Two decades of research on interactions between Xanthomonas phytopathogenic bacteria and their hosts resulted in discovery of a novel Transcription Activator-Like Effector (TALE) protein family, which confers bacterial virulence in plants. TALEs bind selectively to plant promoters and activate expression of cognate genes enabling bacterial reproduction and dissemination. TALEs mediate recognition of specific promoter boxes in a simple and predictable manner. The TALE central repeat domain contains tandem repeats, which specifically contact single consecutive nucleotides in the target sequence via polymorphic amino acid residues. Repeats stack together in an unique right-handed superhelical assembly, which wraps around the DNA duplex. Validated TALE-DNA binding code shows, that two polymorphic amino acids NI, HD, NH, NG and NN in each repeat mediate recognition of A, C, G, T and A/G, respectively. The order of repeats determines recognized sequence in DNA sense strand. Custom TALE DNA-binding domains with desired specificities can be created within one week at low cost. Such designed domains fused to nuclease or activation domains are useful in research, biotechnology and gene-therapy for targeted gene editing and gene regulation. Notably, gene editing with custom-designed TALE nucleases (TALENs) allows for extending targeted genome modifications to a broad spectrum of organisms ranging from plants and insect to mammals.