

GeneArt® Precision TALs



TAL Effectors Technology

How TALs function

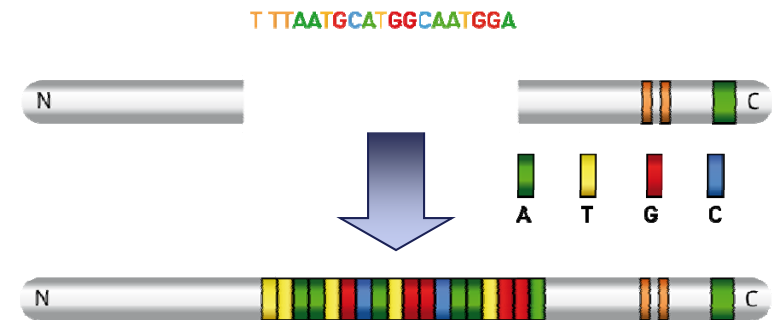
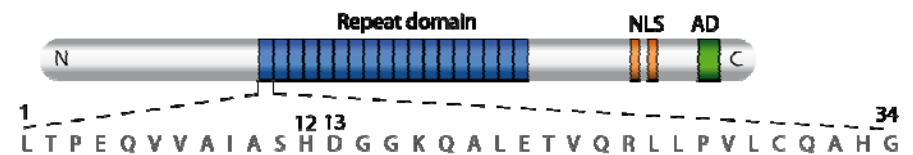
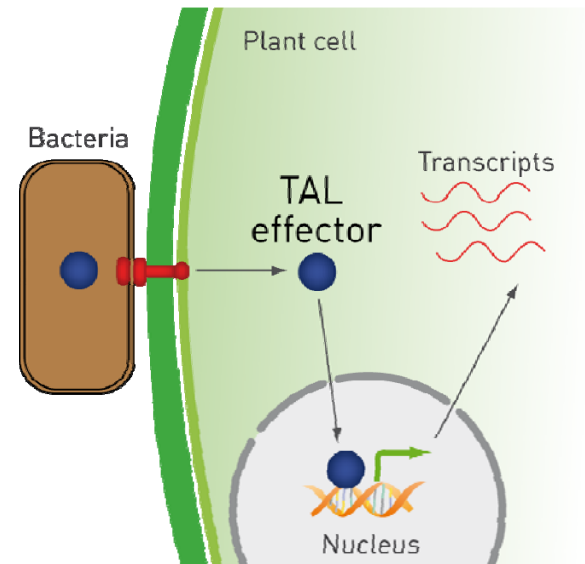
- Bacterial pathogen proteins rewire transcription of host plants upon infection
- TAL proteins use discrete domains to recognize A, T, G, C nucleotides in dsDNA

Engineered System

- Modular assembly of domains allows for creation of sequence specific DNA binding proteins

Why appealing

- Simple code for creating engineered TAL proteins: no bias except for a 5' T
- More predictable than Zn fingers
- One-to-one correspondence between the identity of two critical amino acids in each repeat and each DNA base in the target sequence

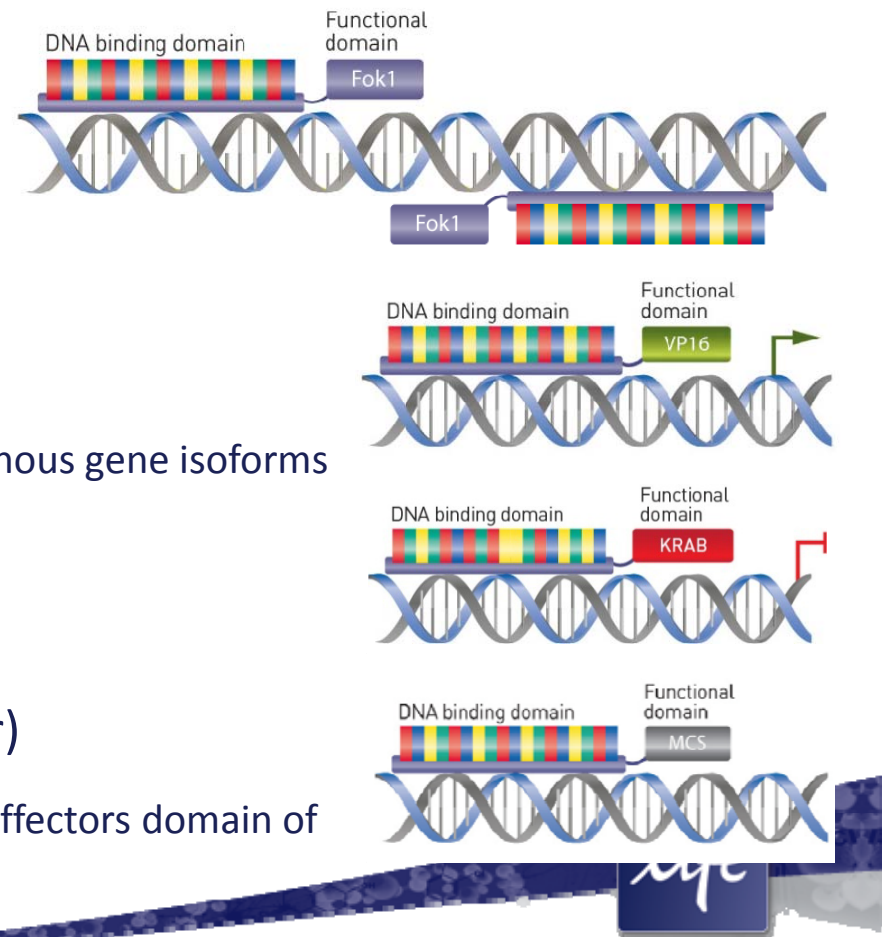


GeneArt® Precision TALs – our new Service

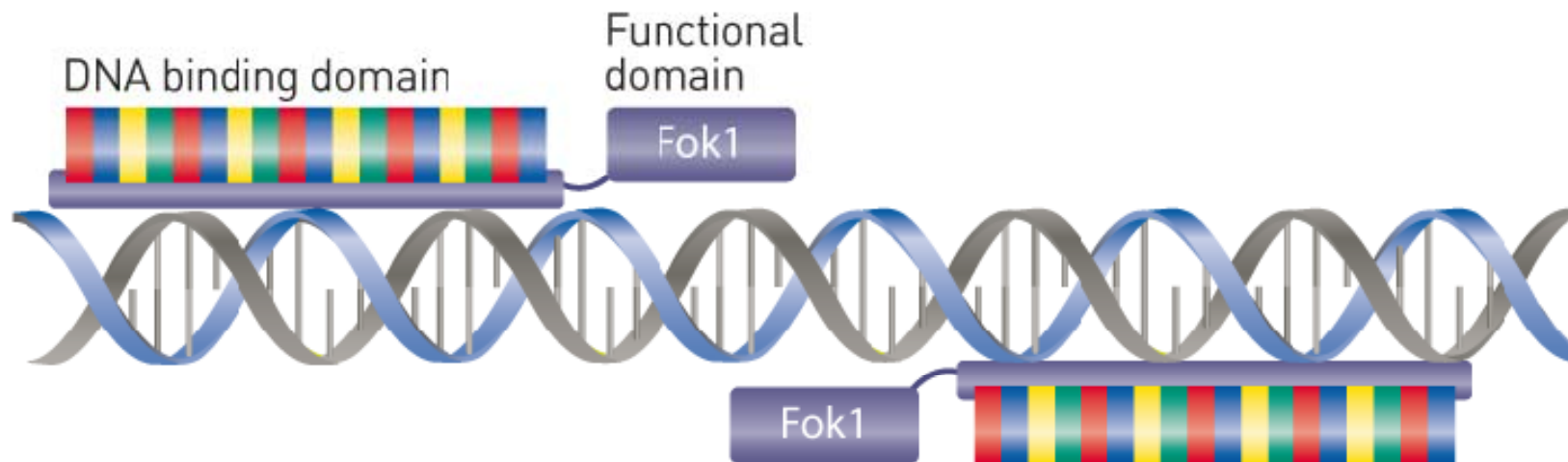
Custom DNA binding proteins for precision DNA targeting

What are they used for?

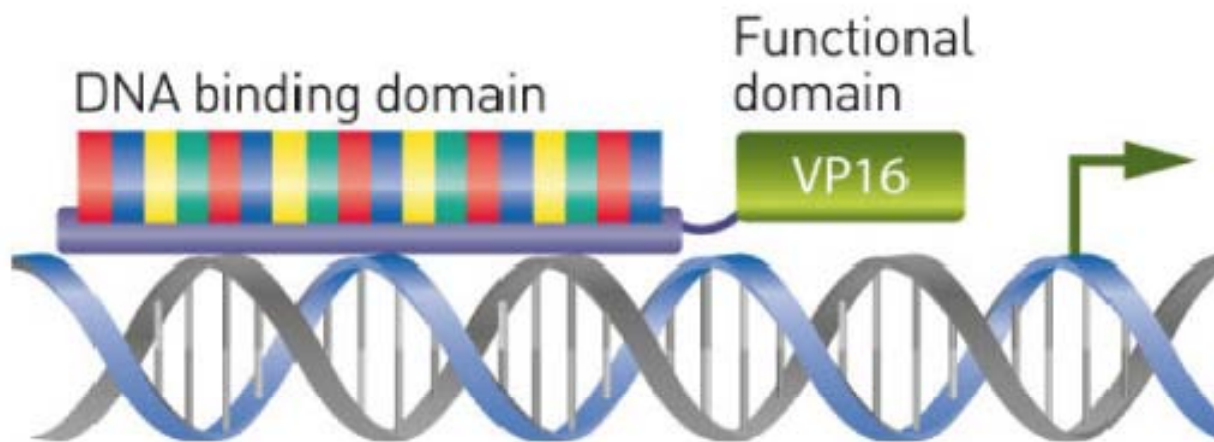
- Gene targeting (Fok1 Nuclease Pair)
 - Silencing
 - Incorporation of exogenous DNA
- Activation (Activator vp16 or vp64)
 - Increasing the expression level of endogenous gene isoforms
- Repression (Repressor KRAB)
 - Down-regulation of gene expression
- Effectors domain targeting (MCS Vector)
 - Target any locus in the genome with the effectors domain of your choice – multiple cloning site vector



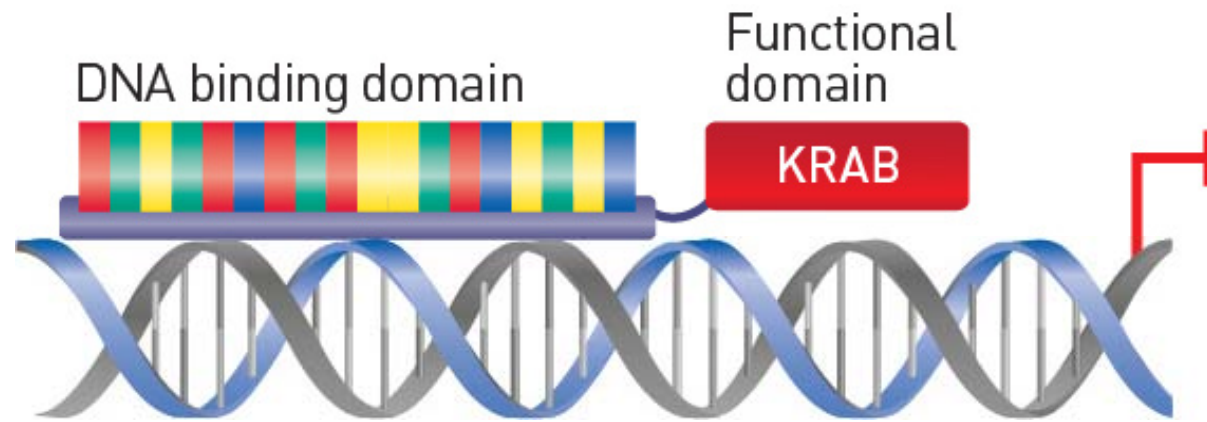
Conceptual Overview - Nuclease Pairs



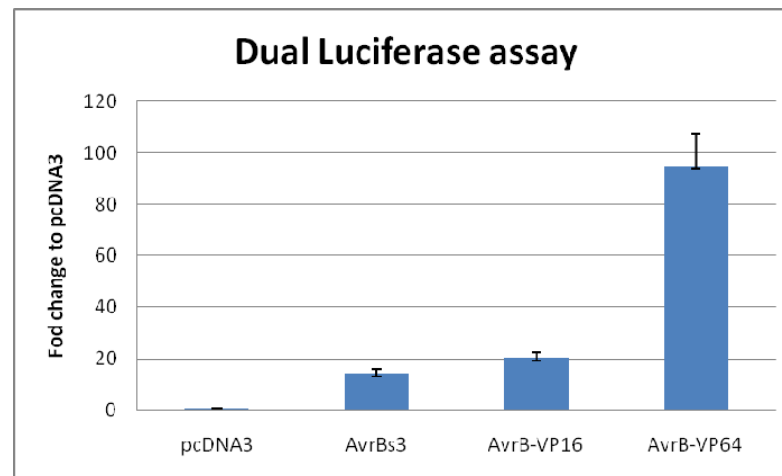
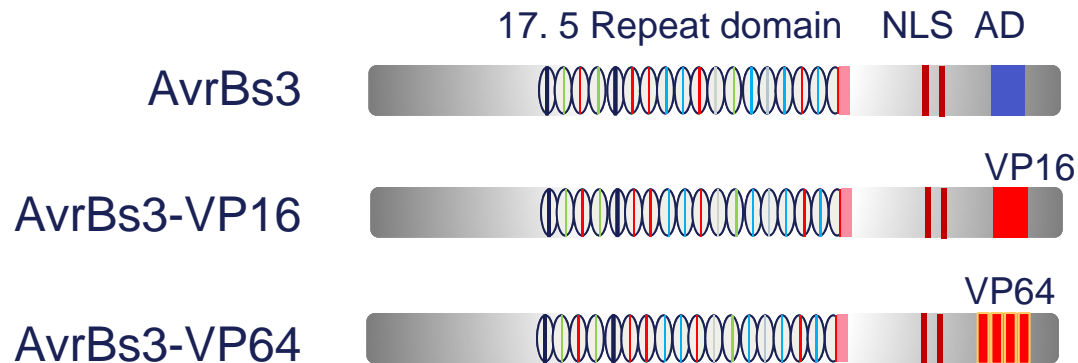
Conceptual Overview - Activator



Conceptual Overview - Repressor



Comparison of TAL transcriptional activators



293FT cells were transfected with reporter and the indicated plasmids. Dual luciferase assay was performed 72h post-transfection. Data was normalized to Rluc readings

Fold Increase
to pcDNA3

1

14

20

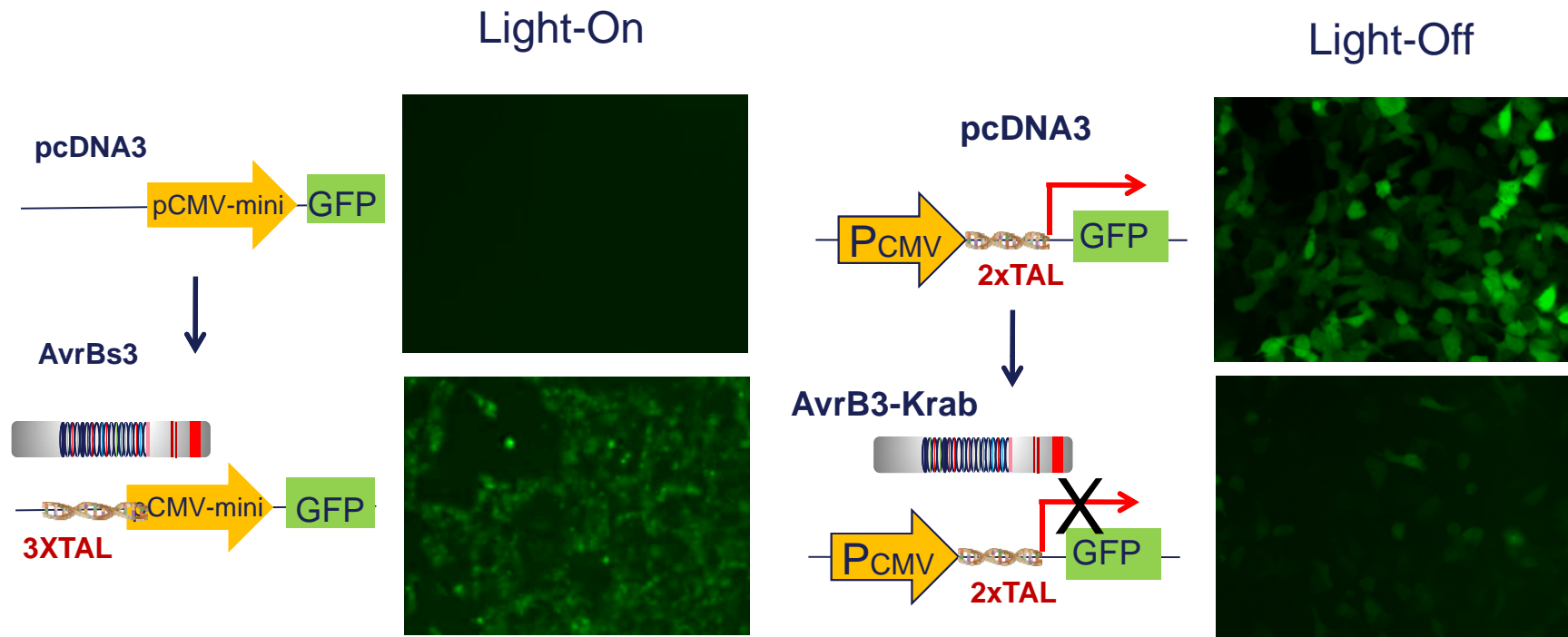
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Wild type TAL or TAL fusion with VP16, VP64 show robust activation of reporter from minimal promoter in mammalian cell lines.



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TAL effectors regulate gene expression in mammalian cells



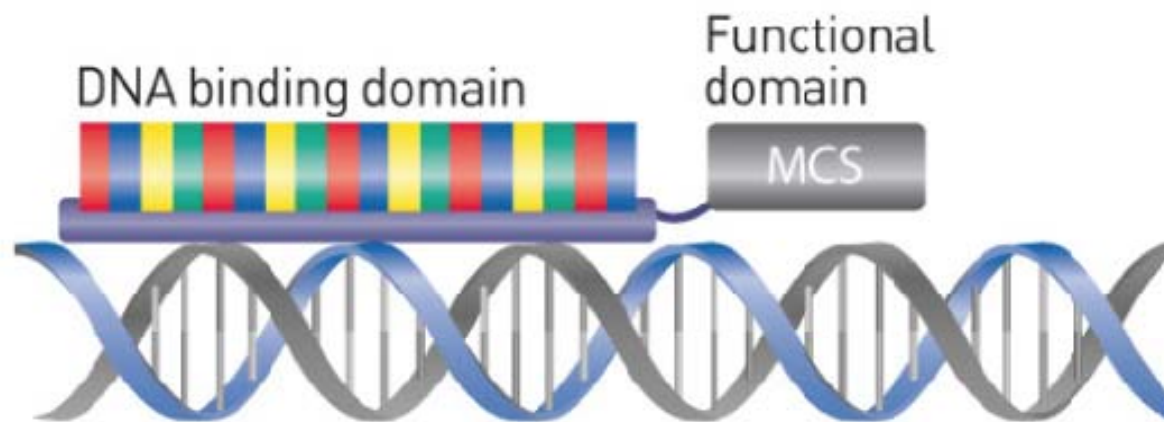
- The indicated plasmids were transfected into 293FT cells. Images were taken 48h post-transfection.

TAL-effectors can regulate reporter gene expression in mammalian cell line transient transfection assays



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Conceptual Overview – MCS Vector



Precision TAL Service

- Production of custom gene encoding TAL
- Time Frame
 - 2 weeks order to delivery
- Delivery Format
 - DNA – same as gene synthesis (5 ug lyophilized)
 - Gateway entry clone
 - 18 or 24 repeats (recognizes 19 or 25 bases with a 5' T)
 - Additional services available
 - LR Swap
 - Maxi Preps
 - Coming soon



GeneArt® Precision TALs: Available Products

Vectors available

Product Name	TAL	Effector Domain
Native TAL FokI	Native	FokI
Truncated TAL FokI	Truncated	FokI
Native TAL vp16 activator	Native	vp16 activator
Native TAL vp64 activator	Native	vp64 activator
Native TAL MCS	Native	MCS
Truncated TAL MCS	Truncated	MCS
TAL repressor	Modified	KRAB

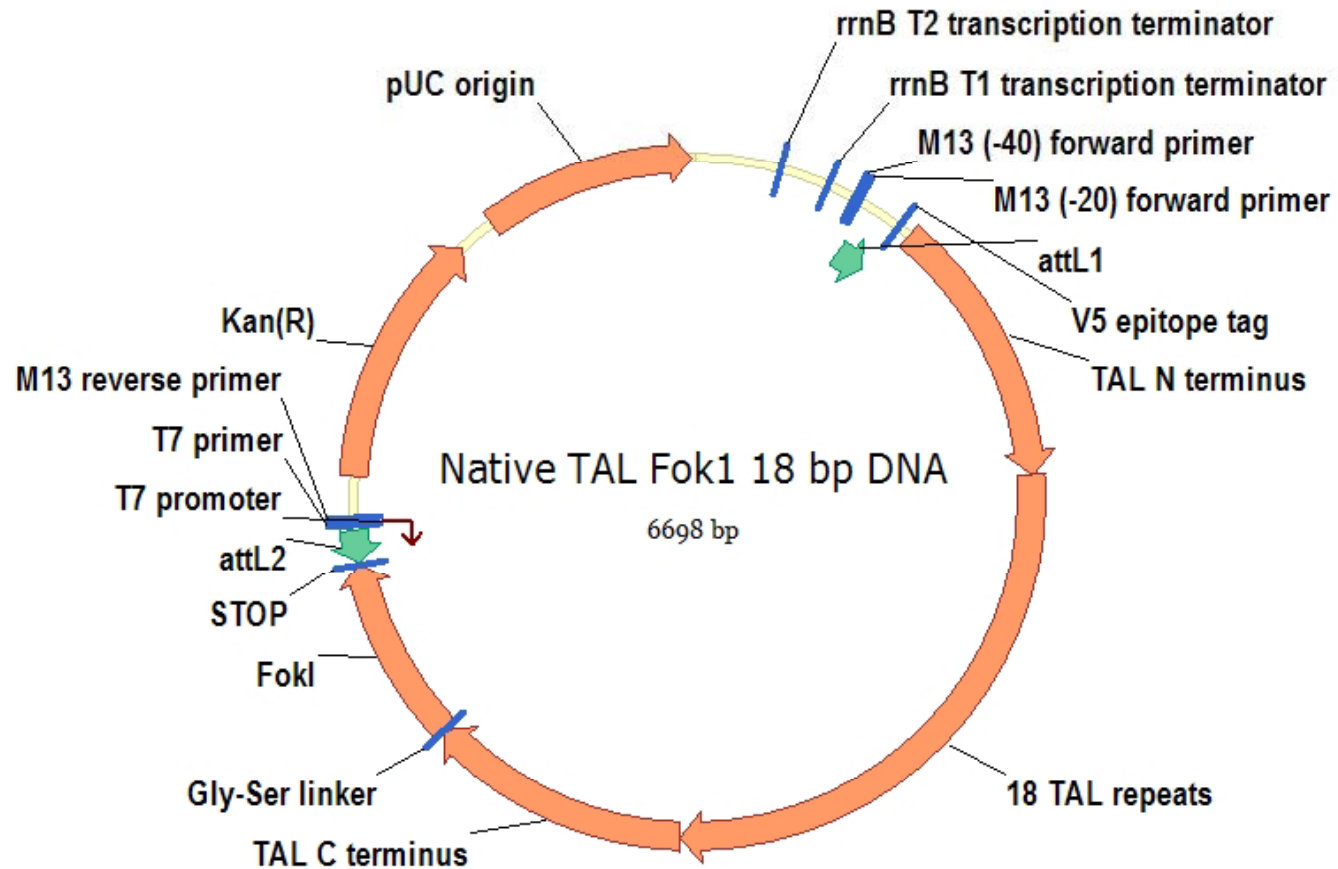
Benefits & Features

TAL Format	Customer Need
Truncated TAL Fok 1	Recommended for mammalian cells
Native TAL Fok 1	Recommended for plants
Native Activators	Higher performance in non mammal systems
Truncated MCS	Removing endogenous activator activity

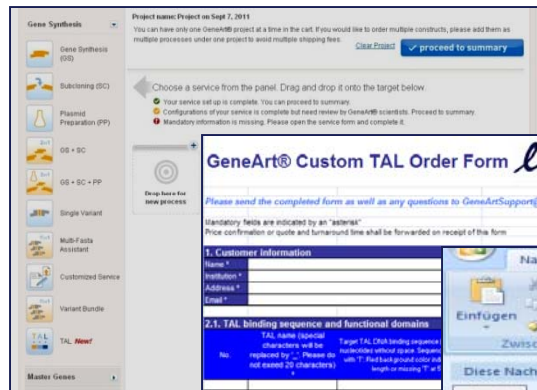


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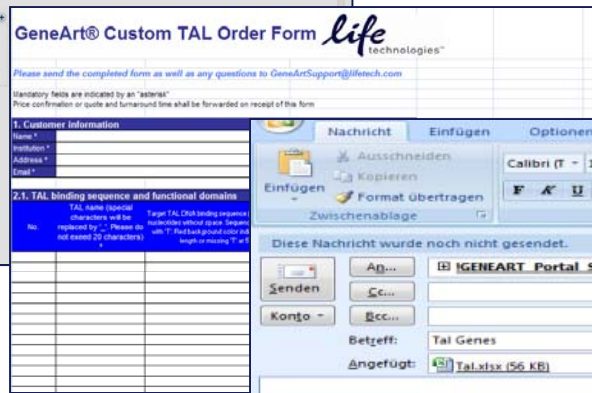
Native TAL Effector Fok1 Entry Vector



GeneArt® Precision TALs - Ordering



- Access the GeneArt Web Portal from the Life Technologies website



- Download and complete the [order form](#)



- Email the completed form to geneartsupport@lifetech.com
- All inquiries will be answered within 24 hours
- Production starts within 24 hours of ordering
- **2 weeks order to deliver**

QC

- 1) Subunit pre verification
- 2) Intermediate assembly sequence
- 3) TAL terminus sequence
- 4) TAL size



Applications

- Gene Targeting gene KO
 - Mouse models
 - Cellular Models
- Gene Activation
 - Disease Models
- Basic R&D
 - Unique DNA modification domains
 - Gene over expression
- Applied Markets
 - Ag Bio gene targeting
 - Enzyme engineering
 - Bio Fuels



Key TAL Literature

- Boch J, et al. (2009) **Breaking the code of DNA binding specificity of TAL-type III effectors.** Science Dec 11;326(5959):1509-12.
- Moscou M, et al. (2009) **A simple cipher governs DNA recognition by TAL effectors** Science, Dec 11;326(5959):1501
- Miller J, et al. (2010) **A TALE nuclease architecture for efficient genome editing.** Nat. Biotech. Online pub.
- Geibler R, et al. (2011) **Transcriptional Activators of Human Genes with Programmable DNA-Specificity.** PLoS ONE 6(5): e19509.
- Hockemeyer D, et al. **Genetic engineering of human pluripotent cells using TALE nucleases.** (2011) Nat. Biotech. Online pub.



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