Uncovering new translational targets across diverse cancers

SCAN ME

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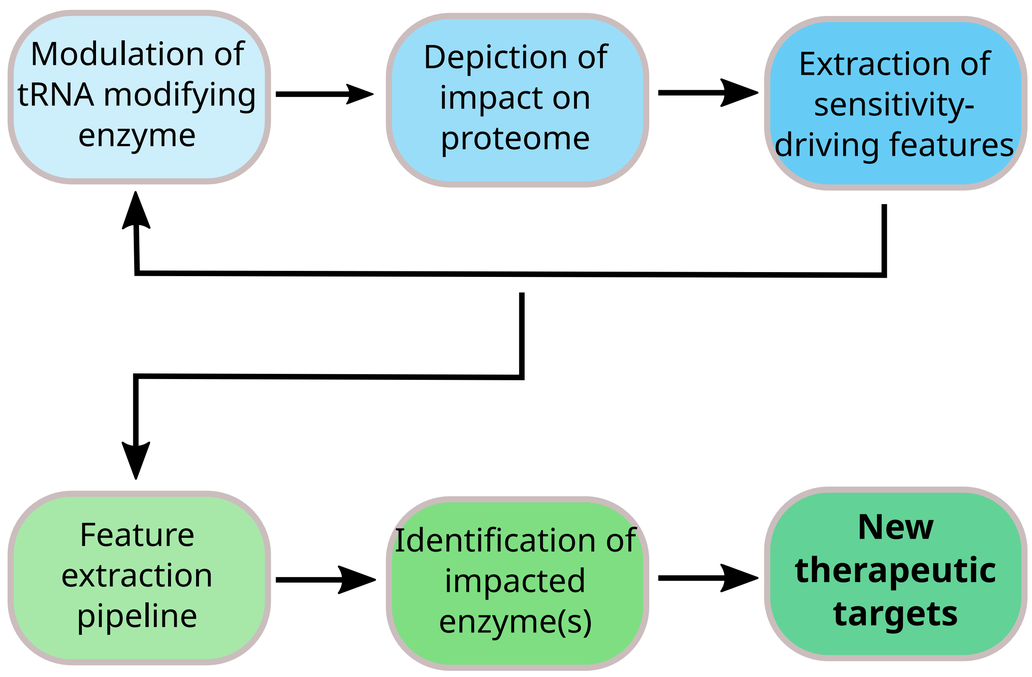
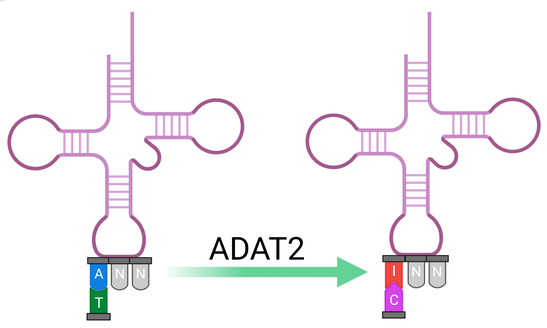
Our aim

In this project, we are developing **a method to determine the features** that condition a **protein's sensitivity** to **tRNA modifying enzyme** modulation in different contexts.

These features can then be used to **discover new therapeutic targets**.



Study case: ADAT2

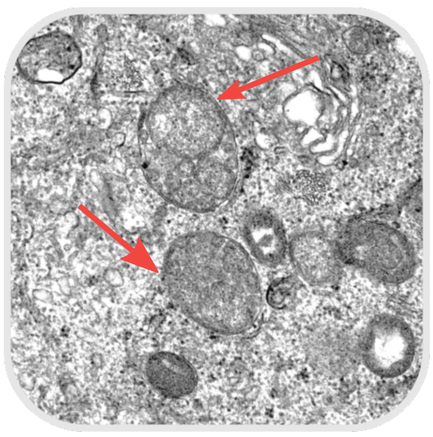


Codon	Amino acid
ACC	THR (T)
GCC	ALA (A)
CCC	PRO (P)
TCC	SER (S)
CTC	LEU (L)
ATC	ILE (I)
GTC	VAL (V)
CGC	ARG (R)

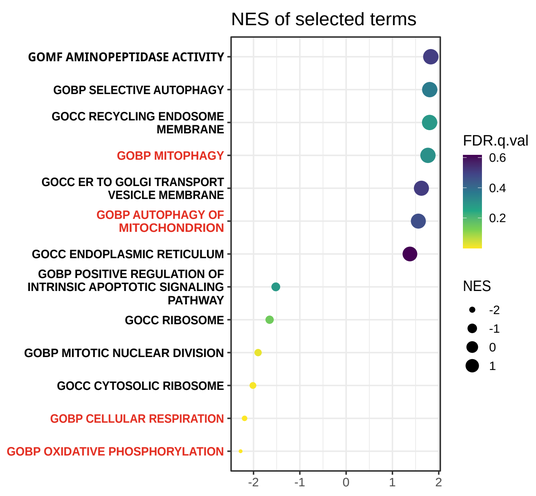
Why ADAT2?
* Multi-omics **data** available for **multiple tissues**
* Biochemically **well-characterized**
* **Dysregulated** in multiple **cancers**

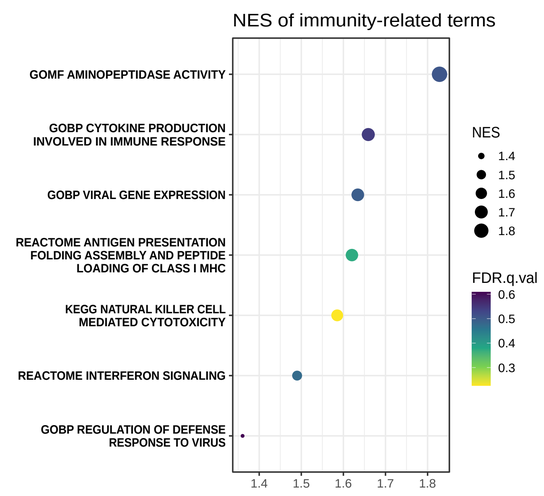
In colon cancer, loss of ADAT2 leads to **increased immunogenicity of cancer cells, oxidative stress,** and **mitophagy.**

⇒ **Interesting target!**



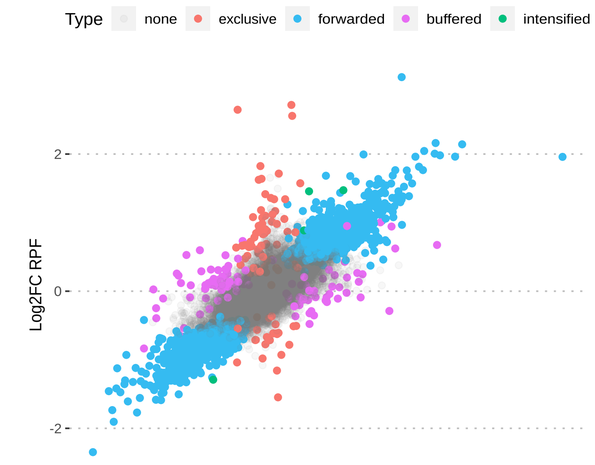
EM shows **mitophagy vacuoles** (red arrows)

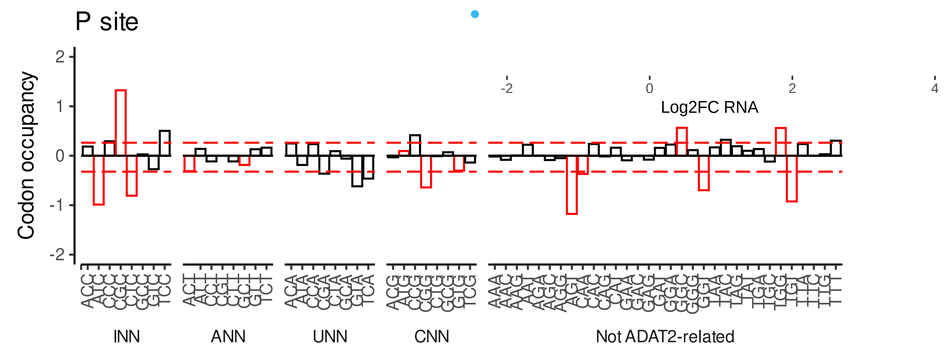




Codons are not enough!

Riboseq experiments indicate that **the loss of ADAT2 has a limited impact on global translation**. Codon occupancy analysis indicates that **ADAT2-related codons are not exclusively impacted**.





Considered features	R^2
Protein abundance in control and treatment conditions (trivial)	0,97
Change in RNA abundance	0,35
Raw codon content	0,065
Codon frequency	0,051

In line with the **usual predicting power of mRNA** abundance on protein levels.

Codon content alone **cannot explain changes** in protein expression!

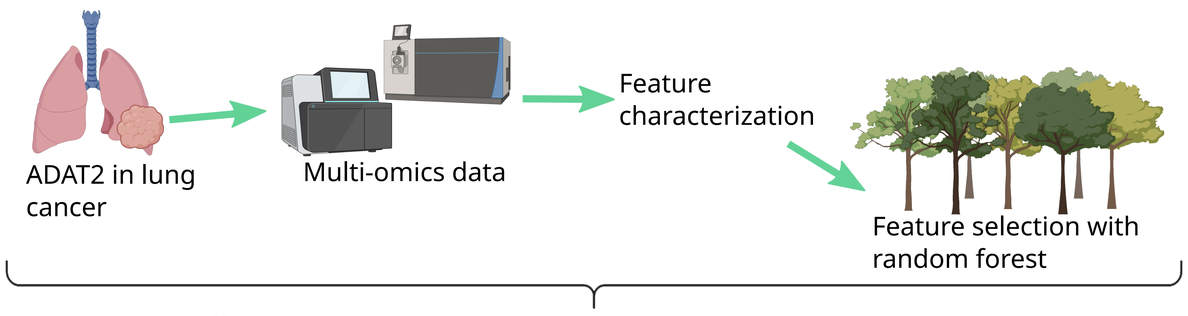
R^2 **accuracy scores** of a random forest **regressor** model trained to **predict changes in protein levels**.

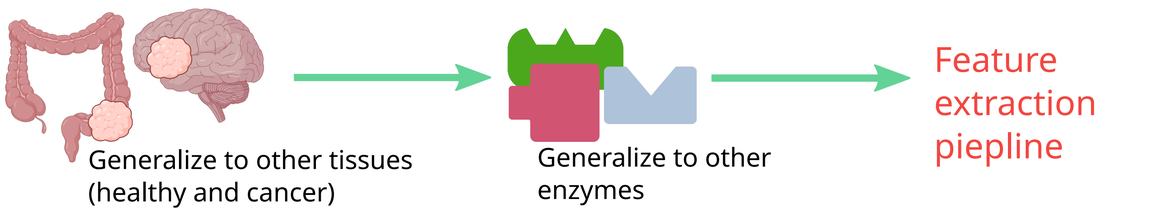
If not codon content, then what are the protein features that drive the changes in their expression ?

What is next

We are building a **pipeline** that will help us **find the important features** that determine a protein's **sensitivity** to **enzymes** such as ADAT2.

1. Analyze





2. Discover