Gene editing, the good first and then the worries

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With the Chemistry Nobel thrusting CRISPRCas9 into the limelight, India needs guidelines for gene-editing research

The Nobel Prize in Chemistry for 2020 (https:// bit.ly/3iR8UfJ) which was announced on October 7, Wednesday, has two women scientists as its recipients. That, in it, is a first in the sciences. Emmanuelle Charpentier, a French microbiologist working at the Max Planck Unit for the Science of Pathogens in Berlin, Germany, and Jennifer A. Doudna, a biochemist from the university of California, Berkeley, U.S. shared the honour "for the development of a method for genome editing".

DISCOVERY, LIKELY OMISSIONS

The two scientists have pioneered the use of CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) – Cas9 (CRISPR associated protein 9) system as a gene-editing tool. In a short period of eight years since its discovery, the method has already made a significant impact in biology, medicine, and agriculture. It is not often that one sees practical applications of scientific findings in such a short time. The only other work with such a quick and revolutionary impact, is PCR (polymerase chain reaction) invented by Kary Mullis in 1983.

The Nobel Prize as the most coveted prize, especially in science, often attracts controversy; this year too is no exception.

The discovery of CRISPR can be traced back to 1987. This was when a group of Japanese researchers observed an unusual homologous DNA sequence bearing direct repeats with spacing in a eubacterial gene. Several important discoveries followed. In subsequent years, Francisco Mojica, Rodolphe Barrangou, Luciano Marraffini and Erik Sontheimer discovered CRISPR and showed it to be a bacterial adaptive immune system and to act on DNA targets. A notable discovery on the use of CRISPR as a gene-editing tool was by a Lithuanian biochemist, Virginijus Siksnys, in 2012. Siksnys showed that Cas9 could cut purified DNA in a test tube, the same discovery for which both Charpentier and Doudna were given the credit.

Thus, the conspicuous exclusion of Siksnys from this year's Nobel, especially when the Nobel Prize can be given to three individuals (the will of Alfred Nobel has it that the Prize can only be shared among a maximum of three individuals), is going to raise discussions. This is especially noteworthy when Siksnys along with Charpentier and Doudna shared another coveted award, the Kavli Prize for Nanoscience, in 2018 (https://bit.ly/36UYnO6). However, the Nobel committee recognized Charpentier and Doudna as the sole discovers for programming a Cas9 protein to cut a piece of DNA at a specific site with the help of a small piece of RNA, thereby Proving the ability of CRISPRCas9 to function as a gene-editing tool.

Other notable early contributors to the field that many believe deserve mention are Feng Zhang of Broad Institute of MITHarvard and George Church of Harvard. Feng Zhang, a past postdoctoral fellow in Church lab, and Church himself, the named inventor of many genome science methods, have made several early contributions to the field. These notable exclusions may raise controversy, but Church described the reason for the exclusion best. He saw it this way — that Charpentier and Doudna made a discovery, which is what the committee prefers to reward, and he and Zhang were inventors.

In the male dominated world of science, this year's Nobel chemistry prize should be widely celebrated worldwide. The recognition that Charpentier and Doudna's work has received will Encourage women to take up science as a career, despite the hard struggle to balance family life and an arduous life in a scientific career. Although CRISPR became a household name for its ease of use, other systems discovered before CRISPR can cleave DNA at specific sites, an example being the Zincfinger nucleases. In this, Dana Carroll, who developed the system, is another notable exclusion from this year's chemistry prize. It would have been an excellent and befitting reply to all who say that women cannot compete with men in science if the Nobel committee had named Carroll alongside Charpentier and Doudna.

WHEN THE WORLD WAS SHOCKED

In India, there is a long way to go before realising the utility of gene editing for therapeutic applications. That said, we cannot be complacent and wait for a rogue individual or entity to try it out in humans. The world was alarmed by such a mission in 2018 when Chinese scientist He Jiankui edited genes in human embryos using the CRISPRCas9 system that were subsequently

implanted and resulted in the birth of twin girls. He claimed this was ostensibly to prevent them from contracting HIV, and the incident became known as the case of the first gene edited babies of the world. Following a global outcry, the World Health Organization formed a panel of gene-editing experts which said "a central registry of all human genome editing research was needed in order to create an open and transparent database of ongoing work". It called upon WHO "to start setting up such a registry immediately".

SITUATION IN INDIA

In India, several rules, guidelines, and policies backed by the "Rules for the Manufacture, Use, Import, Export and Storage of Hazardous Microorganisms/Genetically Engineered Organisms or Cells, 1989" (https://bit.ly/33OIuXx) notified under the Environment Protection Act, 1986, regulate genetically modified organisms. The above Act and the National Ethical Guidelines for Biomedical and Health Research involving human participants, 2017 (https://bit.ly/34LykGI), by the Indian Council of Medical Research (ICMR), and the Biomedical and Health Research Regulation Bill implies regulation of the gene-editing process. This is especially so in the usage of its language "modification, deletion or removal of parts of heritable material". However, there is no explicit mention of the term gene editing. It is time that India came up with a specific law to ban germ-line editing and put out guidelines for conducting gene-editing research giving rise to modified organisms.

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