

Gene Expression Modulation via CRISPR/Cas9

ANSC 691

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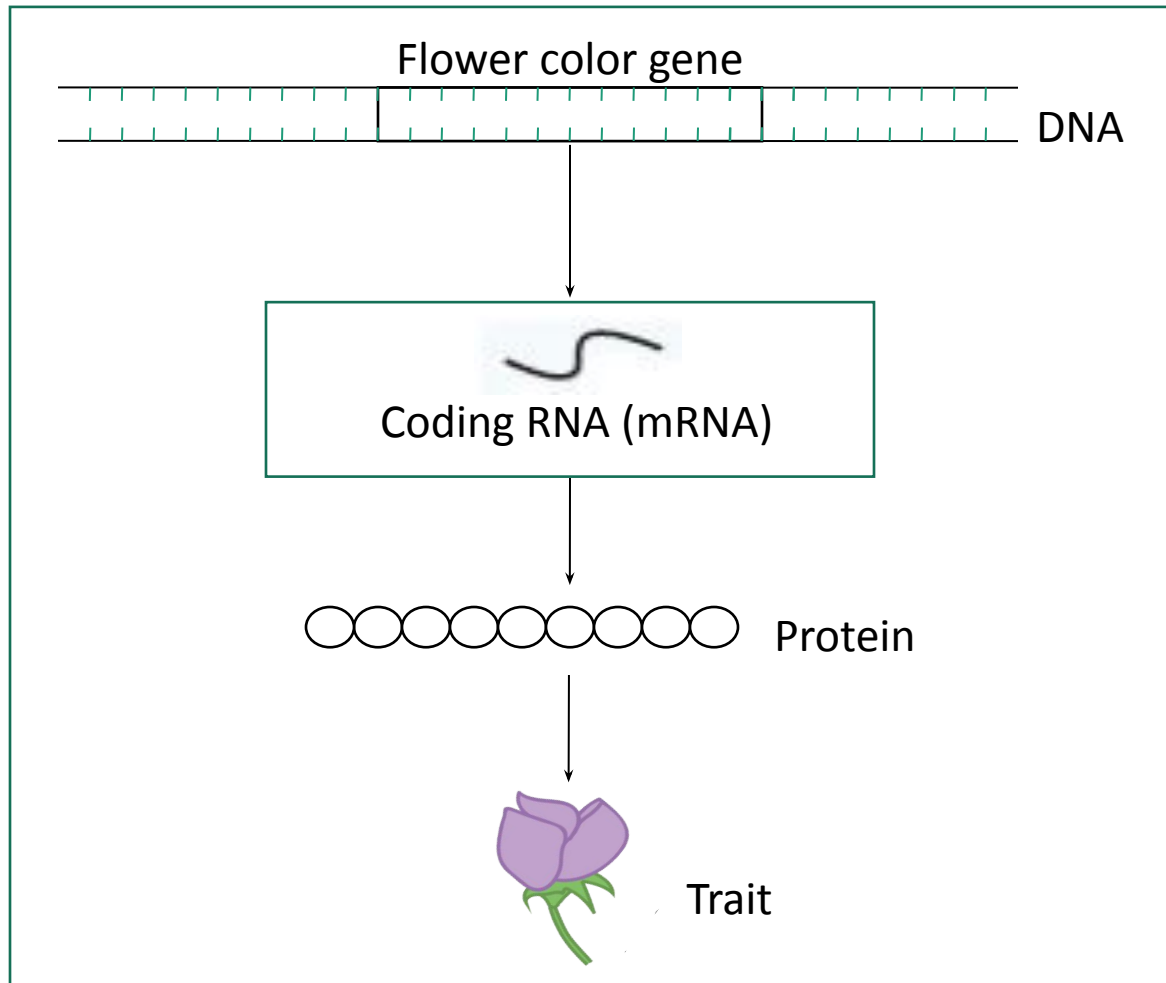
McGill
UNIVERSITY



We Are Different But Reside Together On Earth



Gene Function



Outline



Gene Expression Variation



DNA Modification & Post-transcriptional Control

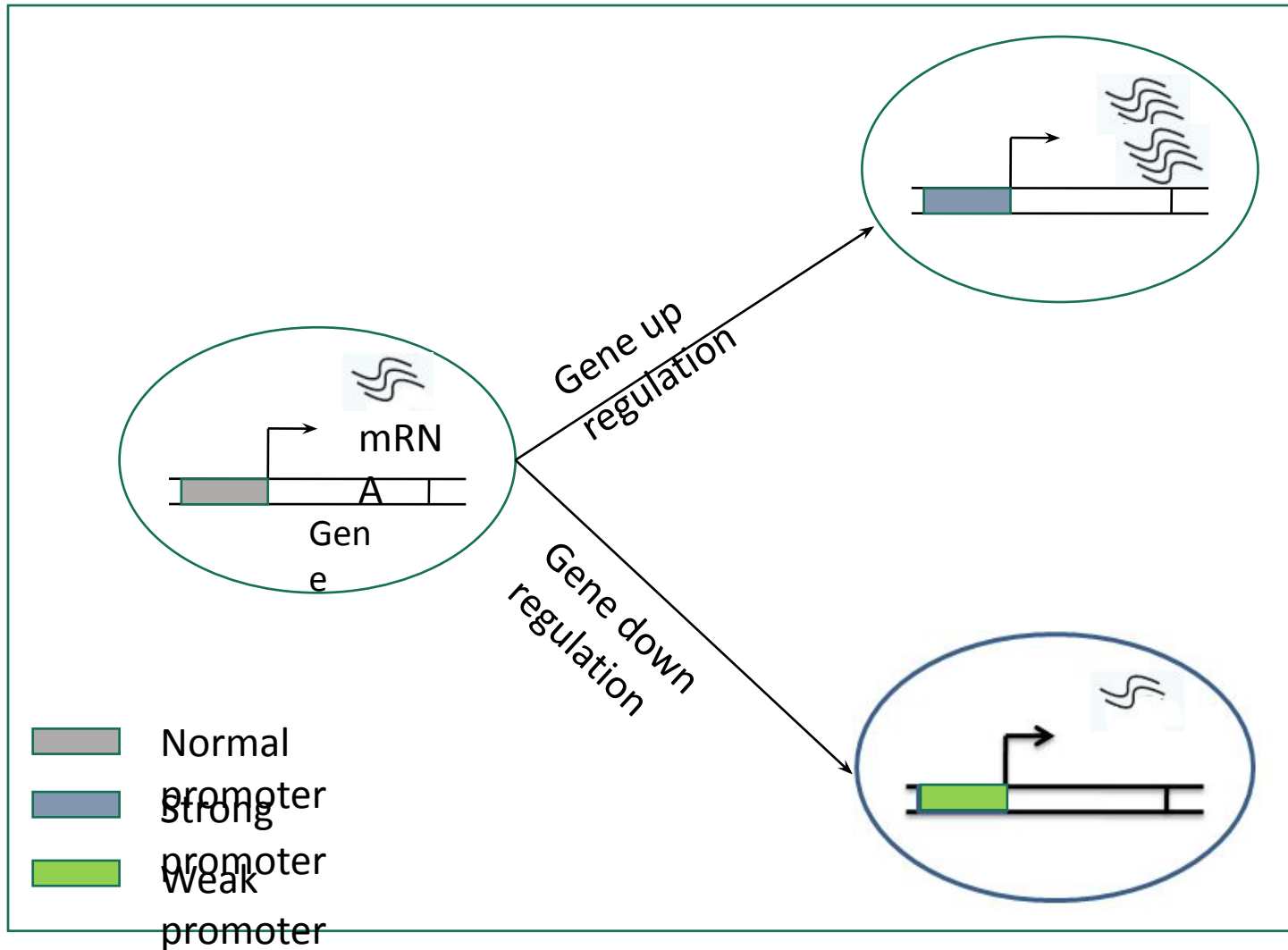


CRISPR/Cas9 Application in Gene Regulation

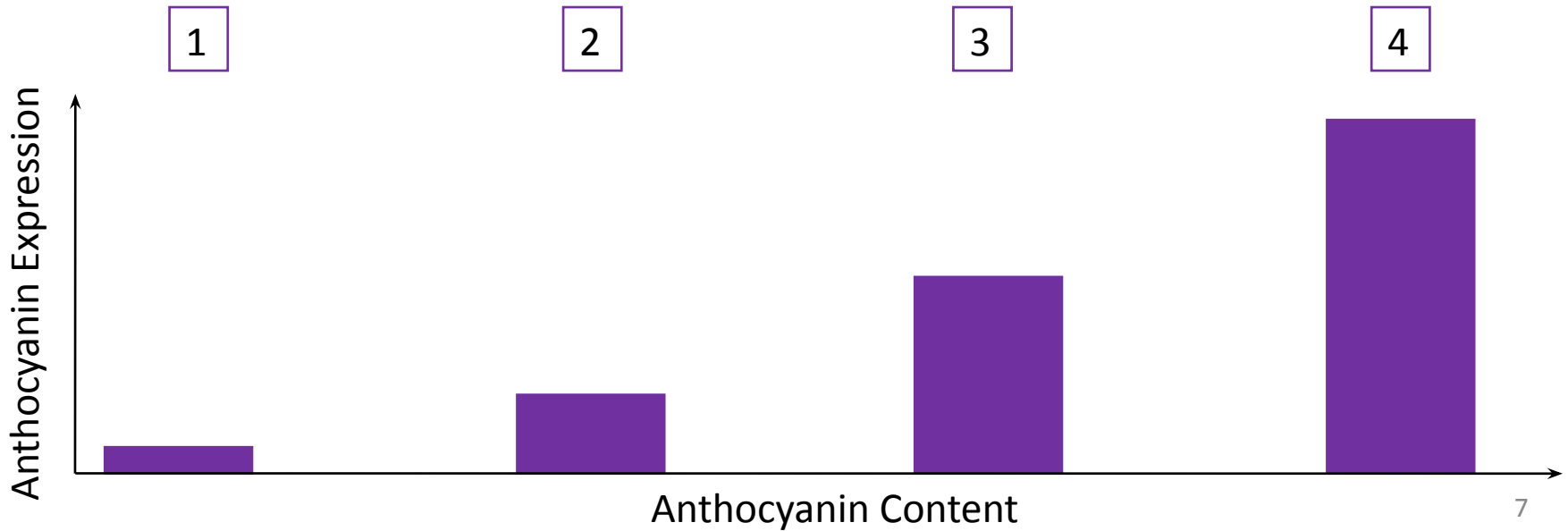


Challenges & Future Prospects

Gene Expression Level



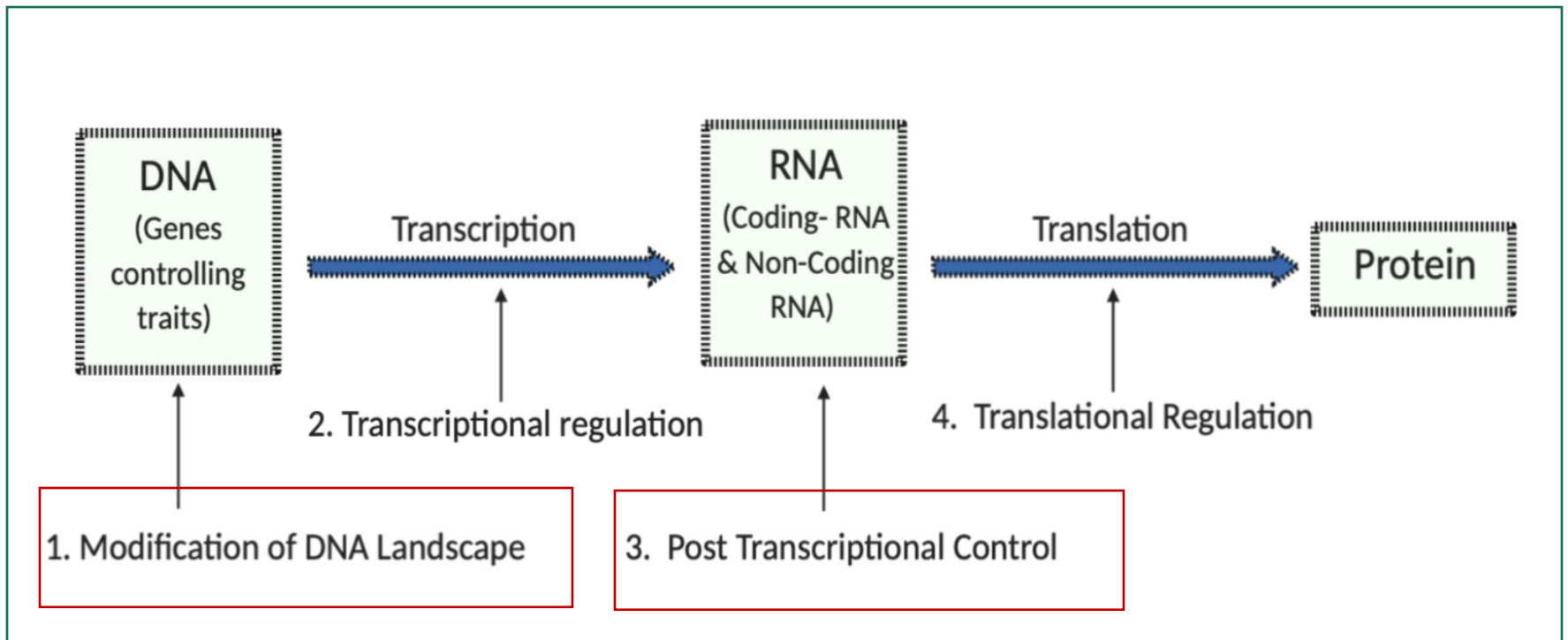
Gene Expression and Level of Phenotype



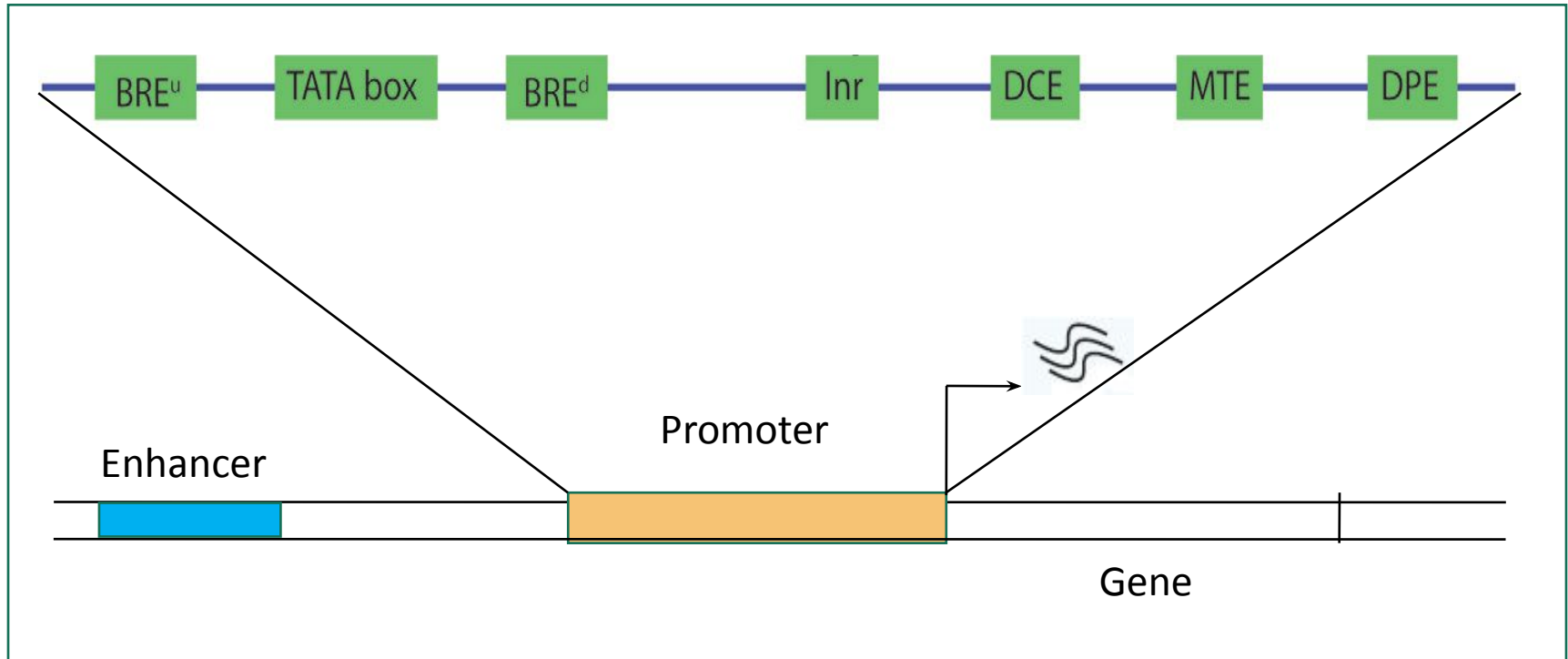
Why Varied Gene Expression Occur



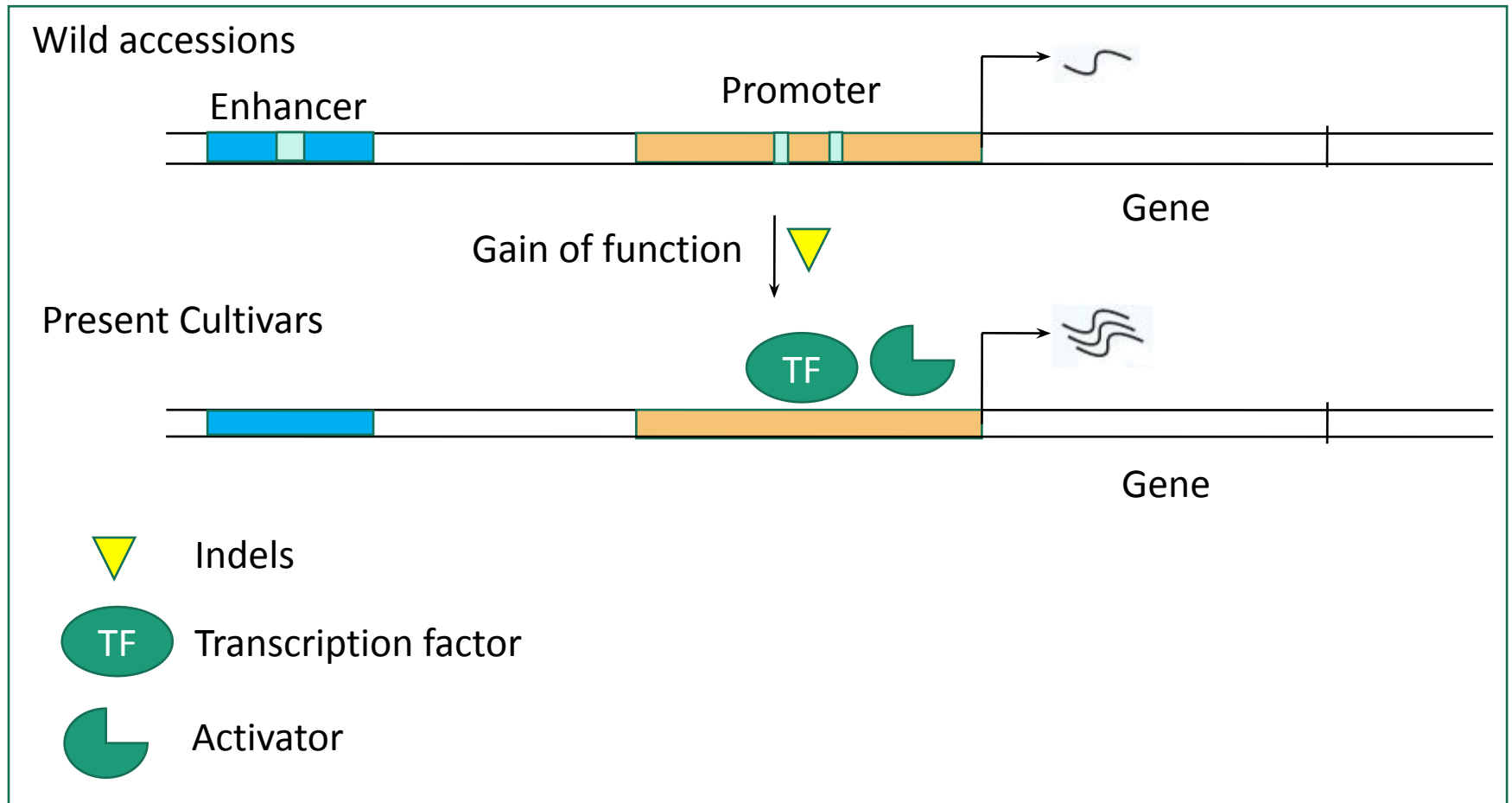
Genetic Expression Control



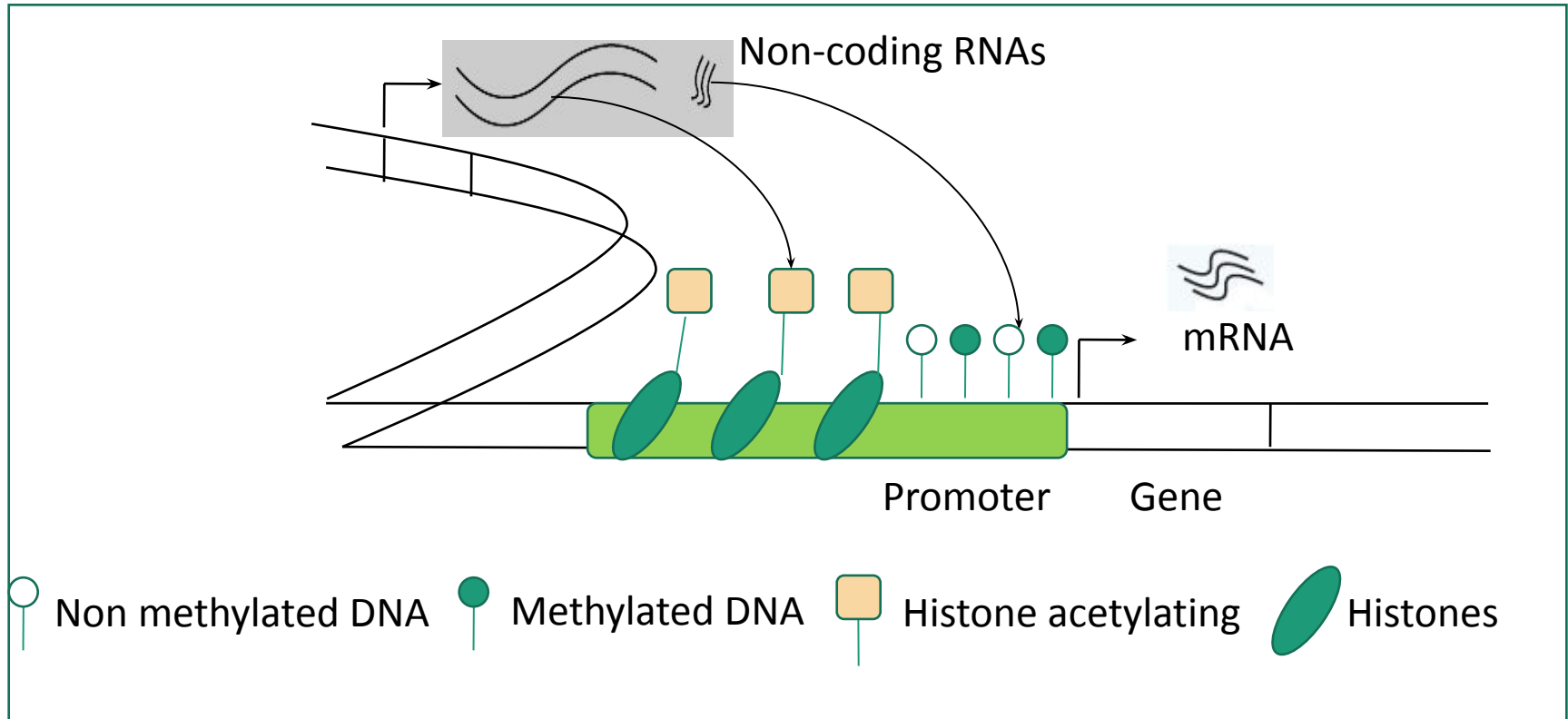
DNA Landscape Controls Gene Expression



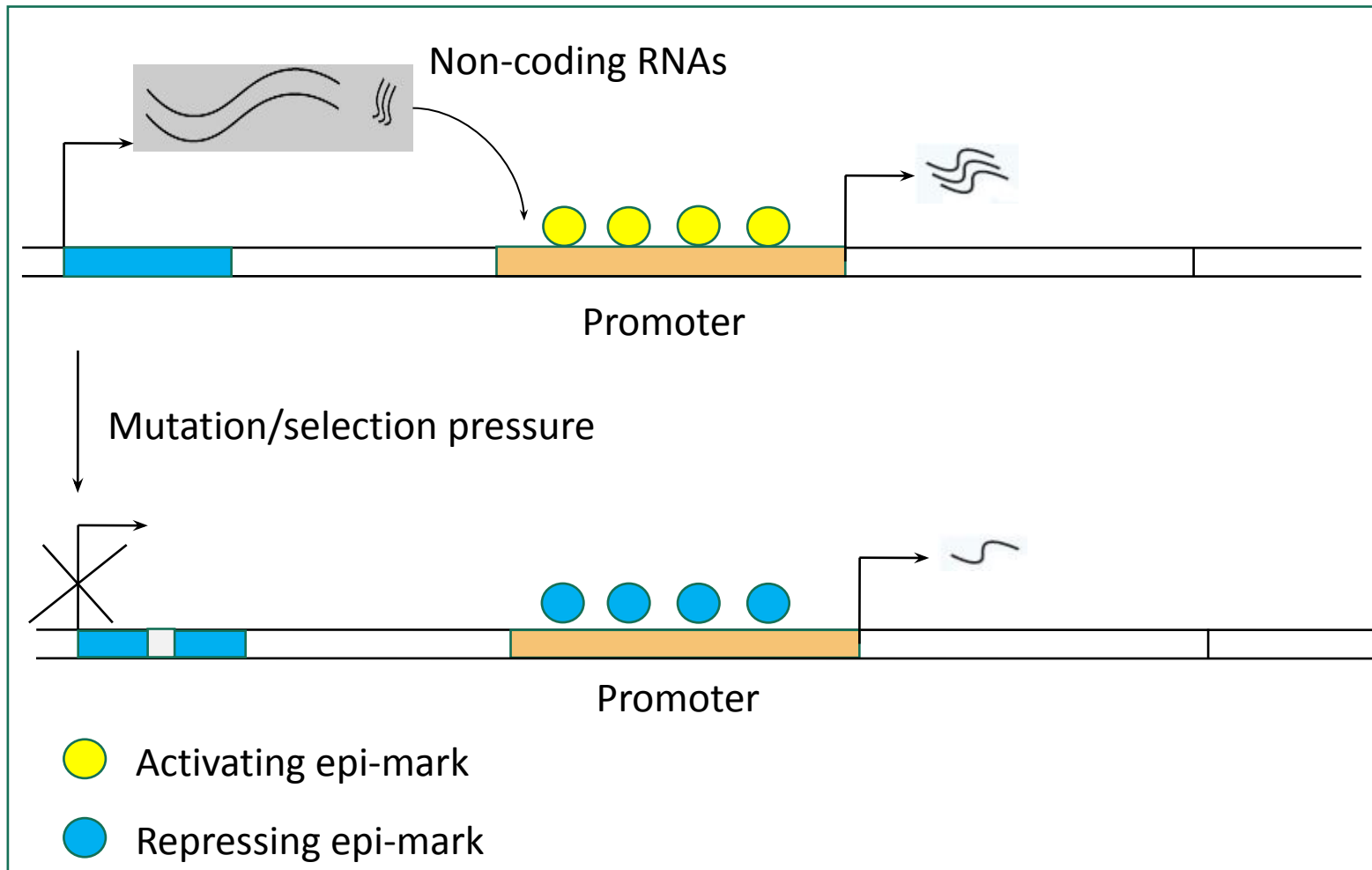
DNA Landscape Controls Gene Expression



Post-transcriptional Control



Post-transcriptional Control



Methods to modify gene expression

Induced mutations

Gamma rays, EMS (Genomic mutations) and 5-aza Cytidine (Epigenomic mutations)

Transgenics

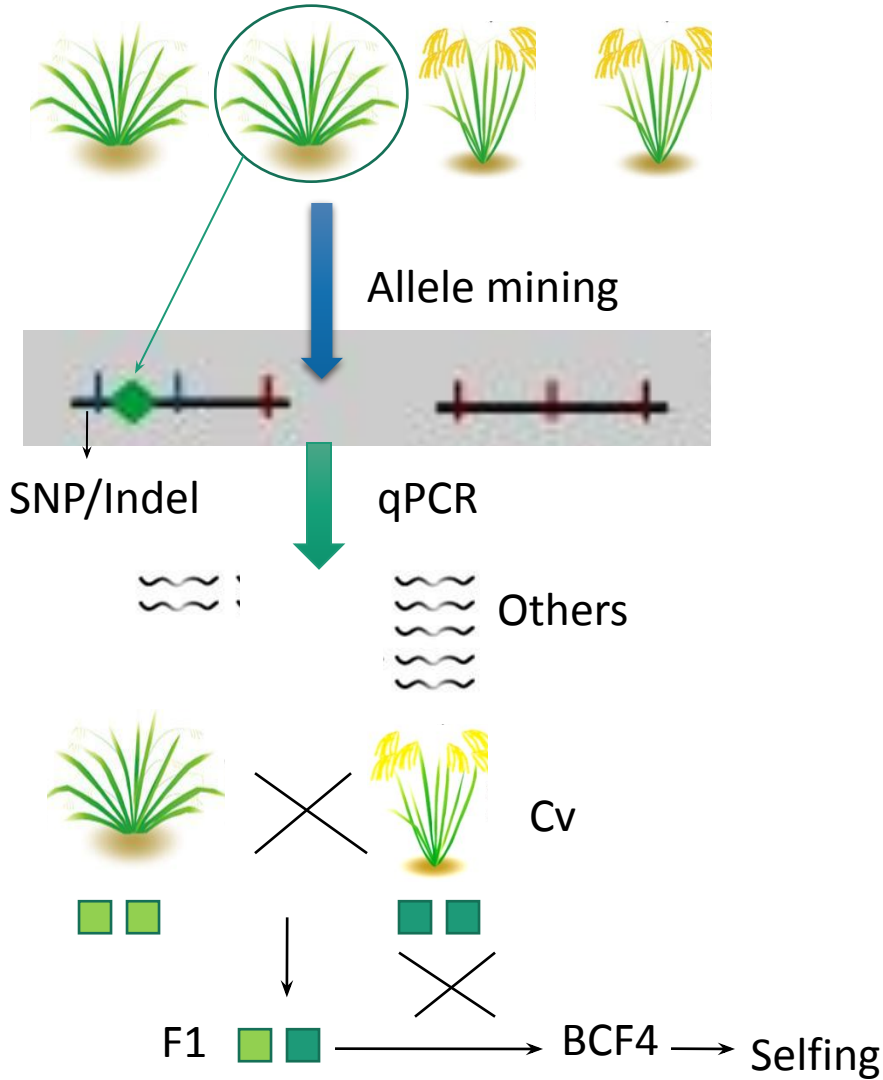
Synthetic promoters, TFs, Poly A stretch, RNAi

Genome/
Epigenome
editing

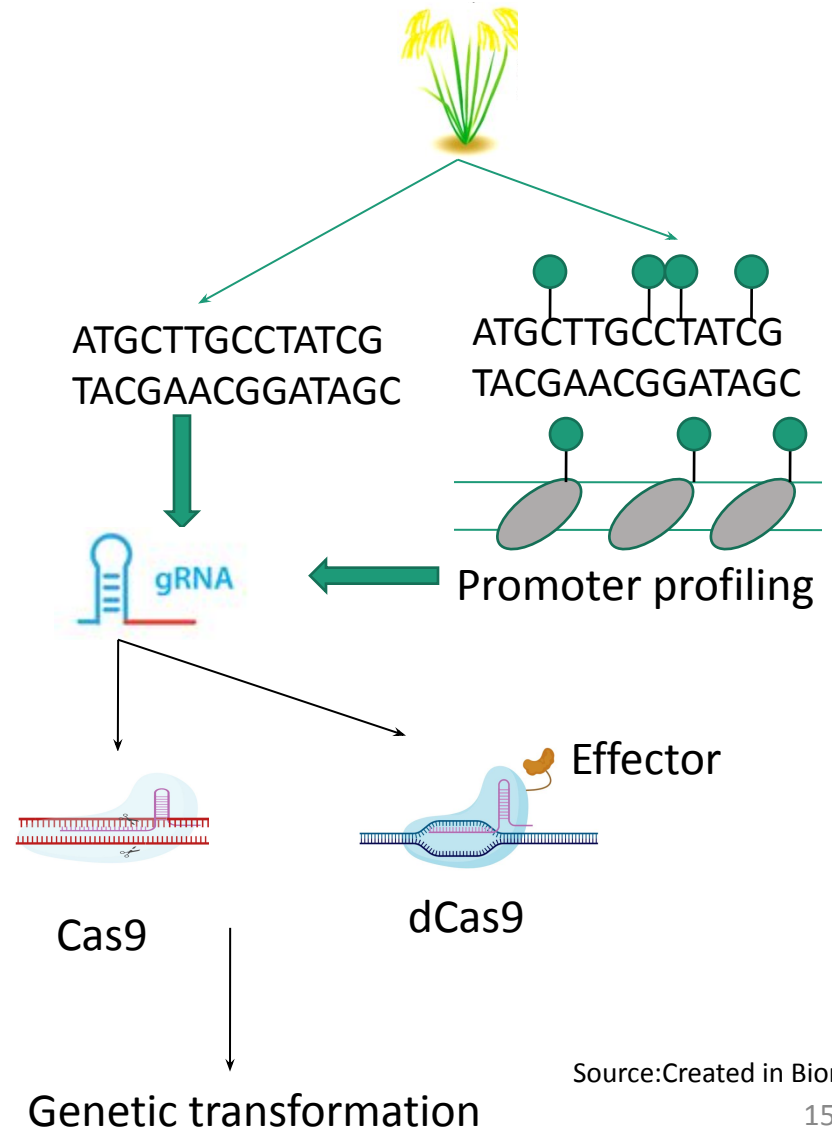
ZFNs, TALENs, CRISPR-Cas9/dCas9

CRISPR Vs Breeding

Molecular Backcross Breeding, 5-6 years

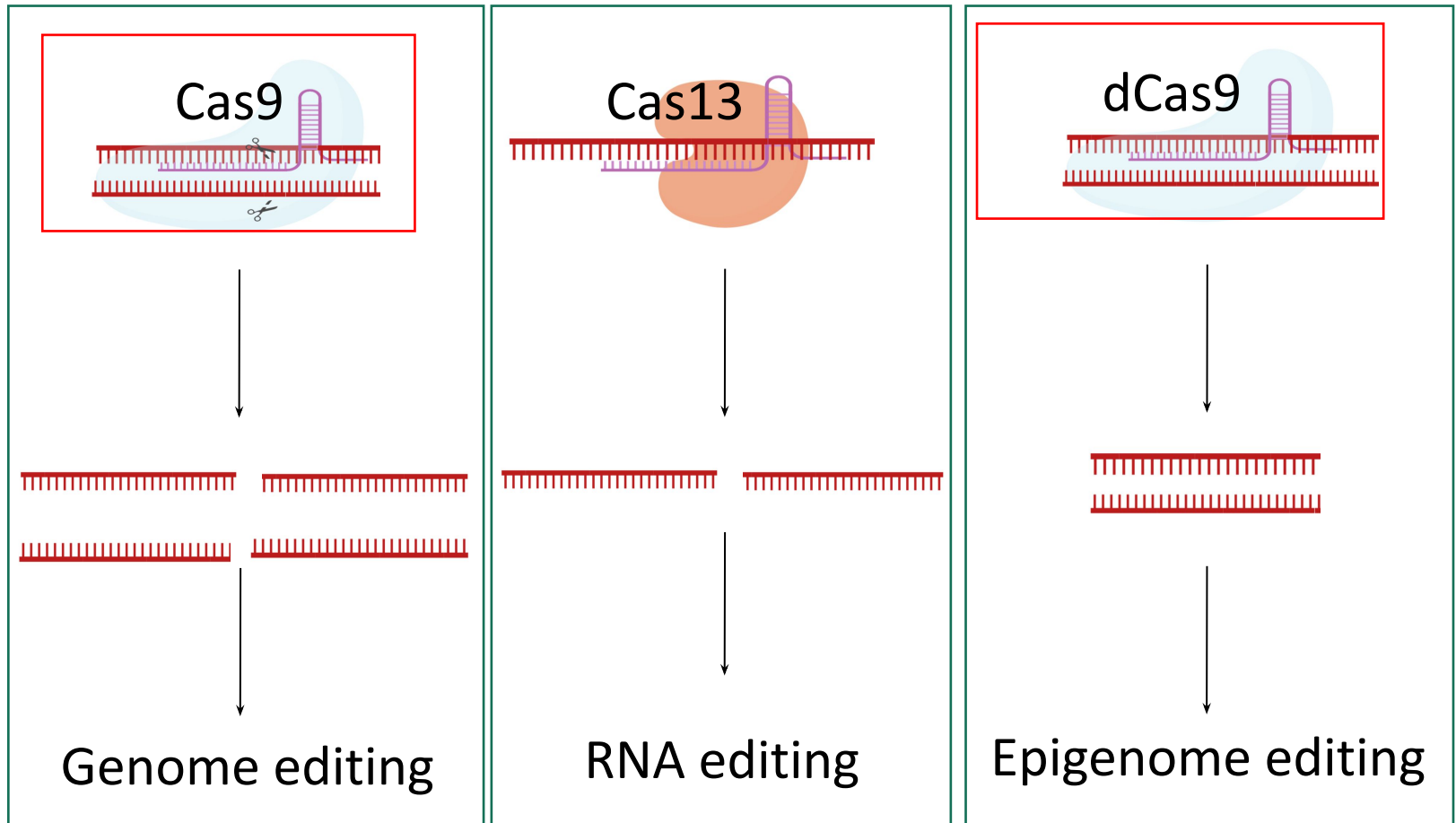


CRISPR Editing, 2-3 years

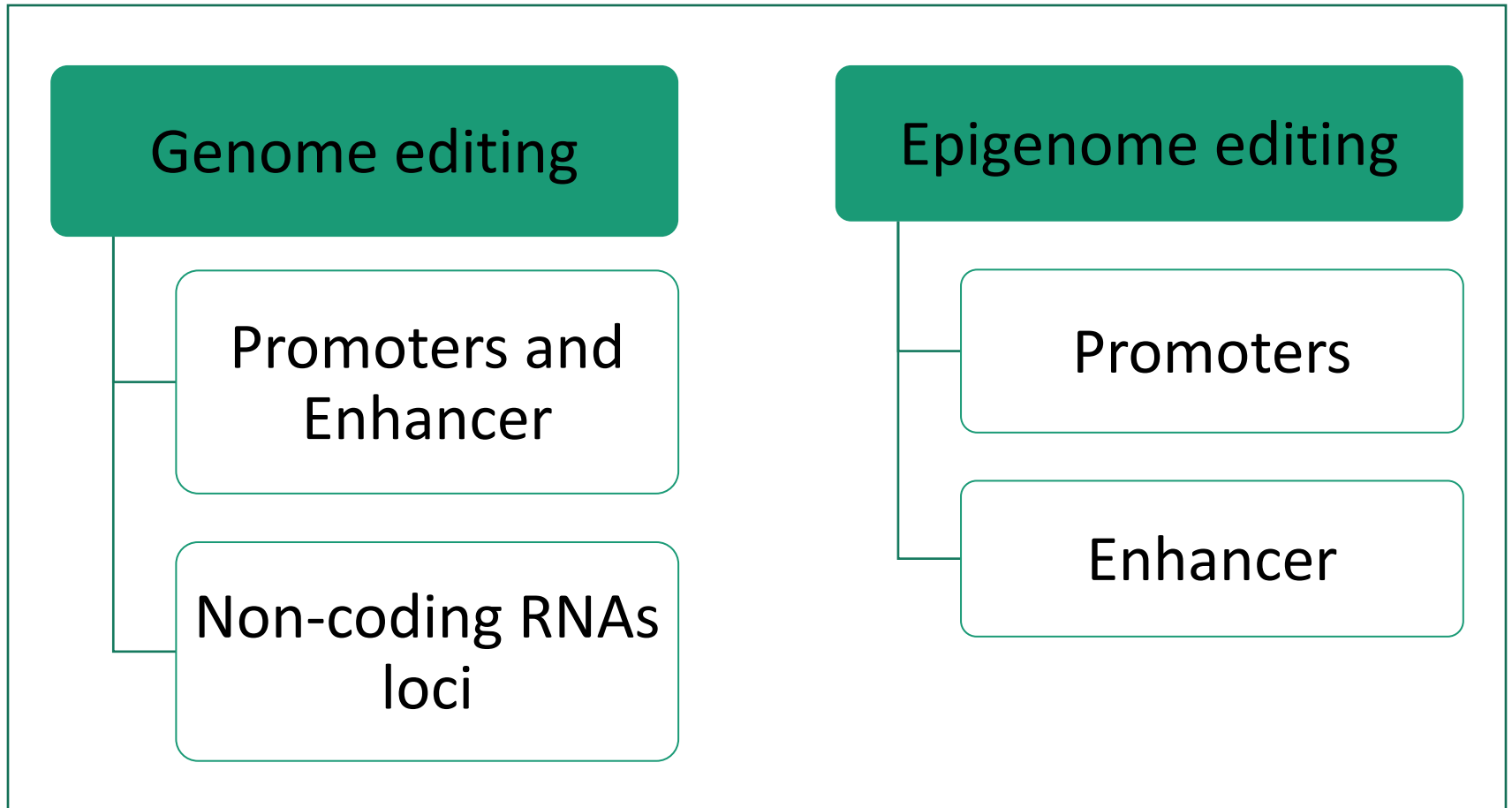


Source: Created in Biorander

CRISPR/cas Variants



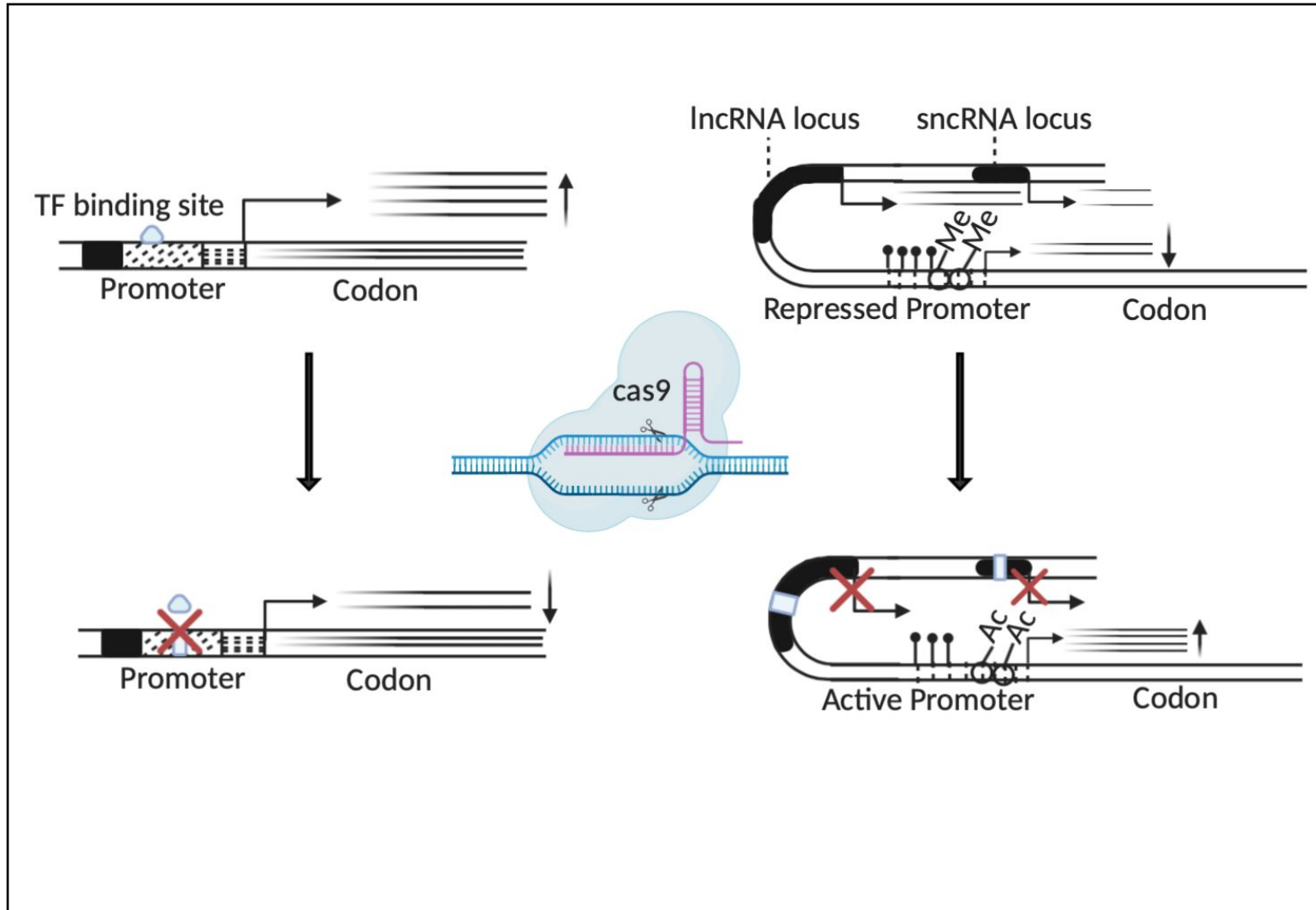
CRISPR Toolbox Targeting DNA Regions





Genome Editing

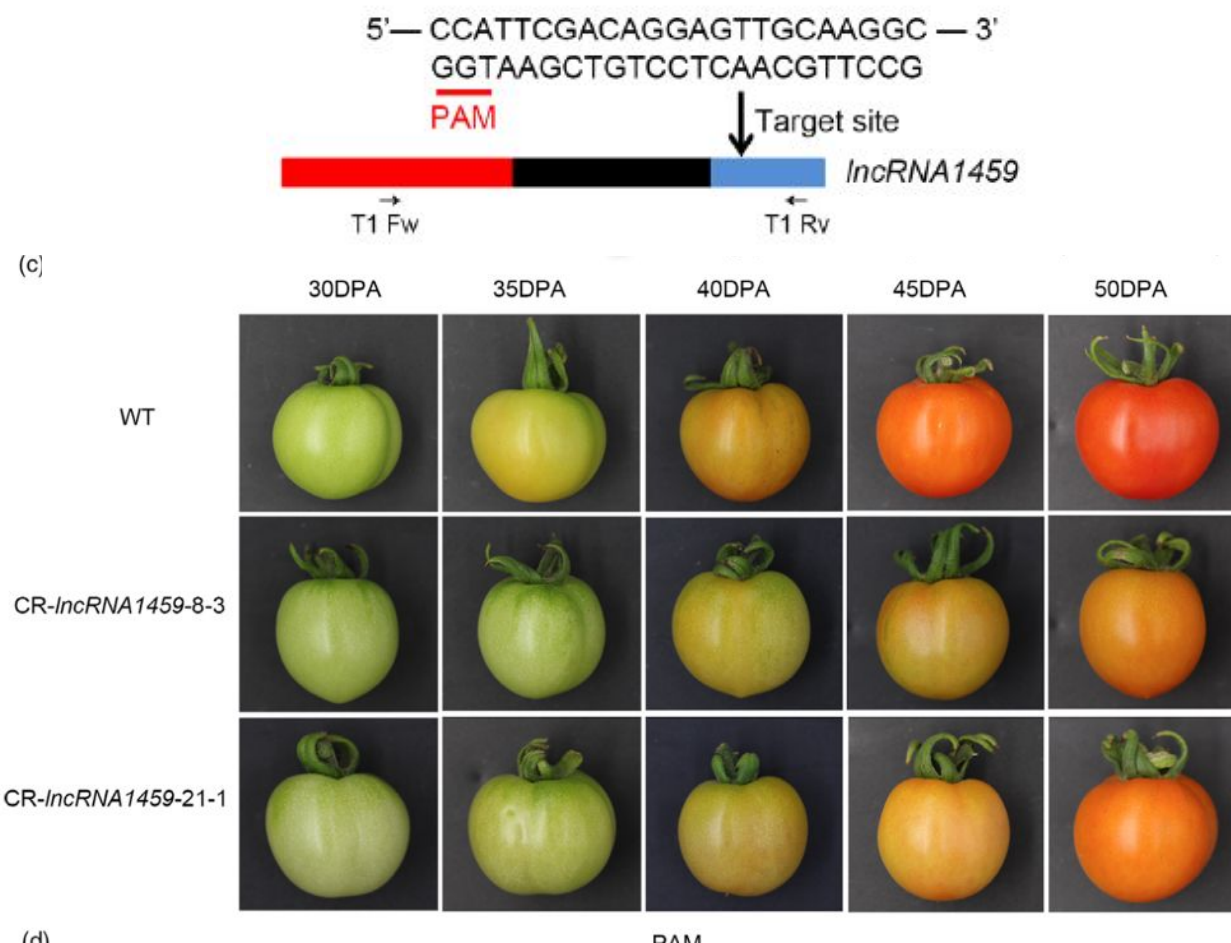
Genome Editing Model



CRISPR/Cas9-mediated mutagenesis of *IncRNA1459* alters tomato fruit ripening

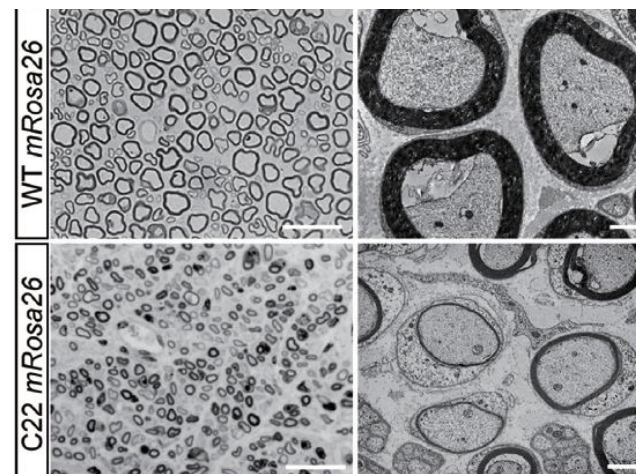
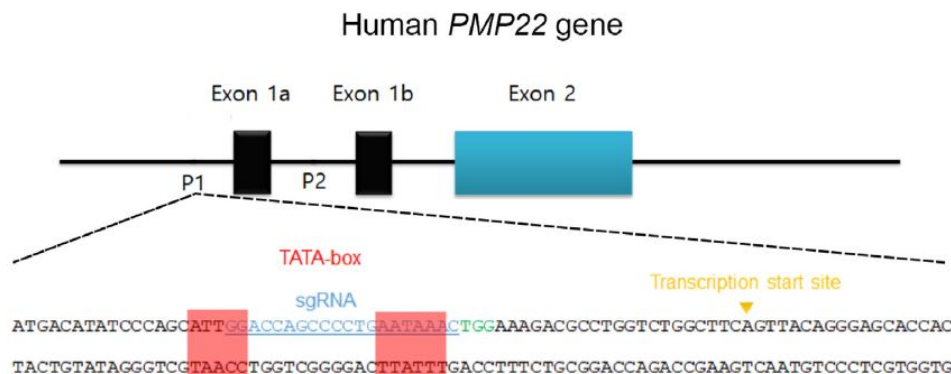
Ran Li, Daqi Fu, Benzhong Zhu, Yunbo Luo and Hongliang Zhu*

The College of Food Science and Nutritional Engineering, China Agricultural University, Beijing 100083, China



Targeted PMP22 TATA-box editing by CRISPR/Cas9 reduces demyelinating neuropathy of Charcot-Marie-Tooth disease type 1A in mice

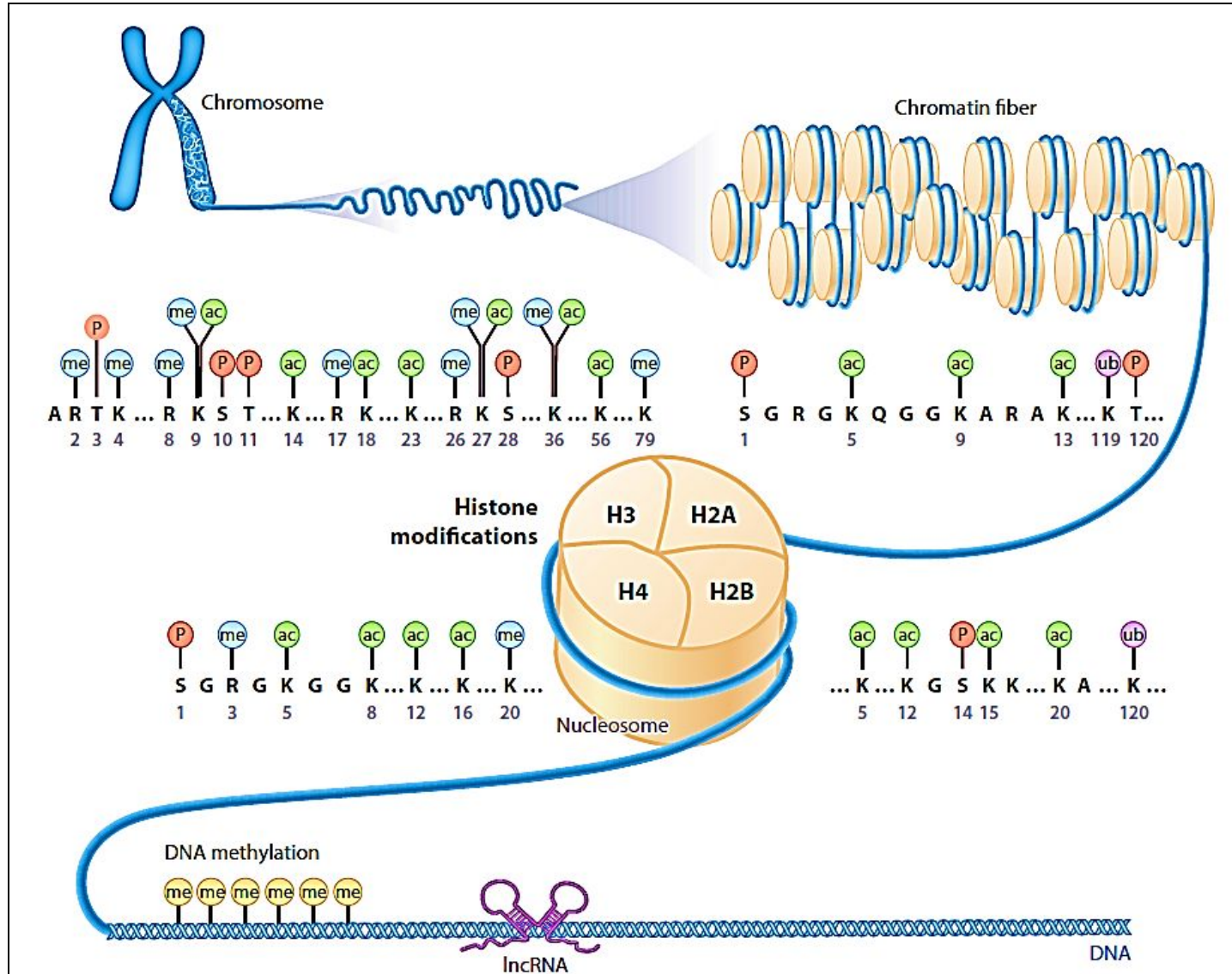
Ji-Su Lee^{1,†}, Jae Y. Lee^{2,*†}, Dong W. Song^{2,†}, Hee S. Bae², Hyun M. Doo¹, Ho S. Yu²,
Kyu J. Lee², Hee K. Kim³, Hyun Hwang³, Geon Kwak¹, Daesik Kim^{4,5}, Seokjoong Kim²,
Young B. Hong^{6,*}, Jung M. Lee^{7,*} and Byung-Ok Choi^{1,3,*}





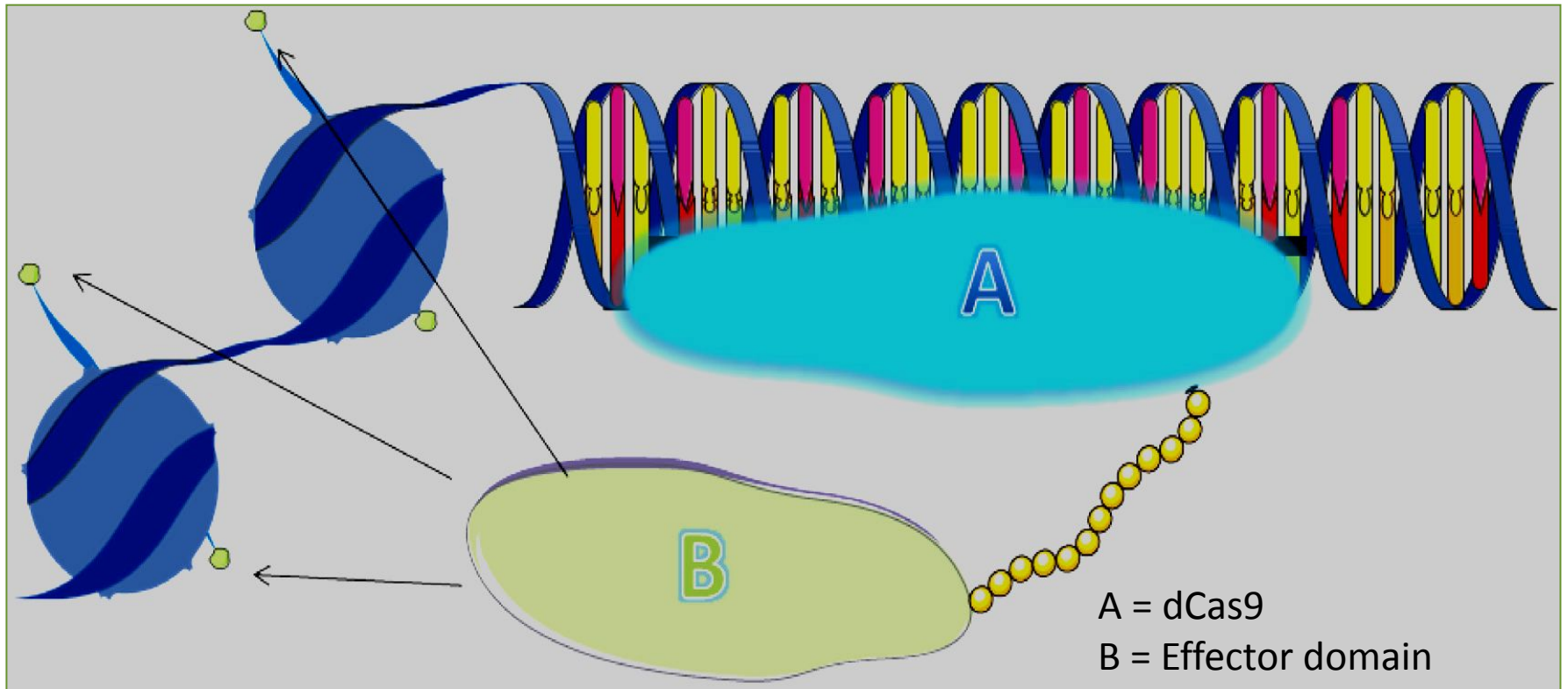
Epigenome Editing

Epigenome



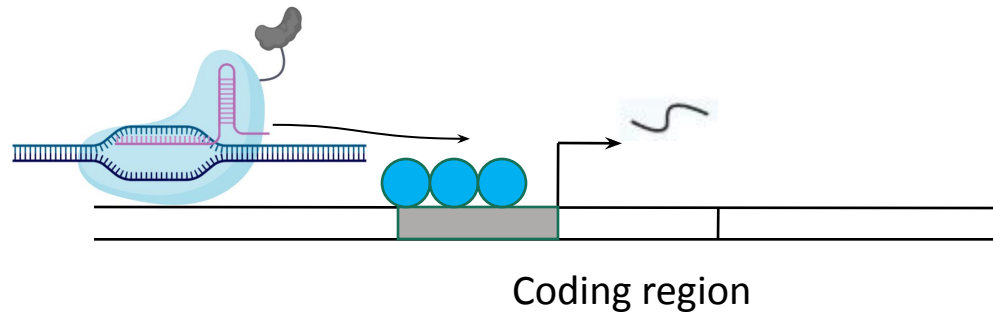
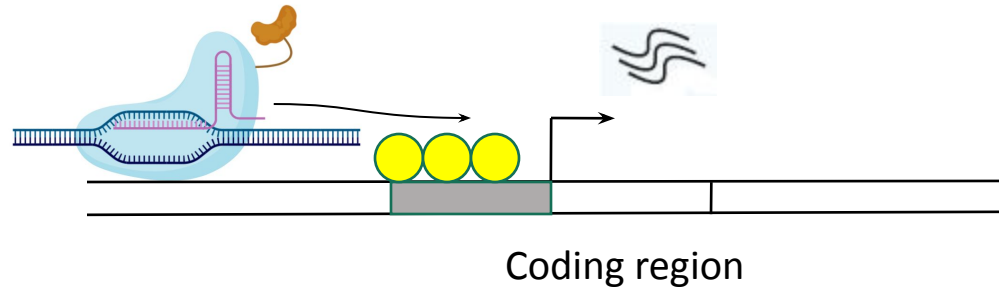
Chen Z, Li S and Subramaniam S *et al* (2017)
Annu Rev Biomed Eng **19**:195–219

Epigenome Editing



Goubert D *et al* (2017) *Converg Sci Phys Oncol* **3** (3): 1-6

Effectors and their Function



Activator



Activating epimark

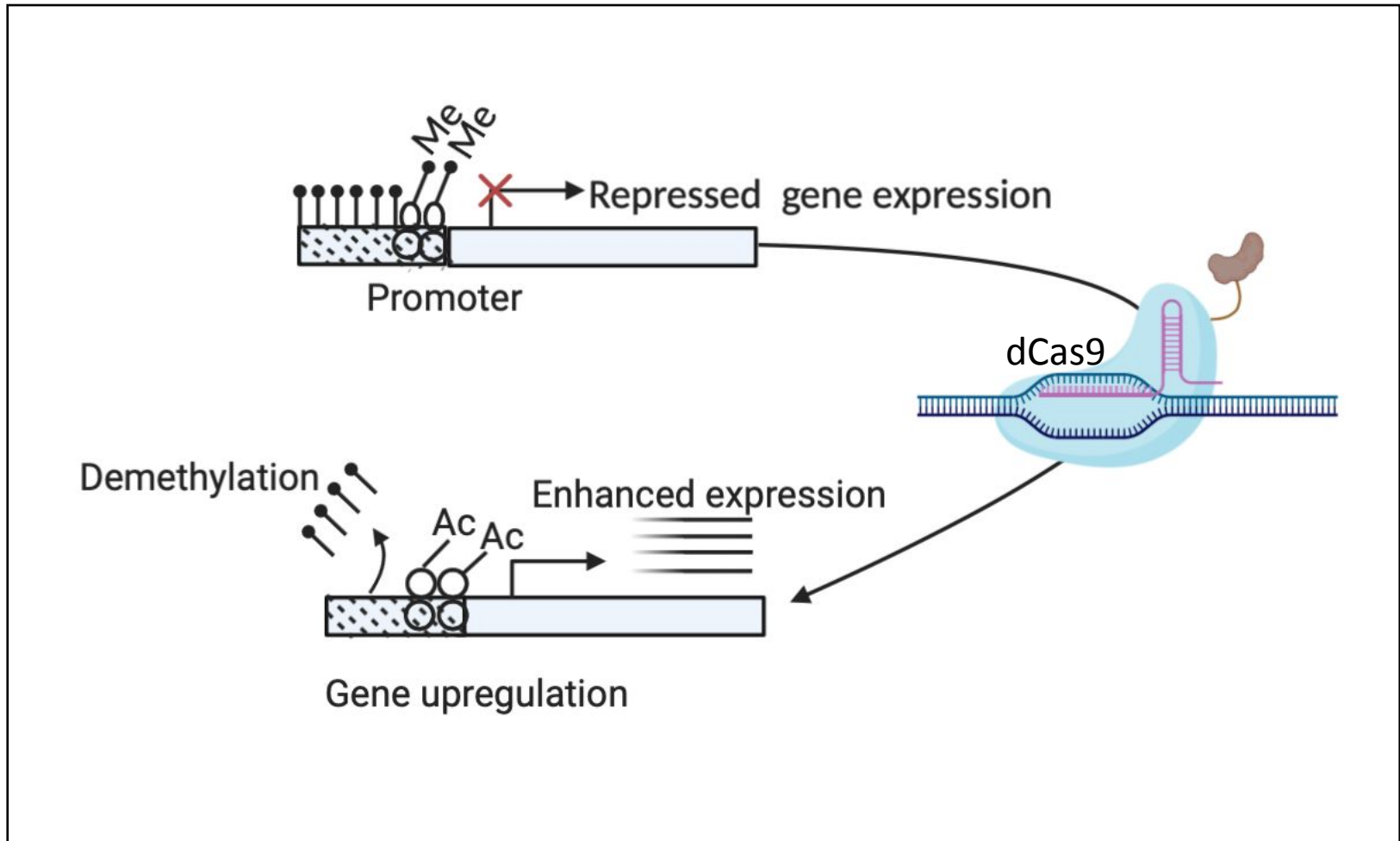


Repressor



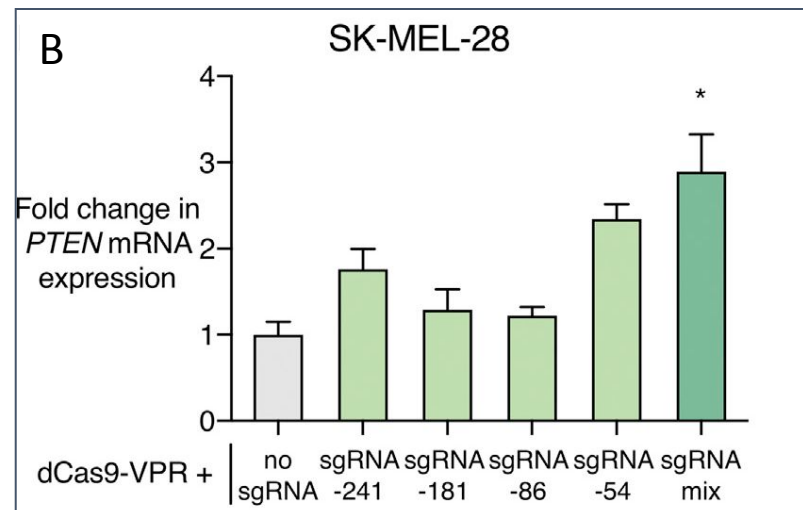
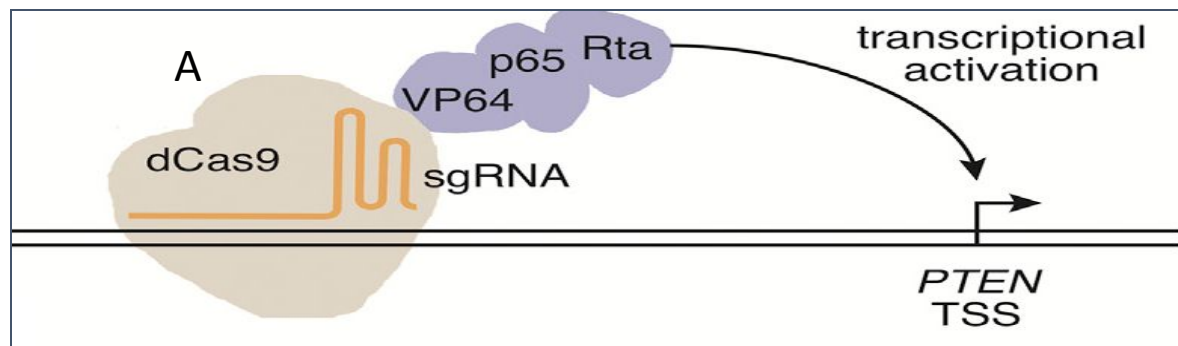
Repressing epimark

Epigenome Editing Model



Activating *PTEN* Tumor Suppressor Expression with the CRISPR/dCas9 System

Colette Moses,^{1,2} Fiona Nugent,^{1,3} Charlene Babra Waryah,¹ Benjamin Garcia-Bloj,^{1,4} Alan R. Harvey,^{2,5} and Pilar Blancafort^{1,2}

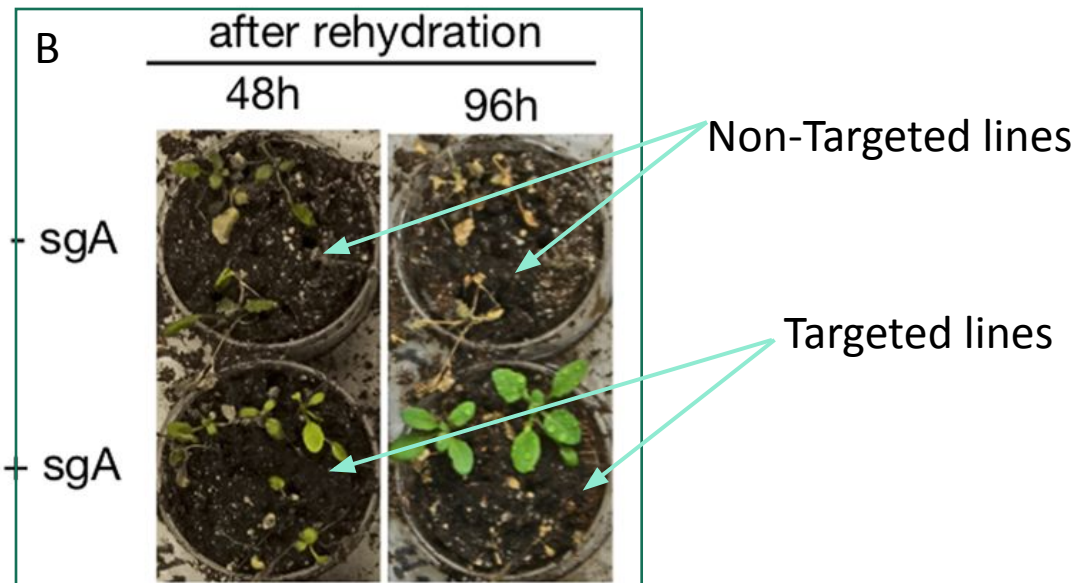
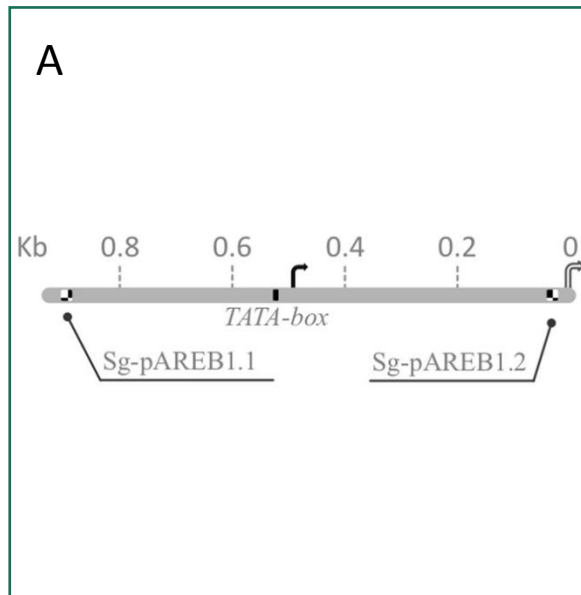


OPEN

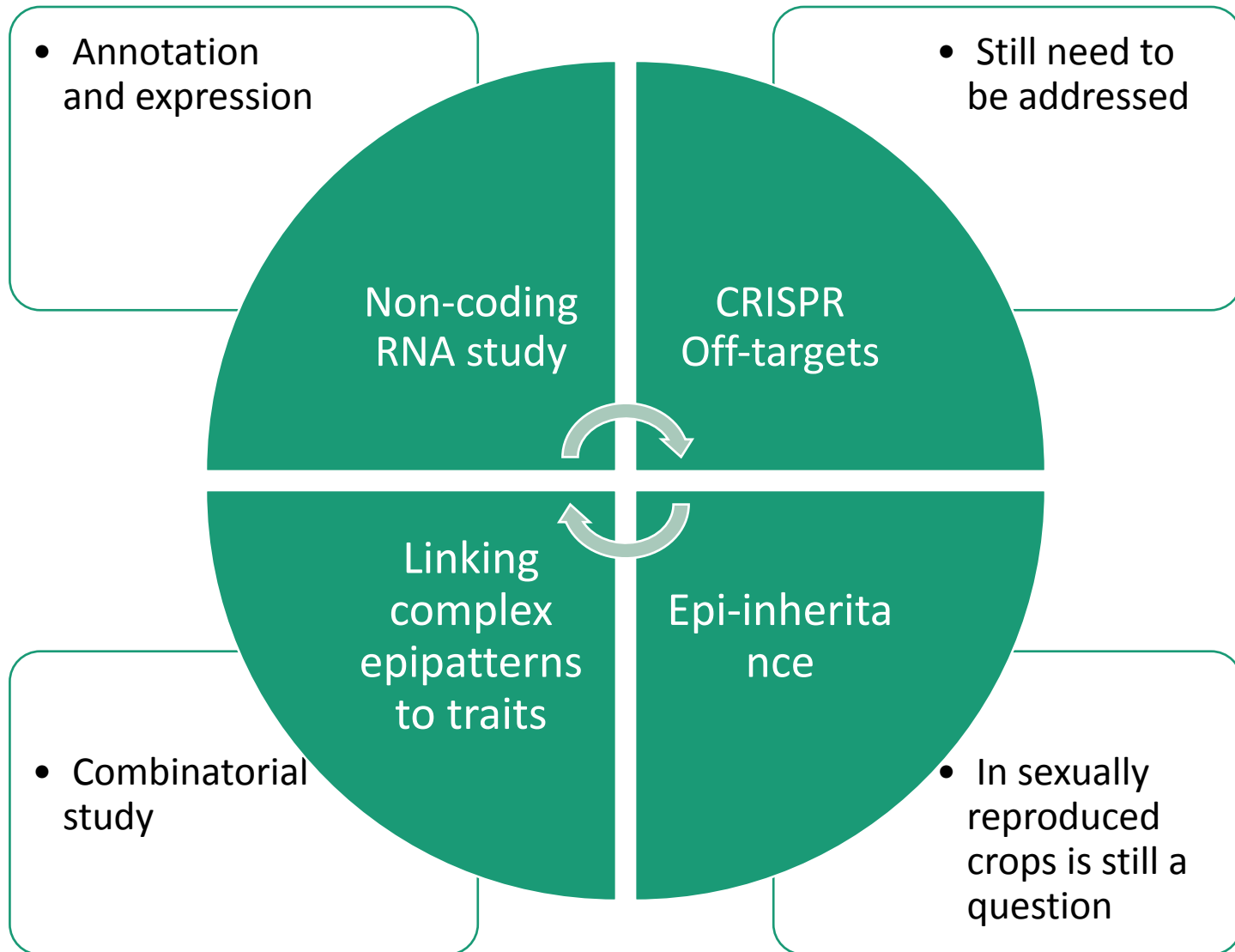
Improved drought stress tolerance in *Arabidopsis* by CRISPR/dCas9 fusion with a Histone Acetyltransferase

Received: 11 September 2018
 Accepted: 9 May 2019
 Published online: 30 May 2019

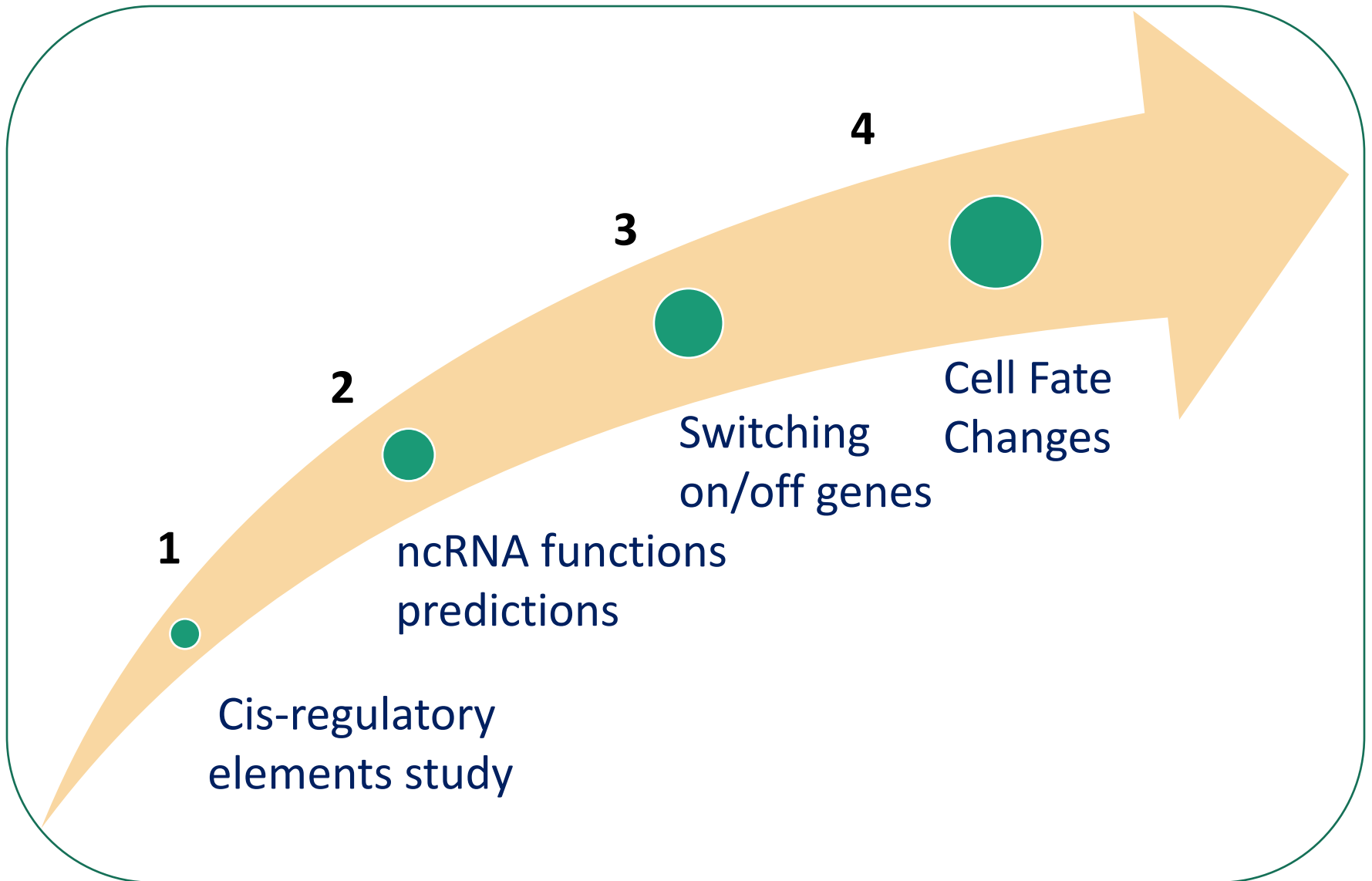
Joaquin Felipe Roca Paixão^{1,2}, François-Xavier Gillet¹, Thuanne Pires Ribeiro¹,
 Caroline Bournaud¹, Isabela Tristan Lourenço-Tessutti¹, Daniel D. Noriega¹,
 Bruno Paes de Melo¹, Janice de Almeida-Engler² & Maria Fatima Grossi-de-Sa^{1,3}



Challenges



Future Prospects



Summary

- ❖ mRNA is a key gene product, whose level decides the trait extent
- ❖ The gene expression is effectively controlled at DNA structural and epigenetic levels
- ❖ CRISPR could precisely target gene regulatory elements
- ❖ CRISPR can modulate existing gene expressions and design new ones

Take Home Message

“Nature may have insufficient resources sometimes, but we should learn to be a generator than borrower”.

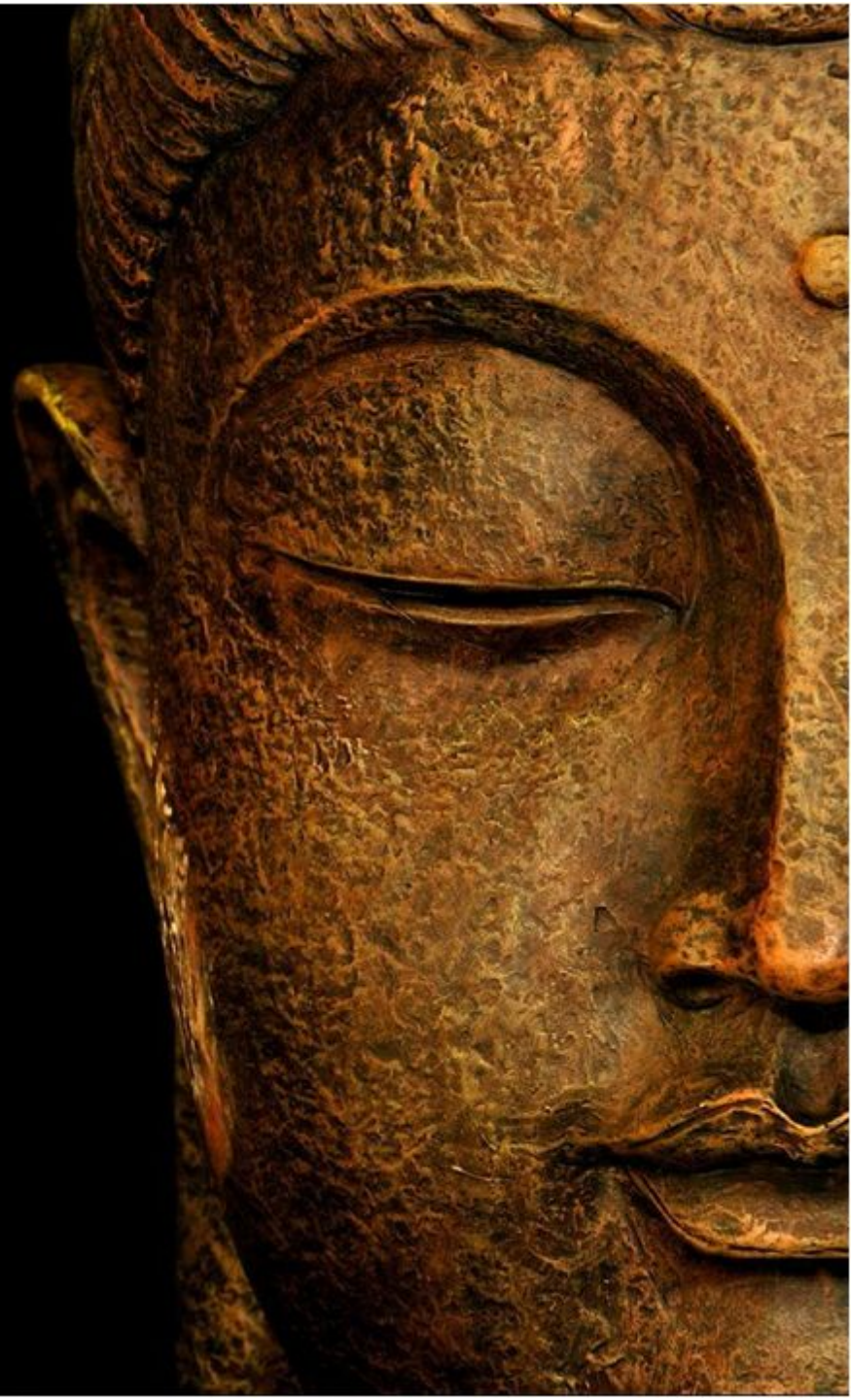




**NSERC
CRSNG**

Acknowledgement





Thank You

Any questions ?

