

## PRESS RELEASE

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### Genetic map of the heart opens new ways of understanding heart disease

Singapore, 3 September 2020 - Heart disease is the top cause of death worldwide. In Singapore, it accounts for one third of all deaths each year.<sup>1,2</sup>

It is a complex set of diseases that is influenced by many different genes.<sup>3</sup> To figure out the genetic basis of such complex diseases, researchers study how different parts of the genome (made up of both genes and the non-coding elements between them) interact physically with one another inside the tight, small space of the nucleus.

The human genome is incredibly vast, as evidenced by the fact that a single human genome print-out occupies over a hundred volumes of minuscule text housed at the Wellcome Collection in London, U.K. (see **Image 1**). Superimpose the network of physical contacts formed from the connections between different sections of a single genome and one gets a sense of the enormous challenge in understanding which interactions are important for a particular disease.

To help identify the important interactions involved in heart disease, Professor Roger Foo of the Department of Medicine, NUS Yong Loo Lin School of Medicine and Senior Consultant at the National University Heart Centre, National University Hospital (NUH), has led a research team to develop the first heart genomic “connectome.” This connectome is a map of the genes in the heart and the “switches” that connect to and control them. This work was published as two companion publications in the journals *Circulation* and *Circulation Research*.

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1. World Health Organization. Cardiovascular diseases (CVDs) Fact Sheet. [https://www.who.int/en/news-room/fact-sheets/detail/cardiovascular-diseases-\(cvds\)](https://www.who.int/en/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds)). Updated May 17, 2017. Accessed June 18, 2020.
  2. Singapore Heart Foundation. Heart Statistics - Singapore Statistics. <https://www.myheart.org.sg/my-heart/heart-statistics/singapore-statistics/>. Updated 2020. Accessed June 18, 2020.
  3. Kathiresan S, Srivastava D. Genetics of Human Cardiovascular Disease. *Cell*. 2012;148:1242-1257.

The papers were co–first-authored by Assistant Professor Chukwuemeka George Anene-Nzelu, PhD students Wilson Tan and Mick Lee, as well as Dr Eleanor Wong.

“Humans have the same number of genes as flies or worms—around 20,000,” explained Prof Foo. “What makes us more complex than a fly is that we have a lot more switches that turn these genes on or off.”

The switches are mostly in the non-coding elements in the genome, i.e. the portions of DNA between genes. They can be flipped on or off according to differences in the DNA code at the section of the switch, which are called variants. For example, in one individual, a variant G may mean that the switch is flipped on. In another individual, a different variant A may mean that the switch stays off (see **Image 2**). To make things more complicated, each gene has more than one switch, and switches may be very far away from the genes they control, making it difficult to identify which switch controls which gene just from looking at the DNA code.

The connectome map developed by the NUS Medicine team shows where these switches are and also pinpoints the most important switches for each gene in the map. Significantly, they found that a series of 59 new variants influencing key switches for particular genes may play an important role in the function of those genes in heart disease.

“Our connectome helps to make sense of the human genome by highlighting the sections and interactions that are relevant for various organs, such as the heart. This could make it possible to analyse the functions of the entire genome someday,” said Prof Foo.

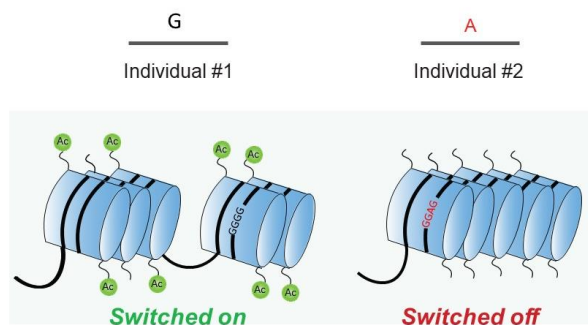
Added Asst Prof Anene-Nzelu, “Using the connectome, we were also able to identify new genes associated with heart disease. These could serve as targets for the development of novel treatments for these diseases.”



**Image 1**

The first printout of the human genome to be presented as a series of books, displayed in the 'Medicine Now' room at the Wellcome Collection, London. The 3.4 billion units of DNA code are transcribed into more than a hundred volumes, each a thousand pages long, in type so small as to be barely legible.

Credit: Roger Foo



**Image 2**

These switches are in turn controlled by changes in the DNA code (either G or A in this example).

Credit: Mick Lee

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Our multidisciplinary and real-world approach to education, research and entrepreneurship enables us to work closely with industry, governments and academia to address crucial and complex issues relevant to Asia and the world. Researchers in our faculties, 30 university-level research institutes, research centres of excellence and corporate labs focus on themes that include energy, environmental and urban sustainability; treatment and prevention of diseases common among Asians; active ageing; advanced materials; as well as risk management and resilience of financial systems. Our latest research focus is on the use of data science, operations research and cybersecurity to support Singapore's Smart Nation initiative.

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Through a dynamic and future-oriented five-year curriculum that is inter-disciplinary and inter-professional in nature, our students undergo a holistic learning experience that exposes them to multiple facets of healthcare and prepares them to become visionary leaders and compassionate doctors and nurses of tomorrow. Since the School's founding in 1905, more than 12,000 graduates have passed through its doors.

In our pursuit of health for all, our strategic research programmes focus on innovative, cutting-edge biomedical research with collaborators around the world to deliver high impact solutions to benefit human lives.

The School is the oldest institution of higher learning in the National University of Singapore and a founding institutional member of the National University Health System. It is Asia's leading medical school and ranks among the best in the world (Times Higher Education World University Rankings 2019 by subject and the Quacquarelli Symonds (QS) World University Rankings by Subject 2019).

For more information about NUS Medicine, please visit <https://medicine.nus.edu.sg/>