Chiral inorganic particles used for gene editing

With the support by the National Natural Science Foundation of China, the research team led by Prof. Kuang Hua (匡华) from the State Key Laboratory of Food Science and Technology, International Joint Research Laboratory for Bio interface and Bio detection, Jiangnan University, discovered that the truncated morphology semiconductor nanocrystals could work mimetically as restricted incision enzyme to cut the specific site of DNA sequence. The work was published in *Nature Chemistry* (2018, 10: 821—830).

Restricted endonucleases are one of the most important tools in the recombinant DNA technology toolbox. Although current techniques have been developed to biomimick various functions of the bio system, it is still out of imagination to create an inorganic system to recognize the specific site of DNA and incise DNA with high selectivity. In terms of primary structure, natural restricted enzymes and inorganic particles share many similarities such as size, surface charge, surface ligand, crystal network, conformation, and chirality. Thus, it is very possible to realize elaborate DNA cutting by well-designed inorganic particles.

Regarding the above analysis, Kuang's group synthesized semiconductor nanoparticle cadmium telluride (CdTe). By modification of L/D cysteine on the surface of CdTe particles, the morphology of chiral particles was uniformly truncated, with mean diameter of 4.5 nm. 1839 bp DNA from salmon sperm was used to incubate with CdTe to find potential binding sites. Excitingly, the chiral particles selectively bound at (5'end) GAT^ATC(3'end) site and cut the phosphodiester bond between T and A under photo irradiation. Moreover, the scissoring did not happen if the DNA sequence was less than 90 bp, which mimicked the length restriction of a natural enzyme.

To understand the whole cutting mechanism, they set up a molecular dynamics model, and found that A and T bases preferred to absorb along the edge of truncated tetrahedral particles, while C and G bases preferred to be closer to the nearest corner. In DNA chemistry, the TATA box was the most flexible site due to the existence of only two hydrogen bonds in individual T-A pairs. The truncated CdTe particles (4.5 nm) well matched with the GAT^ATC pocket in scale and conformation. With the entry of CdTe particles into the "pocket", the phosphodiester bond between T and A was prolonged and weakened. Under irradiation, the photo active ROS attacked the weakened bond, resulting in the specific cutting between T and A.

Notably, the cutting activity of inorganic CdTe particles is independent of ion concentration and temperature. The cleavage efficiency was highly increased when circular polarized light (CPL) was applied for irradiation because of the chiral absorption properties of L/D cysteine modified CdTe particle. Furthermore, cell line and mice model experiments showed that the semiconductor particles perform well *in vivo*. This discovery opens up a new approach for gene editing by designing varied shaped, scaled and ligand inorganic particles.

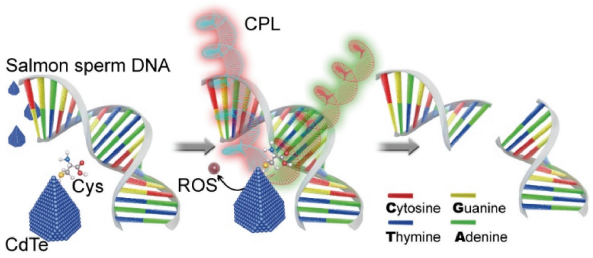

Figure Schematic illustration of chiral CdTe-based specific DNA cleavage under CPL irradiation.