San Diego VA Healthcare System identified a gene variation that may be linked to increased risk of suicide attempts. They studied the mapped genomes of a large group of soldiers to look for similarities in those who had attempted suicide. They found similar variations in two genes (CEP162 and MRAP2) in one genome location. This gene variation may increase the risk of suicide and may also show a genetic link between the risk of suicide and bipolar disorder. (*American Journal of Medical Genetics*, December 2017)

Two related cytokines and associated markers may explain why some people develop multiple sclerosis,

according to a study by VA Portland Health Care System researchers and their colleagues. Cytokines are small, specific proteins released by cells that have a specific effect on the interactions and communications between cells. The two cytokines, MIF and D-DT, can worsen MS by increasing inflammation within the central nervous system. The research team also identified two genetic markers that enhance the expression of both cytokines that occurred more frequently in MS patients with the progressive form of the disease, suggesting that a simple genetic test could be used to identify patients at risk of developing this form of MS. (Proceedings of the National Academy of Science USA, Oct. 3, 2017)

For more information on VA studies on genomics and other key topics relating to Veterans' health, please visit <u>www.research.va.gov/topics</u>

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Updated September 2018 • For a digital version of this fact sheet with active links to sources, visit www.research.va.gov/topics

