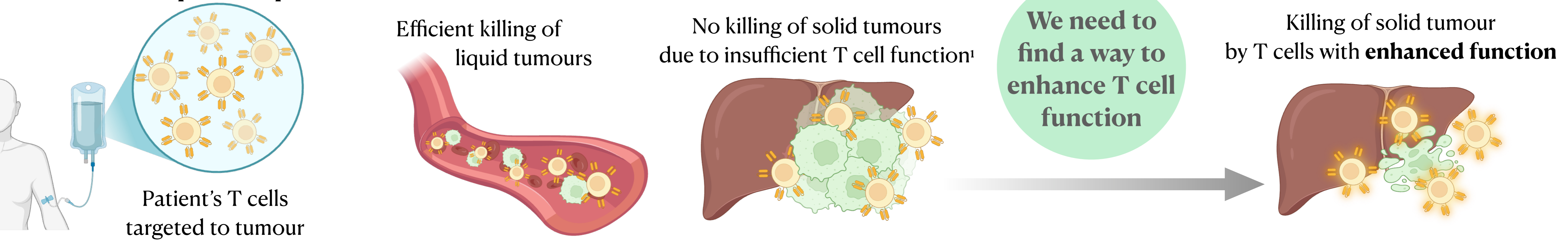


Motivation

Cellular therapies use patient's immune cells to treat cancer



Problems

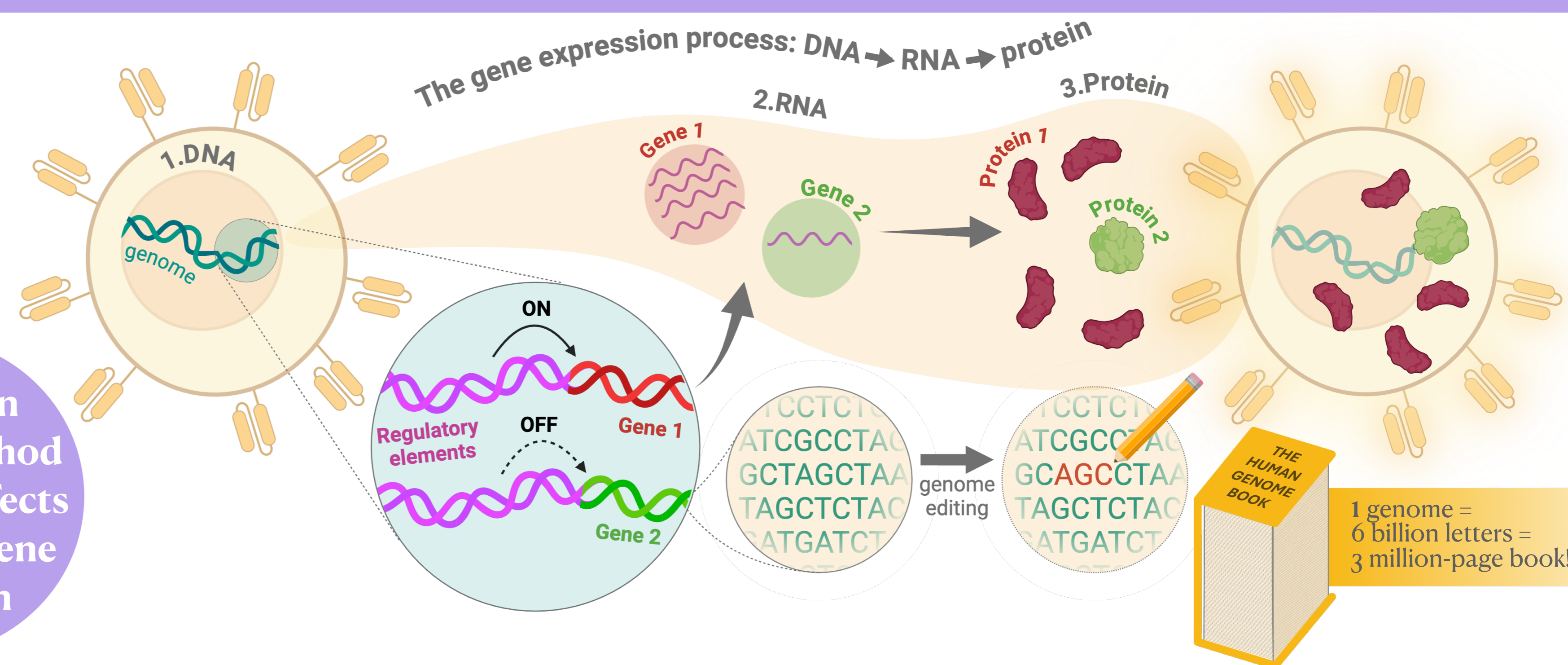
How can T cell function be enhanced?

T cell function is determined by the expression levels of different genes and can be enhanced by modulating gene expression².

How can gene expression be modulated?

We can edit regions of the genome that regulate gene expression. However, we don't know what edits will lead to the desired effects. Testing edits one at a time would take too much time.

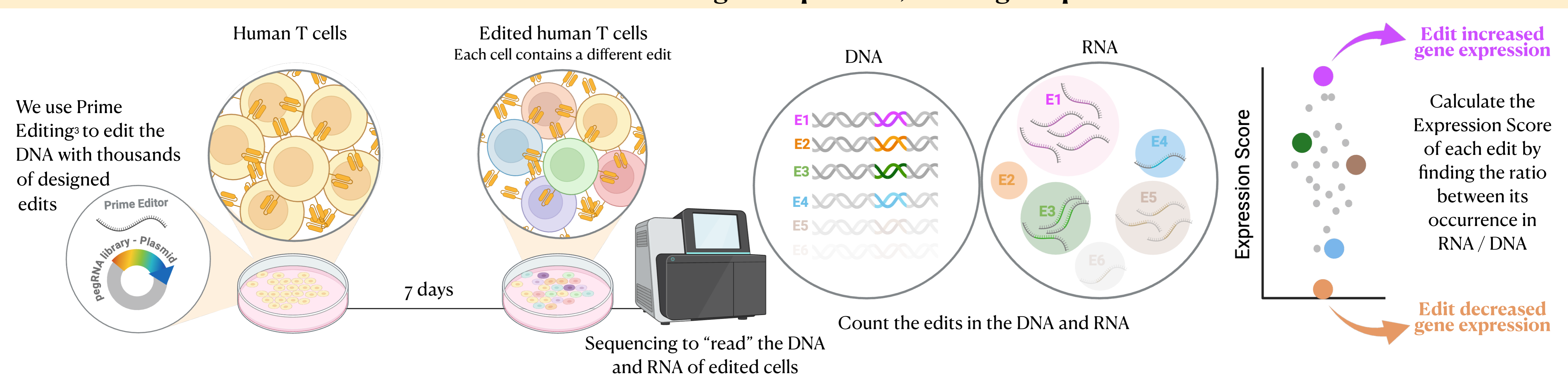
We need an efficient method to test the effects of edits on gene expression



Our solution: PETRA

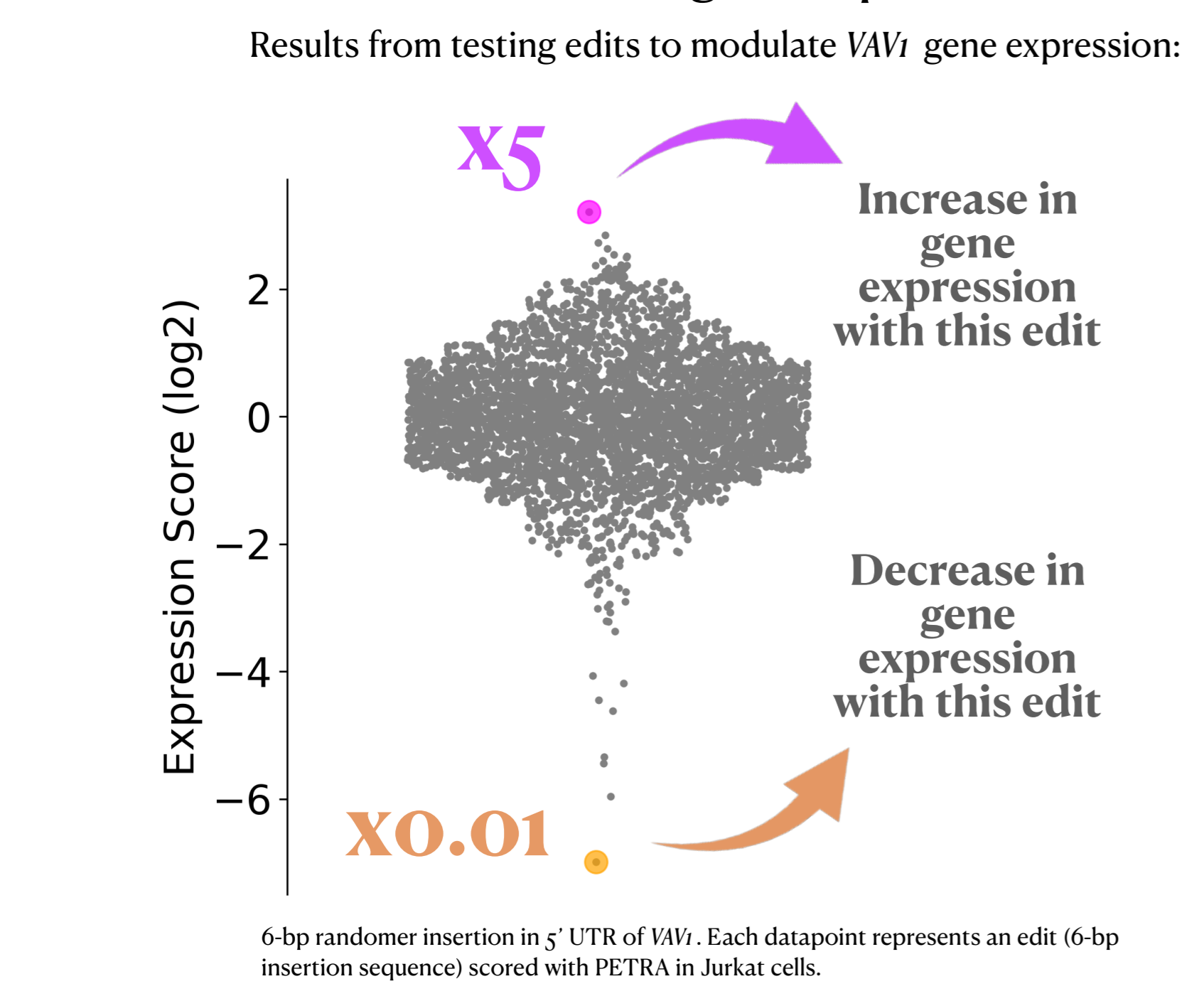
Prime Editing of Transcribed Regulatory elements to Alter expression

PETRA allows us to test the effects of thousands of edits on gene expression, in a single experiment

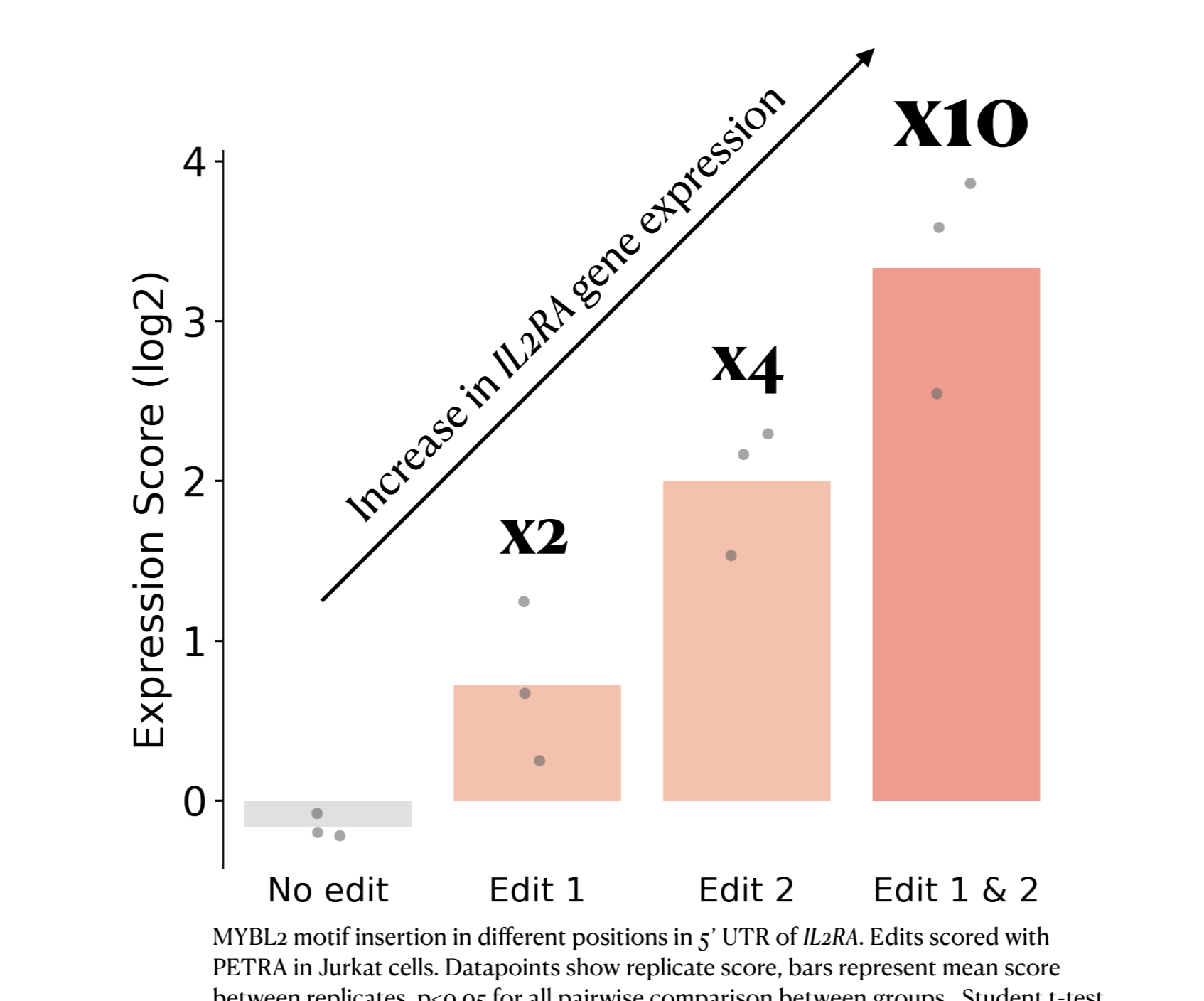


Using PETRA we tested the effect of 11,000 edits on the expression of 4 genes with key roles in T cell function

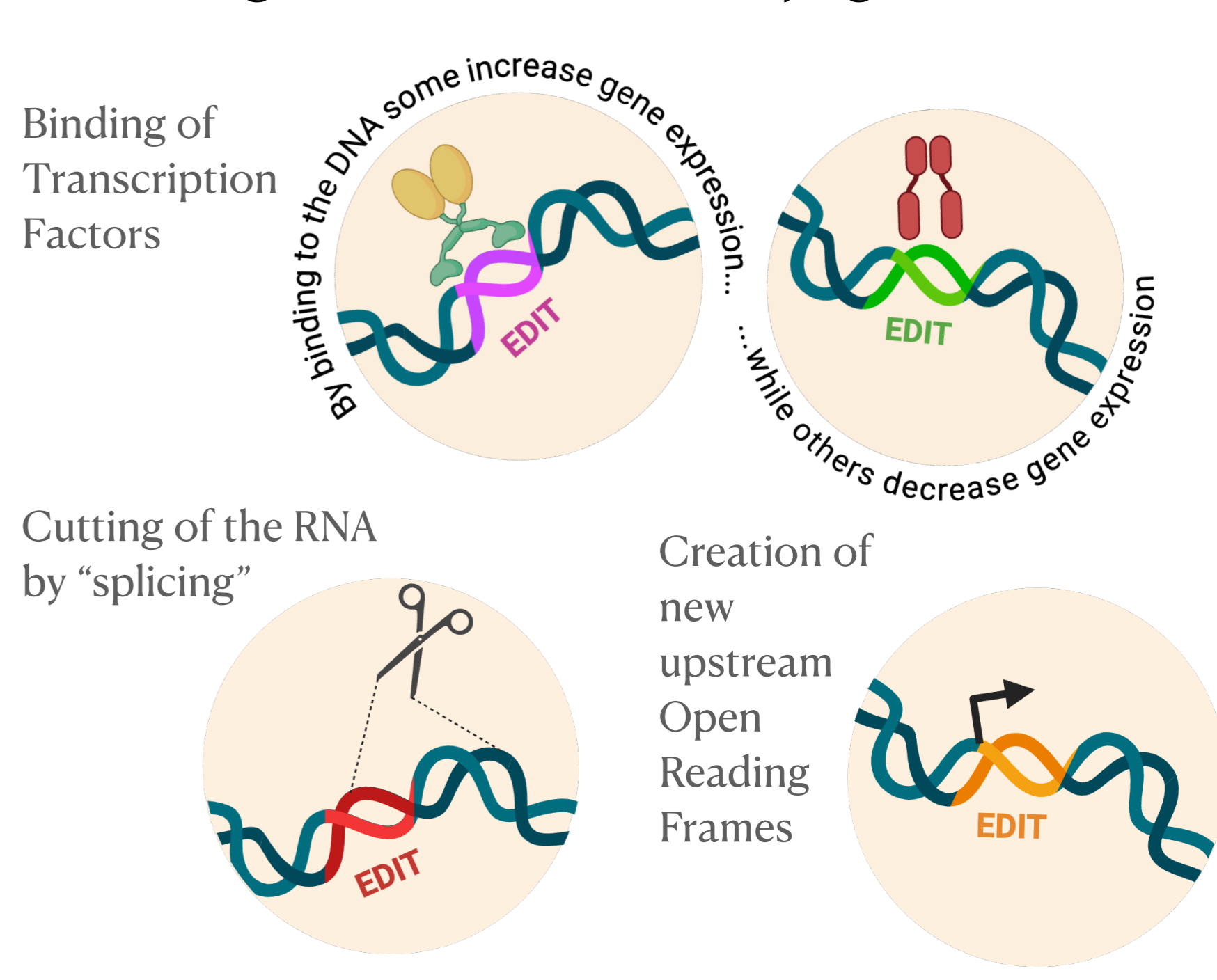
We discovered edits that both increase and decrease gene expression



Edits can be combined for enhanced effects



Combining PETRA scores with AI models reveals biological mechanisms underlying edit effects



Implications and future applications

PETRA generates large datasets linking edits to their effects, which provide a valuable source of information about gene expression...

...and can be used to train new Machine Learning models to better predict edit effects on gene expression in the future.



Edits discovered using PETRA could provide a solution to enhance T cell function and improve cellular therapies.

