PERSPECTIVE

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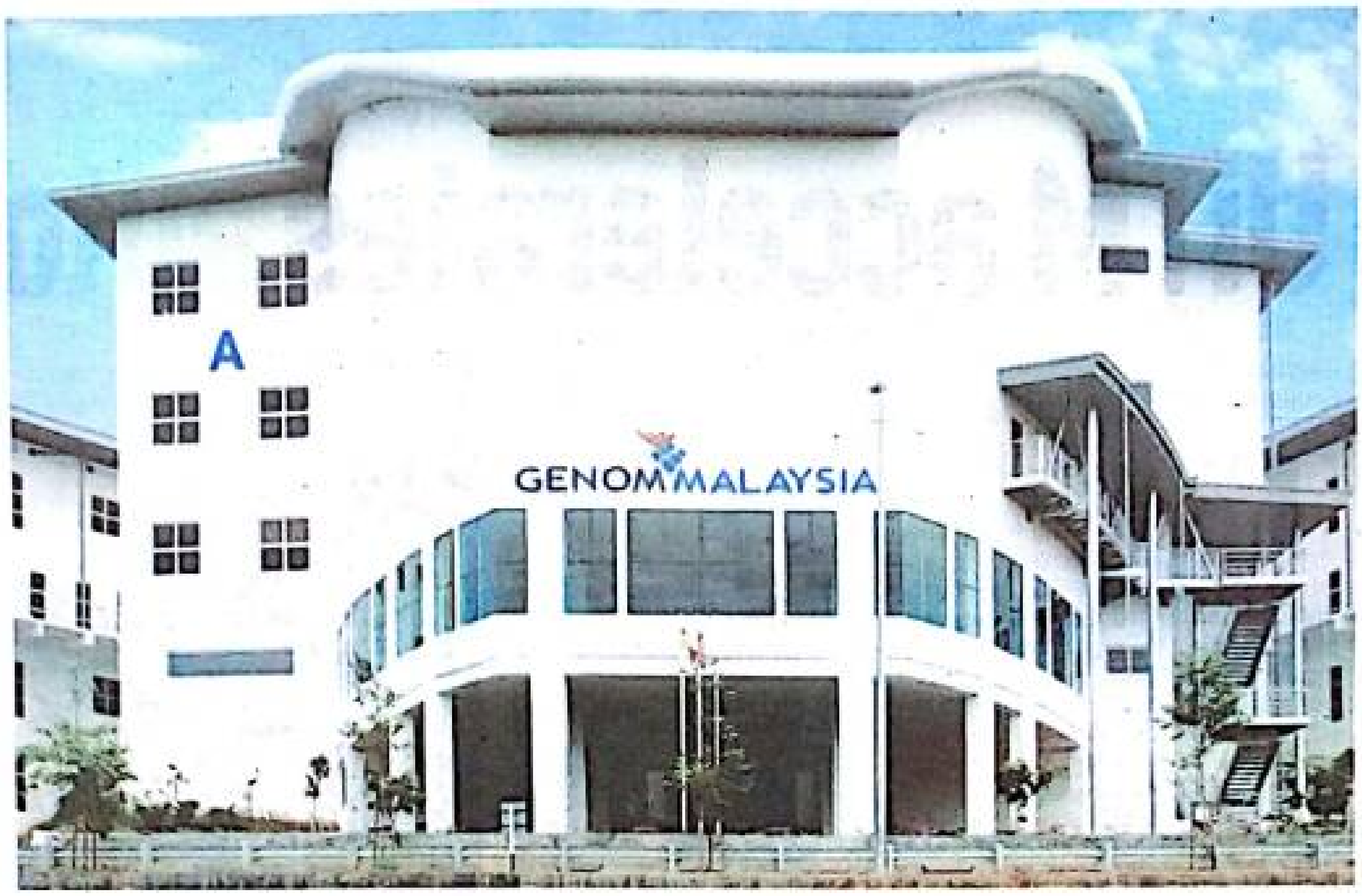

Malaysia Genome Institute

Obviousness of unobvious research

A MULTI-INSTITUTIONAL consortium, which consists of core members from Universiti Kebangsaan Malaysia (UKM) and the Malaysia Genome Institute, has reported the successful sequencing of the genome for a species of Antarctic yeast called *Glaciozyma antarctica* in a research article in the journal *PLOS ONE* on Jan 31. Members of this consortium included scientists from Universiti Sains Malaysia and Universiti Teknologi Malaysia.

This particular yeast species can be found in the sea ice of the persistently cold Antarctic regions. Microorganisms that can survive and thrive in the extreme cold are called pyschrophiles. The term itself comes from the Greek words "psukhrós" meaning "cold" or "frozen" and "phila" meaning "loving".

Every living organism has a genetic blueprint called a genome that is made up of a chemical polymer called DNA or deoxyribonucleic acid. By experimentally deducing the order of the components in the chemical polymer of the genome - a process called genome sequencing — scientists can then figure out the functional molecules, such as proteins or other compounds, that the organism can produce. The genomes for thousands of organisms have been sequenced, including those of humans.

Microorganisms such as yeasts are called eukaryotes, a group that includes humans as well as other animals and plants. The organisation of their genomes is more complex than those of bacteria. Very few of the genomes for eukaryotic psychrophiles have been sequenced compared to those of psychrophilic bacteria. The *G. antarctica* genome is believed to be only the second eukaryotic psychrophile genome that has been sequenced to date.

Studying a microorganism that is found thousands of kilometres away in the frozen southern polar-regions may seem like an odd research enterprise for Malaysian scientists. However, understanding how life is able to persist and thrive in such cold temperatures has wide ranging implications and applications.

In order to survive freezing temperatures, psychrophiles can produce proteins that prevent ice formation called anti-freeze proteins. By analysing the *G. antarctica* genome sequence, nine different genes for anti-freeze proteins (AFPs) were discovered. The group was then able to isolate these genes and confirm that the proteins were indeed able to prevent ice crystals from forming — this molecular level defence mechanism can protect the cell from being destroyed by ice because these microbes lack the insulative barriers of skin and fat that animals have as protection from the cold. AFPs can be used in the future for protecting cells from cold damage such as preserving organs for transplant or long term storage of tissues for medical applications. In such situations, chemicals used for anti-freeze protection may result in damage that proteins such as AFPs will not cause.

The scientists also reported the discovery of enzymes that can withstand and be active at cold temperatures. They can potentially be used as biochemicals called enzymes that can tenderise meat while it remains in the freezer without thawing. Such enzymes can also be used in the production of frozen foods — here's to a future of tastier ice creams. The genome data also revealed more complex mechanisms as to how the organism is able to survive the fluctuations in temperature of the sea ice.

By carrying out fundamental research such as this, what may originally seem like a curiosity-driven search for answers to questions such as how a cell survives and thrives in the cold may actually yield applications that have great impact on fields that range from medicine to the food industry. Such fundamental research is the backbone of discoveries that can lead to various technological breakthroughs and solve humanity's myriad of problems, although such solutions may not be immediately obvious at first.

The yeast cells used for the genome sequencing were first isolated from samples obtained from sea ice brought back to Malaysia by the late Omar Pozan, a Universiti Putra Malaysia scientist, during a voyage to Casey Station, an Australian Antarctic Base. The Australian Antarctic Division had collaborated in the Malaysian Antarctic Research Programme to facilitate Malaysian scientists to study various aspects of Antarctica.

The analysis of genome data falls under what we now refer to as big data analytics. The volume of genome data is expected to exceed all other data combined including videos in sites such as YouTube and physics data. The specific field of data science that analyses and extracts useful knowledge from such data is called bioinformatics.

The *Glaciozyma antarctica* project was funded by the Ministry of Science Technology and Innovation under a funding programme called the Genomics and Molecular Biology R&D Initiatives during the Ninth Malaysia Plan. Work has been ongoing since then to acquire the genome sequence and to analyse the data. Even after the genome had been reported, the scientists of this consortium continue to explore the biology of this mysterious organism and extracting other information from the genome.

The research project and spin-offs that evolved from it have not ceased since the yeast was first isolated in 2001 to this day. Exciting discoveries continue to be made more than a decade on. The vast new knowledge being developed from the study and the lessons we learn from this survivor of the cold may in turn enrich and help save human lives.

> *The pursuit of knowledge can take time and the applications for the acquired knowledge are not always immediately clear.*

The projects that some scientists are up to may sometimes seem like pointless academic exercises — Malaysians studying Antarctic microbes probably counts as one of them. One might ponder what were they thinking! It is not like we have run out of things to study in sunny tropical Malaysia that they needed to make their way down to the icy polar regions to find subjects to study. However, many such curiosity-driven projects are key to discoveries that can revolutionise our industries and health care.

By studying microbes that could survive near extreme heat such as near boiling temperatures, scientists were able to isolate enzymes that allow for DNA to be amplified. Such enzymes are now widely used for applications that range from paternity testing, diagnostics to synthetic production of biochemicals.

A few days after the report of the *Glaciozyma* genome, a team led by a German group published the genome of a salamander called the Mexican axolotl. Many of us may have never heard of it. But by understanding how this amphibian is able to regenerate its body parts, we may one day be ale to treat disabilities such as those caused by spinal cord injuries.

Currently, impactful research is commonly carried out by international teams with a wide range of expertise. Such research can also take time. Some take several years, maybe even decades and longer. In fact, the axolotl specimen was first collected by the Prussian naturalist Alexander von Humboldt and has been cultivated in the laboratory since 1864 (yes — that's 18 and not 19). The pursuit of knowledge can take time and the applications for the acquired knowledge are not always immediately clear. The obviousness of scientific research is not always obvious.

This article was written with input from senior members of the Glaciozyma antarctica genome project — Professor Emeritus Nor Muhammad Mahadi (UKM) and Professor Nazalan Najimuddin (Universiti Sains Malaysia).

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