Using Big Data to understand immune system responses

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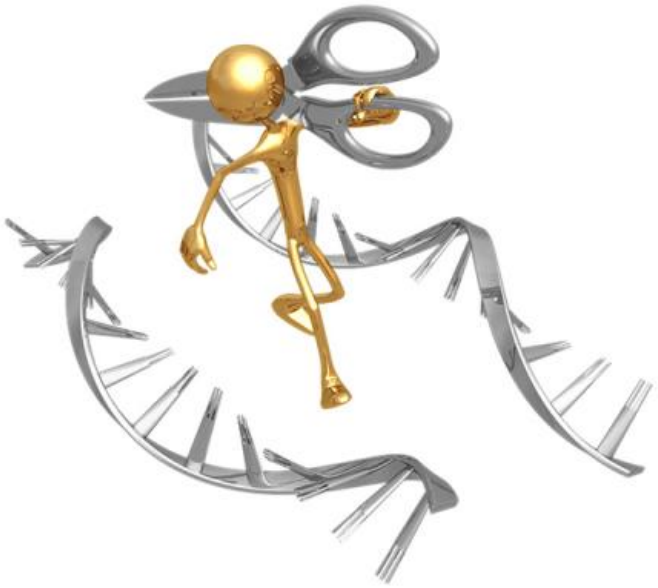

CRISPR technology allows researchers to edit our genetic code, with the potential of eliminating diseases. Credit: Thinkstock

An enzyme found in many bacteria, including the bacterium that gives us strep throat, has given mankind a cheap and effective tool with which to edit our own genes. This technology, called CRISPR, is also being used to understand how the immune system responds to a viral attack.

It has been called the century's biggest biotech breakthrough, and you

might as well learn the name right off the bat: CRISPR.

It may sound like the name of an American breakfast cereal, but it actually refers to a cheap, efficient and highly accessible method of modifying the genes of all living organisms, whether fish, humans, insects or mammals.

This genome editing tool can be used in mosquitoes to stop the spread of malaria, or it can cut out cancer. Only ethical considerations limit its uses. Who knows where this technology will lead? And who should decide? The possibilities are vast. Inherited diseases can be removed forever.

The Norwegian Biotechnology Advisory Board has held many discussions on how to handle genetically modified foods. Genetically modified maize for animal feed – yes or no? Genetically modified soy – yes or no?

Now, the question looms even larger. Yes or no to genetically engineered humans?

To date, the Biotechnology Advisory Board has decided that Norwegian scientists can conduct research on genes in fertilized human eggs.

Many scientists from around the world have contributed their individual pieces of the CRISPR puzzle to the point where genome editing technology is now here – and ready to use. But it was Jennifer Doudna's and Feng Zhang's breakthrough with the Cas9 (CRISPR associated protein 9) enzyme in 2012 and 2013 that really started the ball rolling.

This enzyme comes from the bacterium Streptococcus pyogenes. This little bug is responsible for hundreds of millions of illnesses in the world every year. These include skin irritations, strep throat, ear infections and

flesh–eating bacteria.

The research group found that they could copy what the bacterium does, whereby a small RNA molecule guides the Cas9 proteins to the target DNA molecule that is to be cleaved.

The journal *Science* named CRISPR technology the scientific breakthrough of the year in 2015.

There is disagreement as to whether or not we should modify the genes of plants and animals that we use for food. A new genetic technology called CRISPR raises a larger question: should we modify our own genetic code? Credit: Thinkstock

The body's minute-by-minute defences

Numerous researchers have begun to use CRISPR around the world. One of them is Associate Professor Richard Kandasamy at the Norwegian University of Science and Technology's (NTN) Centre of Molecular Inflammation Research (CEMIR). He conducts research on inflammatory reactions that occur in many diseases.

Using large amounts of data, his research reveals what happens minute-by-minute when the immune system responds to a virus. The results of his team's research were recently published in the respected online journal Systems Biology and Applications.

When the flu or any other virus attacks the body, it has to react with lightning speed.

"It's not like defence cells are just sitting around waiting in some corner of the body to gobble up viruses – and boom, it's all taken care of," says Kandasamy.

As Kandasamy explains, "What happens inside the defence cells is a very comprehensive step-by-step reaction. Signals are sent to the nucleus to initiate a production of new proteins that will take part in the inflammatory reaction and that the cell will use to destroy the virus. This all takes some time. But even a tiny chemical modification of proteins in the cell also enables the cell to start reacting super quickly."

He and his team can map these reactions in extreme detail from the moment a virus infects a cell. By frequently repeating the mapping process in the hours after infection, they can create a detailed map of the cell's reactions.

Most scientists who are working on CRISPR research either proceed by

analysing one gene at a time, or upwards of 20,000 genes at a time. Kandasamy uses both approaches. He also uses large computing systems to analyse this complex dataset. This approach of combining modern technologies and mapping reactions minute-by-minute is one of the unique approaches his research group uses to understand reactions in the cell.

Kandasamy came to NTNU through the Onsager Fellowship programme, which is designed to recruit some of the most talented international young researchers to the university. Just before Christmas, Kandasamy was awarded a generous grant for independent research from the Research Council of Norway's FRIPRO programme for promising young researchers.

Time will tell what this discovery, and CRISPR, will lead to in fighting and treating the world's diseases. But one thing you can be sure of – the research has already come to a place near you.

More information: Richard K Kandasamy et al. A time-resolved molecular map of the macrophage response to VSV infection, *npj Systems Biology and Applications* (2016). DOI: 10.1038/npjsba.2016.27

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