EG – MEGANUCLEASES

Meganucleases are endodeoxyribonucleases characterized by a large recognition site (double-stranded DNA sequences of 12 to 40 base pairs); as a result this site generally occurs only once in any given genome.
Meganucleases are therefore considered to be the most specific naturally occurring restriction enzymes.

In short **Meganucleases** are going to produce a cut in a very specific DNA site, thereby making it possible for genetic editing to occur.

Zinc-finger nucleases (**ZFNs**) are artificial restriction enzymes generated by fusing a zinc finger DNA-binding domain to a DNA-cleavage domain. Zinc finger domains can be engineered to target specific desired DNA sequences and this enables zinc-finger nucleases to target unique sequences within complex genomes. By taking advantage of endogenous DNA repair machinery, these reagents can be used to precisely alter the genomes of higher organisms. Alongside CRISPR/Cas9 and TALEN, ZFN is a prominent tool in the field of genome editing.

Transcription activator-like effector nucleases (**TALEN**) are restriction enzymes that can be engineered to cut specific sequences of DNA. They are made by fusing a TAL effector DNA-binding domain to a DNA cleavage domain (a nuclease which cuts DNA strands). Transcription activator-like effectors (TALEs) can be engineered to bind to practically any desired DNA sequence, so when combined with a nuclease, DNA can be cut at specific locations. The restriction enzymes can be introduced into cells, for use in gene editing or for genome editing *in situ*, a technique known as genome editing with engineered nucleases. Alongside zinc finger nucleases and CRISPR/Cas9, TALEN is a prominent tool in the field of genome editing.

In short both TALENs and ZFN work based on the fusion of a **DNA recognizing domain** and **a DNA cleavage domain.** The **DNA Cleavage Domain** in both **TALEN and ZFN is FokI** (The FokI nuclease functions as a dimer, and therefore two zinc-finger arrays must be designed for each target site).
While the **DNA recognizing domain** is TALE repeats in TALENs and Zinc-Finger in ZFN. TALE repeats only recognize a single nucleotide and Zinc Fingers recognize 3 nucleotide at a time.

Therefore TALENs are going to have a **higher specificity** and are going to make for **better tools in genomic engineering.** Henceforward we can conclude that there is a **Evolution of molecular** tools that with each generation there is a higher specificity and better reconnaissance ability of the DNA sequence and consequently a **better genomic editing.**

Recently, it was shown that **TALEN can be used as tools to harness the immune system to fight cancers** TALEN-mediated targeting can generate T cells that are resistant to chemotherapeutic drugs and show anti-tumor activity.