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APRI researcher Dr. Sanghwa Lee's joint research team identifies DNA target searching and cleavage mechanism of Cas12a, one of the key proteins of CRISPR-based gene editing technology

- Korean researchers have identified DNA target searching and cleavage mechanism of Cas12a, one of the key proteins of CRISPR-based gene editing technology.
- GIST (President Seung Hyeon Moon) - Dr. Sanghwa lee of the Advanced Photonics Research Institute (APRI) in collaboration with Dr. Chul-hyun Jung of the Theragnosis Lab at the Korea Institute of Science and Technology (KIST) and Professor Sangsoo Bae of Hanyang University used single-molecule fluorescence imaging technology to observe in real time the entire DNA target searching and cleavage mechanism of Cas12a, one of the key proteins of CRISPR-based gene editing technology.
- The CRISPR/Cas9 gene editing technology has developed rapidly and has been widely used in various fields such as gene therapy and development of new breeding plant. However, in general, it has limitations such as off-target DNA cleavage that have base sequences

similar to the target DNA, and it also has limited operable targets within the entire genome.

- To overcome these technical limitations, the researchers have improved the gene editing technology by discovering and developing various alternative proteins. Among them, the Cas12a protein is known to have higher target specificity than Cas9, and thus it has been widely considered. Therefore, to understand the relatively high target specificity of Cas12a and to develop more improved gene editing techniques, research was needed to identify the target searching and cleavage mechanism of Cas12a.

- In this study, the researchers used a single-molecule fluorescence imaging technique to observe in real time the entire target searching and cleavage mechanism of Cas12a. Through this process, it was shown for the first time that the Cas12a protein cleaves a specific target through one-dimensional diffusion motion on long DNA and, after stable binding with target DNA, cleaves sequentially in time sequence from the non-target strand to target strand sequence.

- Dr. Sanghwa Lee said, "The results of this study on the target searching and cleavage mechanism of the Cas12a protein are expected to contribute to the improvement of CRISPR gene editing technology by showing how the molecular mechanism of Cas12a protein is distinct from Cas9."

- The research led by GIST Dr. Sanghwa Lee (APRI), Dr. Chul-hyun Jung (KIST), and Professor Sangsoo Bae (Hanyang University) was supported by supported by the National Research Foundation of Korea, the National R&D Program for Cancer Control, the GIST Research Institute, Next Generation BioGreen 21 Program, and the Korea Healthcare Technology R&D Project and was published in *Nature Communication* (IF 12.353) on July 17, 2018.

