Green tea catechin dramatically promotes RNAi mediated by low molecular-weight polymers

With the support by the National Natural Science Foundation of China, the research team led by Prof. Cheng YiYun (程义云) at the East China Normal University recently reported that green tea compounds could help small interfering RNAs (siRNA) drugs slip inside cells, which was published in *ACS Central Science* (2018, 4: 1326—1333). This work was highlighted by media such as American Chemical Society, ScienceDaily, EurekAlert, GEN, World Tea News, Phys Org, and China Science Daily.

siRNA has great potential to specifically down-regulate target genes for the treatment of various diseases. However, being relatively large and negatively charged makes siRNA molecules fail to across the cell membrane without the assist of vectors. Cationic polymers are one of the most potent candidates for siRNA delivery. Considering the rigidity and short double-helical structures, it is hard to condense siRNAs by polymers. Though efforts such as increasing the charge density and molecular weight to strengthen the siRNA binding affinity have been tried, the efficiency-toxicity correlation for these polymers has been unsatisfactory. Polymers with higher molecular weight suffer from higher levels of cell cytotoxicity. On the other hand, the lower ones with better cell compatibility show poor transfection efficacy due to weak binding affinity with siRNA molecules.

To breakdown the efficiency-toxicity correlation, Cheng's group introduced the natural polyphenol epigallocatechin gallate (EGCG) to formulate the siRNA into negatively charged nanoparticles as the core, and further coated the particles with low molecular polymers to form the shell (Figure). The supramolecular strategy makes it easier for low molecular weight polymers to condense the siRNA into uniform nanoparticles, which is applicable for various polymers with different topologies and chemical compositions. These nanoparticles strikingly silenced several target genes in different cell lines, and next successfully down-regulated the pro-inflammatory enzyme to attenuate chronic intestinal inflammation in an intestinal injury model.

The researchers termed the prepared nanoparticles "Green" nanoparticles (GNPs) because they used EGCG, the major ingredient of green tea and a naturally occurring polymer which was approved as food additives to prepare the nanoparticles, and also because the nanoparticles showed high efficiency and low toxicity during RNAi. Because of the chemical similarity of siRNA with microRNA, DNAzyme, antisense oligodeoxynucleotide, and peptide nucleic acids, the researcher says, the GNPs will work for a wide variety of nucleic acids and become a general and robust platform for gene delivery.

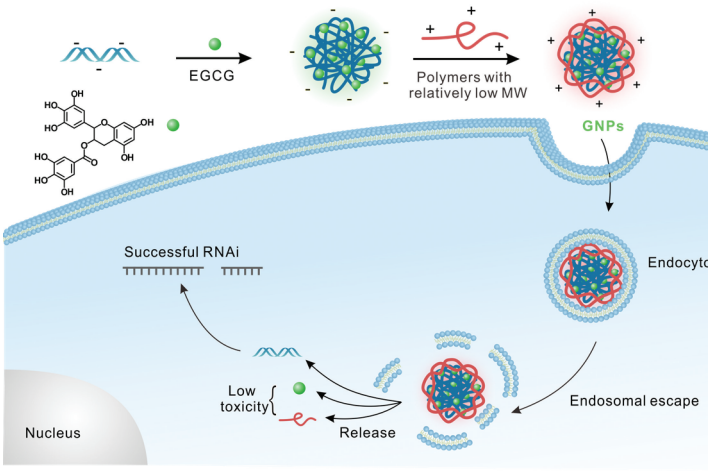

Figure Schematic illustration of GNPs formulation and the proposed gene silencing mechanism.