

## TALE proteins may be used to induce specific gene expression to treat some diseases

**Jacques P. Tremblay**  
Laval University, Canada

Genes coding for Tal effector (TALE) proteins may be engineered to target specific DNA sequences. TALEs are fused with a transcription activator can be used to specifically induce the expression of a gene. This could lead to completely new therapies for several diseases. We have applied this potential therapeutic approach to Friedreich ataxia (FRDA) as an example. FRDA is due to a reduced expression of frataxin following an elongation of a trinucleotide (GAA) repeat in intron

1. Aim: To develop a potential treatment for FRDA by increasing the expression of the frataxin gene. Results: We have engineered 12 TALE genes (TALE<sup>Frat</sup>) coding for TALE<sup>Frat</sup> proteins each specifically targeting different 14 bp DNA sequences within the proximal region of the human frataxin promoter. When the genes of these TALE<sup>Frat</sup> were fused with a transcription activator, i.e., four VP16 peptides (i.e., VP64), the resulting TALE<sup>Frat</sup>-VP64 proteins induced the expression of a mCherry reporter gene fused to a mini-CMV promoter able to be activated by the insertion of the frataxin proximal promoter upstream to the mini promoter. These TALE<sup>Frat</sup>-VP64 also increased by 2 to 3 folds the frataxin gene expression (detected by qRT-PCR) in the cells. Conclusion: TALE<sup>Frat</sup> proteins targeting the frataxin promoter are thus a method to increase the expression of frataxin mRNA and potentially could alleviate the symptoms of Friedreich ataxia. This new methodology of TALE effector opens a new field, which could be used to develop TALE proteins to treat other diseases by inducing the expression of specific genes.

### Biography

Tremblay was born in Montreal in 1946. He completed his B.A. at college Ste Marie in 1967 and a B.Sc. in Honours Biochemistry at Mc Gill University in 1970. He obtained in 1974 a Ph.D. in Neuroscience from the University of California in San Diego (UCSD). He is a professor at Laval University since 1976 and a full professor since 1985. He was the chairman of the department of Anatomy from 1987 to 1997. Dr. Tremblay has published 183 articles in peer reviewed journals and presented 304 communications in congress. He has presented 75 invited conferences in international congress.

[jacques-p.tremblay@crchul.ulaval.ca](mailto:jacques-p.tremblay@crchul.ulaval.ca)