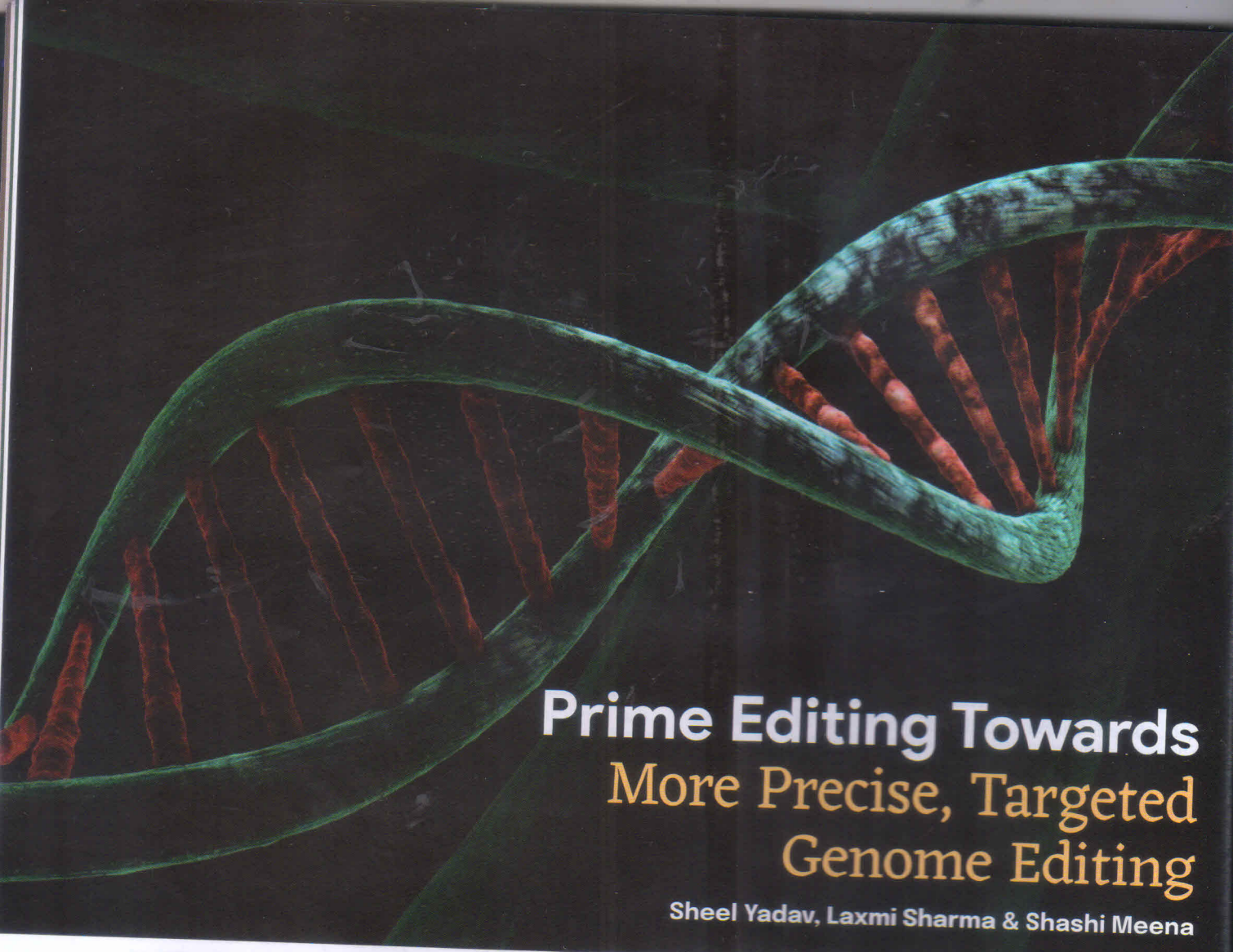

Prime Editing Towards More Precise, Targeted Genome Editing

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OVER the past decade, there has been a lot of scientific experimentation to develop crop varieties that are more adapted to the rapidly changing climatic conditions. With the advent of NGS (Next-Generation Sequencing) technology, the breeding process to develop improved, climate-resilient crop varieties has become more precise and much faster than ever anticipated. The availability of whole genome sequences of most crop species has allowed crop breeders and molecular biologists to target precise regions in the genome and attempt gene modification to bring about desirable changes in the genome and, consequently, the phenotype. Genome editing, a non-transgenic method of genetic modification, has been made much easier and feasible with the recently developed CRISPR-Cas9 system owing to its simplicity. The potential of this technology in genetic improvement was realised as soon as the first reports of successful genome editing started appearing. Due to its profound applicability, this technology was hailed as a breakthrough in 2015.

An advancement of this technique called 'Prime Editing', published in the journal *Nature* in October 2019, allows 'search-and-replace' genome editing. What sets prime editing apart from traditional CRISPR is that it enables targeted editing without generating double-stranded DNA breaks. Moreover, targeted insertions can be achieved without the need for donor DNA templates. It was observed that this technique has a similar efficacy to CRISPR-Cas9 but causes much fewer off-target effects. In simpler terms, this technology enables editing just one or a few bases. It also expands the limited scope of current base editing abilities (4 possible combinations C > T, G > A, T > C, and A > G) to all 12 combination swaps. Though in its infancy, this technology holds immense promise and has garnered much attention (already cited > 250 times) due to its potential uses, especially in medical genetics. Since the first report that appeared in 2019, this technology has captured the interest of molecular biologists across the world who are trying to overcome the hurdles (particularly the off-target effects) they face using the CRISPR-Cas9 system. It is widely believed that this technology will, in no time, overtake CRISPR for genome editing.

Components of Prime Editing

The two basic components of prime editing include:

- A guide RNA (pegRNA) consisting of an extended single guide RNA (sgRNA) containing a Primer