Granted a new patent to Nobel Laureate Jennifer Doudna

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Miércoles, 1 de Diciembre, 2021 | Número #2

It is a honor to grant a Patent to Nobel Laureates Drs. Jennifer Doudna and Emmanuelle Charpentier, the first women to jointly win the Nobel Prize in Chemistry, in 2020

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It is a honor to grant a Patent to Nobel Laureate, Dr. Jennifer Doudna, an American Biochemist, and Dr. Emmanuelle Charpentier, a French microbiologist, who are the first women to jointly win the 2020 Nobel Prize in Chemistry for their pioneering work in CRISPR gene editing. Jennifer's invention was issued as a U.S. Patent No. 11,053,271 on July 6, 2021 and relates to the molecular mechanism of integration of a DNA donor molecule into a host genomic CRISPR locus.

I have been a patent examiner at The United States Patent and Trademark Office (USPTO) for 16 years. I entered the USPTO after a long professional career as a biomedical researcher. As a career civil servant at the USPTO, my job helps foster an environment that creates economic growth and opportunity. My area of technology is molecular biology. Many scientists do not know the relevance of filing for a patent to seek intellectual protection for an invention. However, Dr. Jennifer Doudna and her research team understood that it was critical to protect the invention describing the CRISPR-Cas9 system. She filed her first application jointly with Dr. Charpentier and the University oof Berkeley on May 25, 2012. In fact, in early 2019, the USPTO has granted fifteen patents-based applications that Drs. Doudna and Charpentier had filed in 2012[1].

When I first reviewed U.S. Application No. 15/535,393 after its filing in 2014, scientist did not know the requirements for the integration of a donor DNA molecule into the genome of host prokaryotic cells[2]. I also knew little about the new CRISPR-Cas system and began reading publication by the inventor and other scientists in the field of CRISPR technology. Since 2012, the rapid development of genome-editing by CRISPR-Cas has allowed scientists to specifically target and cleave DNA or RNA, with many potential applications in biomedicine and research. This technology has become very popular today due to its potency, precision, and ease of use[3]. It is used from simple science experiments for high school students to more complex laboratory technologies. For example, my friend Dr. Ana Muñoz, who is a science teacher at Wakefield High School in Arlington, Virginia, has used it to modify the year' genome to introduce into it a gene encoding a green fluorescent protein so students can visualize the emission of green light when yeast growth[4]. Most recently, during the COVID-19 pandemic, a mouse model was created to observe pathological changes resembling those observed in COVID-19 human patients where the human angiotensin converting enzyme 2 (hACE2) replaced the mouse version of the enzyme using the CRISPR-Cas system[5].

"The rapid field of CRISPR technology allows scientists to target and cleave DNA or RNA".

When I started examining U.S. Application No. 15/535,393, I learned that the integration of a donor DNA molecule is the first step in the CRISPR-Cas adaptive immunity in bacteria and archaea. In this process, a foreign DNA donor molecule from a bacteriophage, for example, must be integrated into the prokaryotic host genome. In a second step, the integrated molecules are cleaved to generate short nucleic acid molecules named CRISPR RNAs (crRNAs) which will be responsible for targeting invading DNA or RNA in bacteria and archaea[2]. In a final step, the crRNAs will direct the cleavage of a foreign molecule via Cas proteins at a site complementary to the crRNAs[2].

"The integration of a DNA molecule is the first step in CRISPR-Cas adaptive immunity in bacteria and archaea ".

The subject of U.S. Application No. 15/535,393 relates to the first step, the acquisition of a donor DNA molecule or spacer catalyzed by CRISPR-associated (Cas) proteins, Cas1-Cas2[6]. Jennifer Doudna demonstrate that linear donor DNA molecules or spacers require 3'-OH ends and at least a terminal C 3'-OH end to integrate into supercoiled target DNA comprising an AT rich DNA region. Integration proceeds through a staggered two-step mechanism in which the C3'-OH first attacks the minus strand of the target DNA to produce a half-site intermediate. The 3'-OH on the opposite strand of the integrating DNA then attacks the target DNA away on the opposite side of the target DNA on the plus strand, leading to a full integration of the donor DNA molecules or spacers (figure)[7]. The inventors also demonstrated that a Cas1-Cas2 complex is necessary to integrate double stranded donor

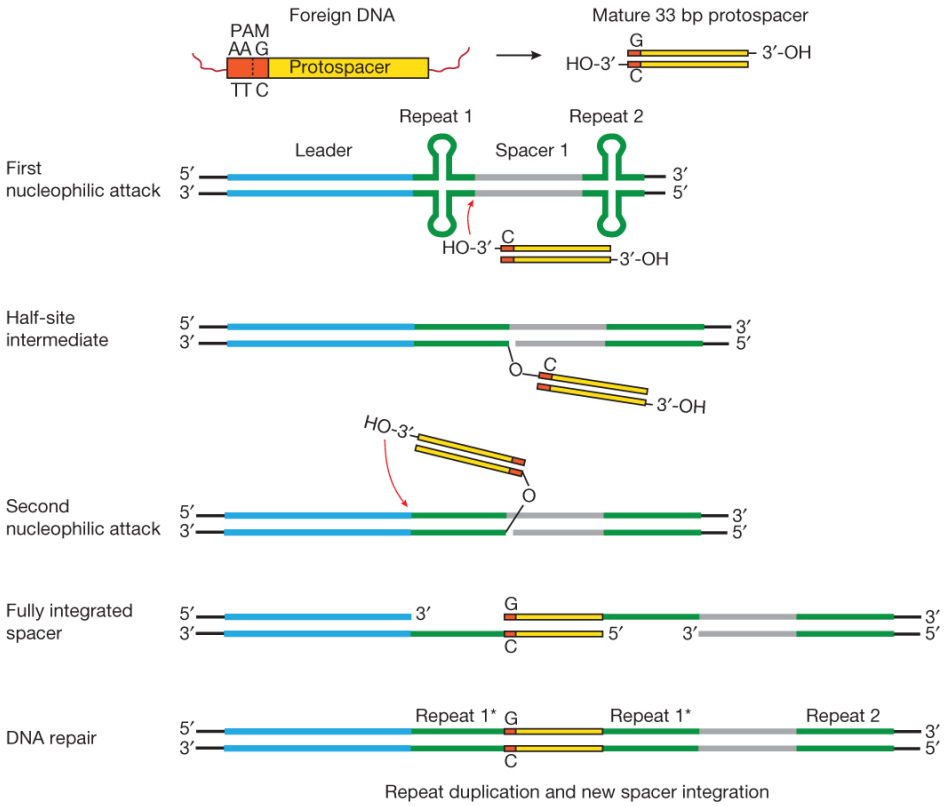

Figure. Explanation of protospacer integration in CRISPR-Cas. Adapted from Nuñez et al., 2015[7].

DNA molecule comprising a 3'-OH overhang with a length of 1 too 5 nucleotides but not with 5'-overhangs[7].

US Patent. 11,053,271 is a public document, it will be seen and reviewed by scientists to contribute to the advancement of the understanding of how a foreign DNA-Cas1-Cas2 complex targets supercoiled DNA in the first step of the adaptation stage of CRISPR-Cas immunity. Today, the CRISPR technology is becoming a powerful tool across all biological fields for identifying and characterizing pathogenic threats, detecting and diagnosis infectious agents, and developing new treatments for their diseases[5].

I can't think of a better way to showcase the value of encouraging innovation in the US through protection of intellectual property than by participating in the examination process of Application No. 15/535,393 filed by Jennifer Doudna and her research team.

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Sobre el autor

Maria Leavitt, Ph.D. works as a Primary Patent Examiner in Biotechnology at the United States Patent and Trademark Office (USPTO) since 2005. She has granted numerous patents in the field of transgenic animals, gene therapy, non-embryonic stem cells, nanotechnology, and polymers for nucleic acid delivery. Maria holds a Bachelor's of Science from Universidad Complutense of Madrid, and MS and BA degrees from Old Dominion University, Virginia, as well as a Ph.D. in Biomedical Sciences from Eastern Virginia Medical School.

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