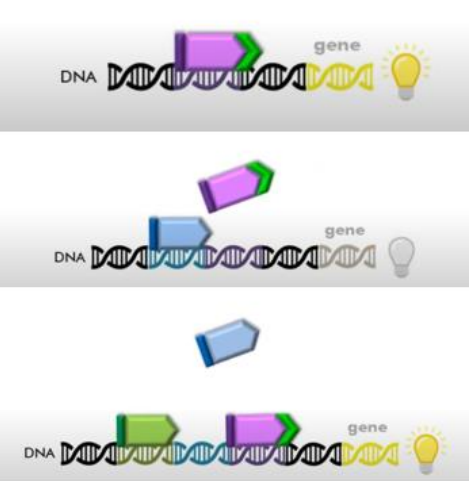
NATIONAL INSTITUTE OF CHEMISTRY

RESEARCH DOMAINS: Synthetic Biology, Genomics

INDUSTRIES: Biotechnology, Healthcare

GENE REGULATION BY MOLECULAR DISPLACEMENT



Gene expression is the process by which instructions in the DNA are converted into a functional product. Regulation of gene expression is vital for cellular development and determines it`s characteristics. Researchers from the National institute of Chemistry discovered a novel way of gene regulation by molecular displacement, facilitating the engineering of "designer" cells with desired characteristics. Cells, designed to exhibit therapeutic effects, can be used in the fields of medicine and diagnostics. Engineered cells could also be designed for drug discovery or production, making them useful in biotechnological applications.

Technology

TALEs (Transcription Activator-Like Effectors) are DNA-binding proteins, that act as molecular switches and control gene expression. Importantly, they can be designed to bind almost any selected DNA sequence, enabling specific control of any gene. We demonstrated that a TALE protein can displace another TALE protein from the DNA in a highly polarized manner when binding to the DNA sequence on its left, but not its right side. Such molecular displacement facilitated highly specific inhibition of gene expression in mammalian cells, which was demonstrated to be more efficient than other frequently used transcriptional silencing methods. The effect is scalable even up to five consecutive TALE proteins and can be used to encode complex genetic circuits within living cells, as demonstrated in mammalian cell culture. Moreover, TALEs are also able to displace other proteins from the DNA. An important example is the Cas9 nuclease, an efficient technology used for genome engineering with the important disadvantage of off-target binding. Displacing the Cas9 complex from off-target sites can prevent undesired cleavage of DNA, resulting in safer gene therapies.

Main advantages

- Precision and specificity - TALEs can be designed to bind any DNA target
- High efficiency compared to other frequently used transcriptional inhibition strategies
- Safety – application for prevention of undesired DNA cleavage by genome editing technologies

Key words

TALE proteins, molecular displacement, gene regulation

TYPE OF COOPERATION
Technology licensing opportunity

INTELLECTUAL PROPERTY
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