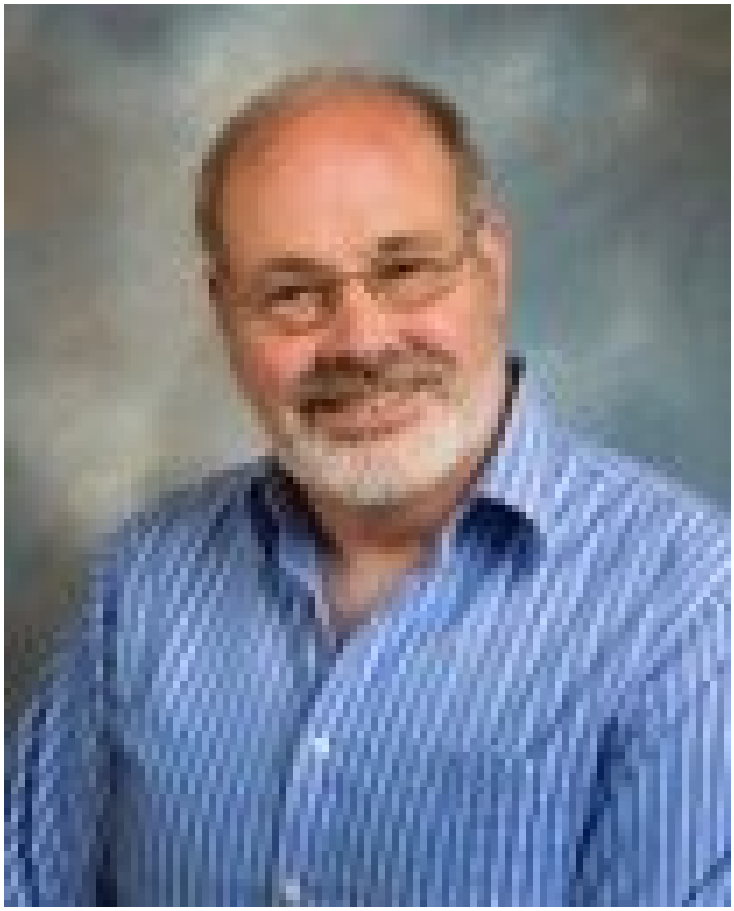
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Limitless potential of gene editing

06 October 2021 | Views | By Eric Rhodes, Chief Executive Officer, ERS Genomics, Ireland

Indian companies have wasted no time when it comes to embracing new technology, and CRISPR is no exception



Published in 2003, the first complete human genome sequence triggered a scientific revolution in our understanding of how differences in gene sequences led to different functional effects within biological systems. We now had the basic sequence information for thousands of genes, but this was like having a complete dictionary of words with associated definitions missing – the understanding of how genes interacted with each other and the impact of small differences at the DNA sequence level was lacking.

To make the most of this wealth of new DNA information, tools for manipulating sequences in the context of living systems were needed. It wasn't enough to simply know that differences at the DNA level existed; knowledge was needed to understand how sequence differences affect gene function.

The Advent of DNA Manipulation

Interestingly enough, it was also in 2003 that the first tool to manipulate DNA in vivo was introduced. Based on a class of proteins called zinc-finger proteins, this first generation tool allowed scientists to introduce a cut in the DNA of a living organism at a pre-designated site and then manipulate certain changes at that location. Zinc-finger nucleases were revolutionary in what they could accomplish, but came with the downside that each unique targeting event required fairly significant design effort, which was neither easy nor inexpensive.

A further development in this space came along in the form of Transcription activator-like effector nucleases (TALENs) several years later. Although much simpler in terms of design for targeting different sequences, the construction of each tool itself was cumbersome and the end-product extremely large and difficult to manipulate in cells.

Enter CRISPR

In 2012 the world was introduced to a third generation gene editing tool courtesy of Dr Emmanuelle Charpentier and Dr Jennifer Doudna. They were awarded a Nobel prize in 2020 for their work on the discovery of the CRISPR/Cas9 gene editing system.

Scientists worldwide now have a platform accessible to all, which can be applied across virtually all species, from bacteria, to plants, to the most complex species, including humans. CRISPR/Cas9 regularly makes the headlines globally. In the last few months highights have included human treatments for Alzheimers (1), Sickle Cell Anemia (2) and HIV (3). There have been innumerable stories of drug discovery, improvements in agricultural science and environmental impact innovation. Precision gene editing has a long reach and will impact many facets of life.

CRISPR/Cas9 in India

In India, at a government level, advances in biotechnology have been a focus for quite some time. As far back as 1982 biotechnology was on the radar of then Prime Minister, the late Rajiv Gandhi. Following extensive deliberations, in 1986 the Indian government created a separate Department for Biotechnology, within the Ministry of Science and Technology. In keeping with this trend, Indian companies have wasted no time when it comes to embracing new technology, and CRISPR is no exception.

Most notably, India is leading the way when it comes to COVID-19 testing. The ground-breaking ‘Feluda’ test was developed by Tata Medical and Diagnostics Ltd. (TataMD), the healthcare venture of the Tata Group in conjunction with the Council of Scientific and Industrial Research’s constituent lab, the Institute of Genomics and Integrative Biology (CSIR-IGIB) based in New Delhi. This was the world’s original paper-based rapid test for COVID-19 detection, and enabled fast, affordable mass testing. The Feluda test has since been adapted to detect mutated variants quickly, owing to the test delivering results in 45 minutes and requiring only a basic PCR machine – more complex machines such as those running RT-PCR take longer to run and return results.

A second truly inspiring use of CRISPR comes from the different, but no less globally important, are of agricultural research. The Indian Council of Agricultural Research (ICAR) and The Department of Biotechnology (DBT) are working together to realize the potential of CRISPR gene-editing technology.

Scientists in India are also enabling a change that will make the world a better place – researchers in India and the US discovered 29 genes in malaria-causing mosquitoes that make the mosquito resistant to insecticides. Around 2 per cent of global malaria fatalities are in India, and up to 1.3 billion Indian people are considered ‘at high risk’ of being infected with malaria. Discovering a way to potentially neutralize and limit the threat of malaria would have an incredible impact on worldwide healthcare.

Researchers from the Institute of Bioinformatics and Applied Biotechnology in Bengaluru, the University of California, and the Tata Institute for Genetics and Society (TIGS) collaborated to produce a new reference genome for a sample of the malaria carrying mosquito from India. With knowledge of the entire genome, researchers are applying CRISPR to edit the “insecticide resistant” genes in mosquitoes with a goal of understanding how they might one day eliminate these forms of resistance.

There are many projects right now with the potential to vastly change day to day life in India. From health to environment to agriculture to bioenergy, use of gene editing is part of the planning to tackle previously seemingly insurmountable challenges.

What’s Next for India: Biosimilars?

Experts believe that biosimilars are essential to the future of affordable healthcare. This is especially true for a country like India, where they lead to greater competition and innovation in the market. Biosimilars cause prices to drop and allow greater access to medication for patients. India has firmly established itself as a global leader in producing similar biologics and, due to its population of 1.39 billion, India is also a huge market for these products.

Although the potential is high and the expectation is huge for India, the challenges are enormous in order to maintain global leadership in this field. To get this right, Indian biopharmaceutical companies need to embrace CRISPR.

Although many Indian companies have cracked the complex production know-how of biosimilars in both microbial and mammalian platforms, there is a need to enhance their focus on gene editing technology. Even companies that are ahead of the game in domestic markets are still grappling with issues related to manufacturing performance and production yield, and are exploring both organic and inorganic ways to improve.

Considering the criticality of time to markets in the biosimilars sector, it is important to support timely access to the technologies that will enable companies to forge a competitive market entry or maintain a leading position. Companies in this field that are not using CRISPR/Cas9 need to embrace this new technology or risk getting left behind.

What’s Next for CRISPR Globally?

By virtue of its ease of use and low cost, CRISPR has already opened up the use of genome editing to disciplines that had previously not even considered it a possibility. Outside of human disease applications, gene editing is being used to create greener chemistries and enable the use of microbes to create industrial products that pre-CRISPR required precious natural resources. To further support a sustainable future, gene editing will be used to modify crops to better withstand the changing world climate conditions and increase food production. Gene editing is likely to become a major player in the treatment of genetic diseases. Perhaps much in the same way that software has evolved to manipulate computer and robotic hardware, so too will gene editing serve as a 'coding tool' for exploring and exploiting the biological hardware of living systems. The potential is limitless.

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