

tRNA biology: a story of translation from fundamental research to drug discovery in cancer

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COO_THERA+RAME

What is cancer: one name for a group of diseases

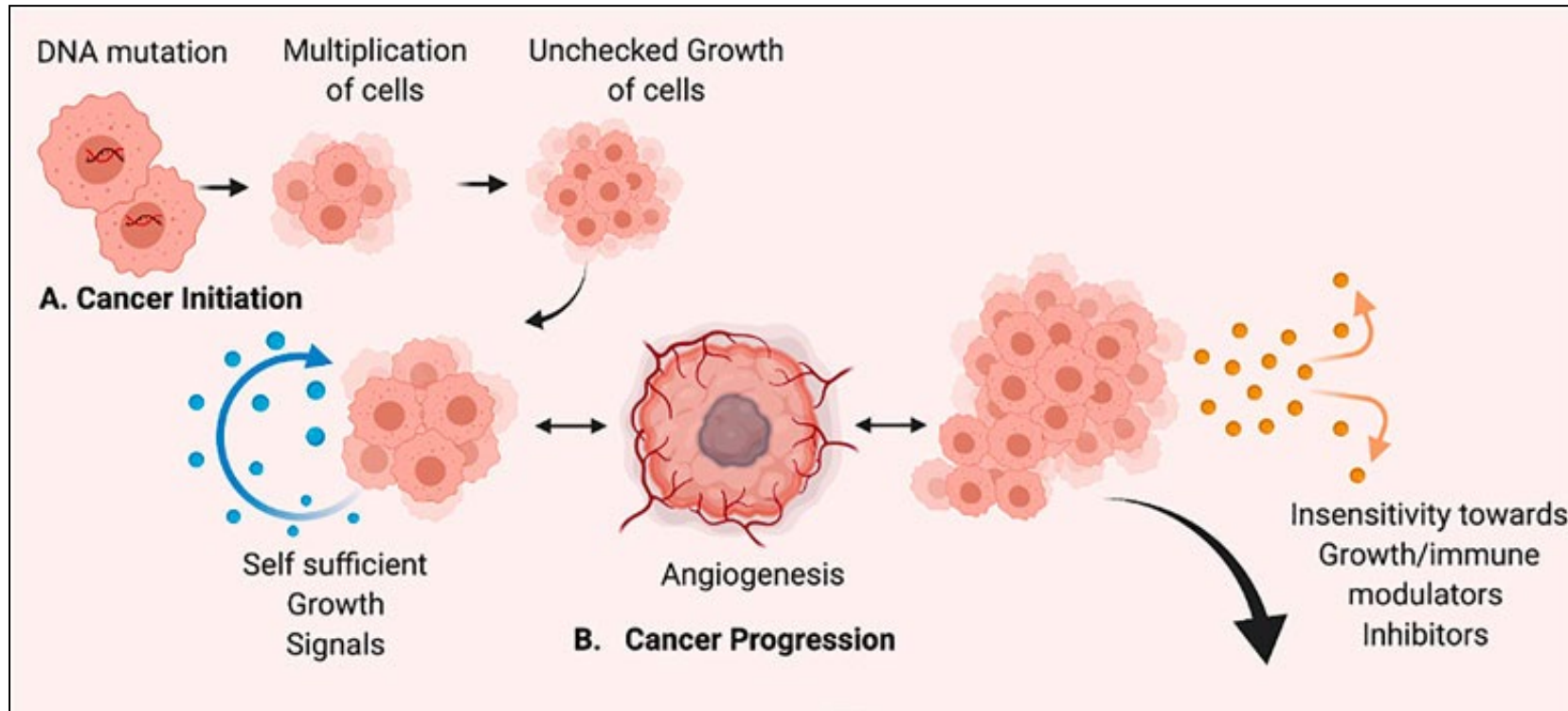
Cancer initiation



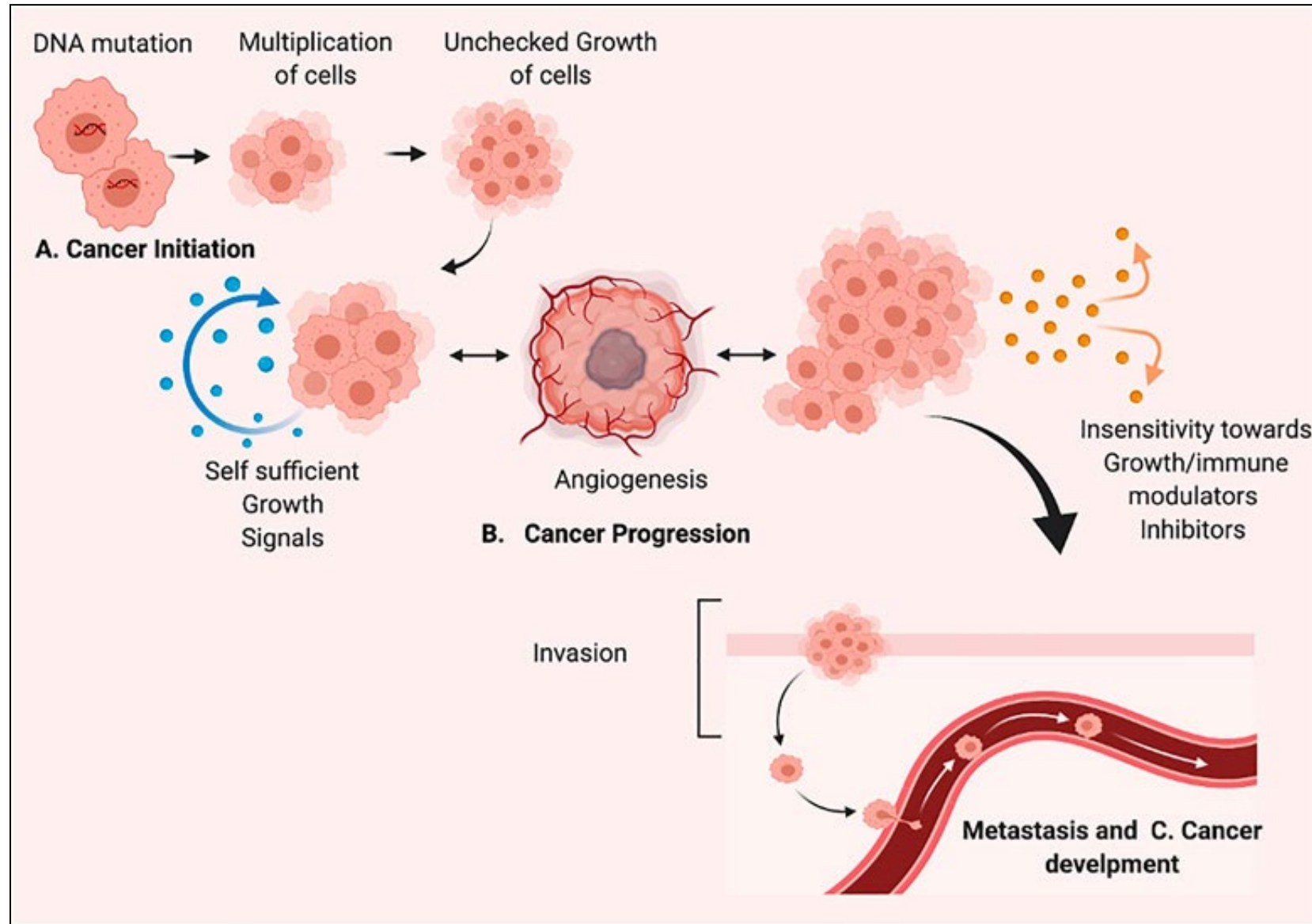
What is cancer: one name for a group of diseases

Cancer initiation

Cancer progression



What is cancer: one name for a group of diseases



Good prognosis

COMPLEXITY OF THE DISEASE

Poor prognosis

Cancer initiation

Cancer progression

Cancer metastasis

Our scientific fundamental question

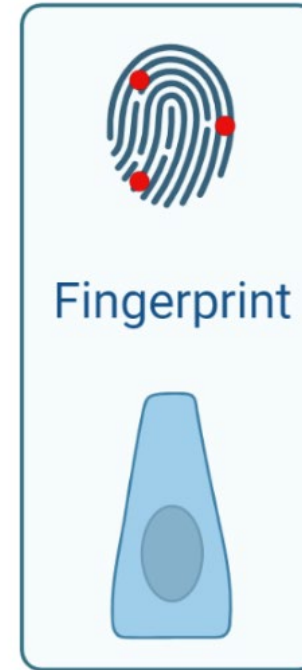
Good prognosis

COMPLEXITY OF THE DISEASE

**CONVERGENT
ADAPTATION
MECHANISMS**

Poor prognosis

Healthy cell



Cancer
transformation

Cancer cell



**Can we identify new players
that are essential for cancer
survival?**

mRNA translation can be highly optimized: central role of tRNAs

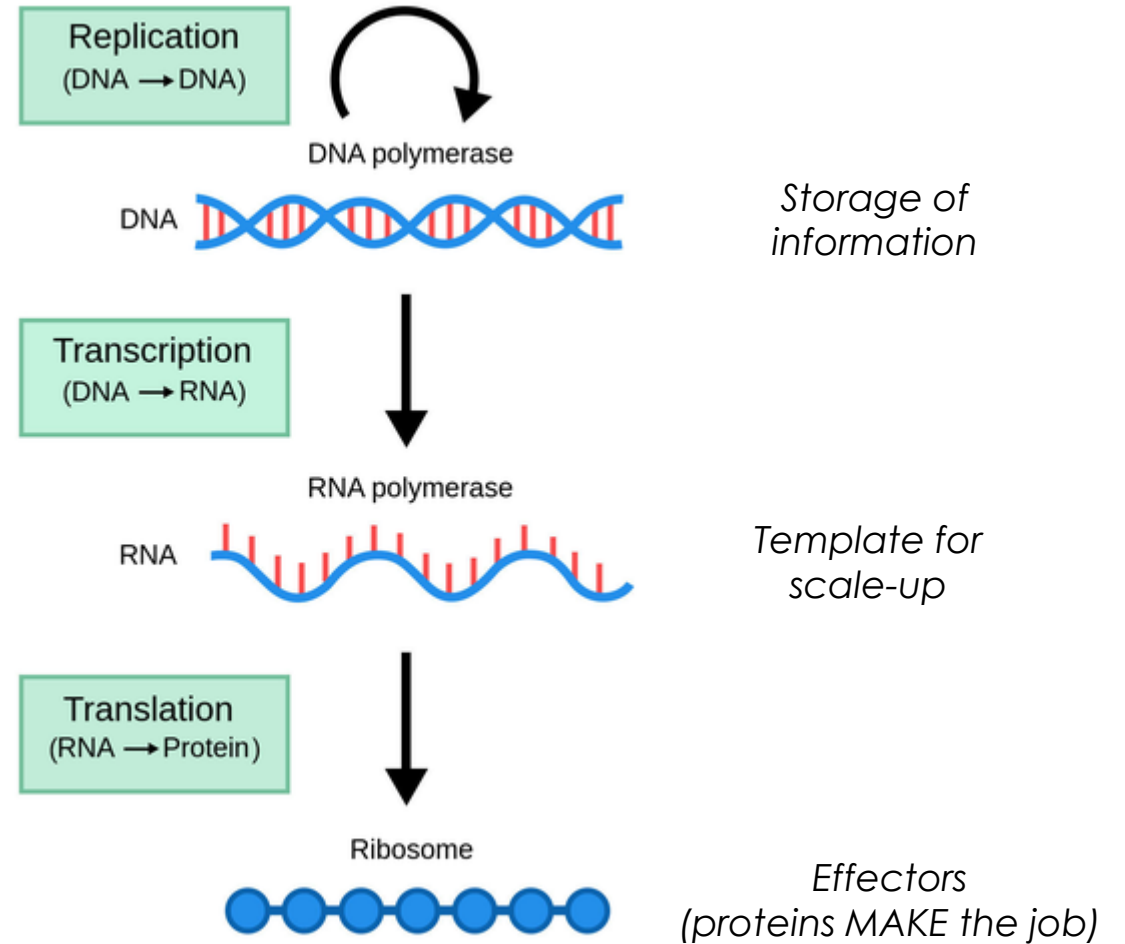
Good prognosis

COMPLEXITY OF THE DISEASE

**CONVERGENT
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Poor prognosis

Central dogma of biology



mRNA translation can be highly optimized: central role of tRNAs

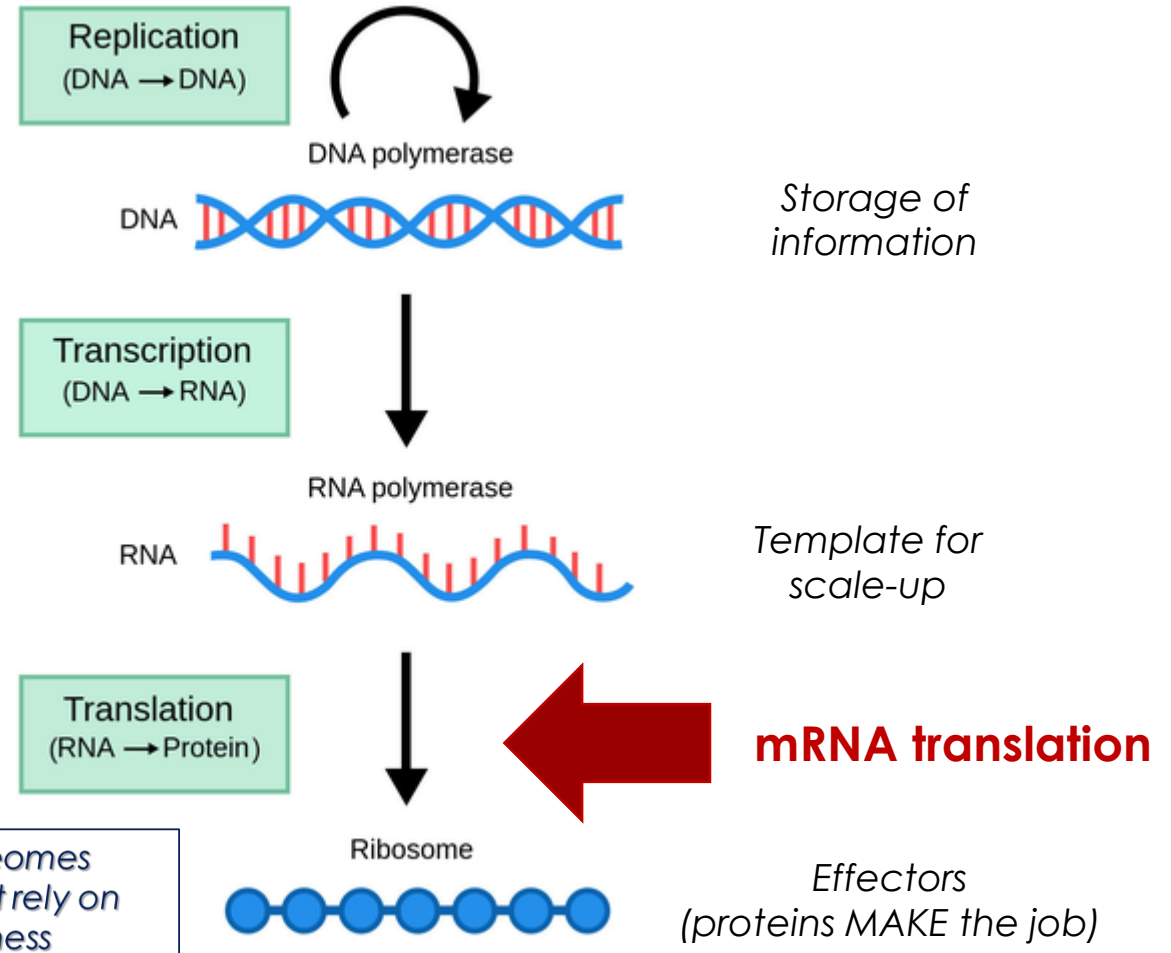
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Central dogma of biology

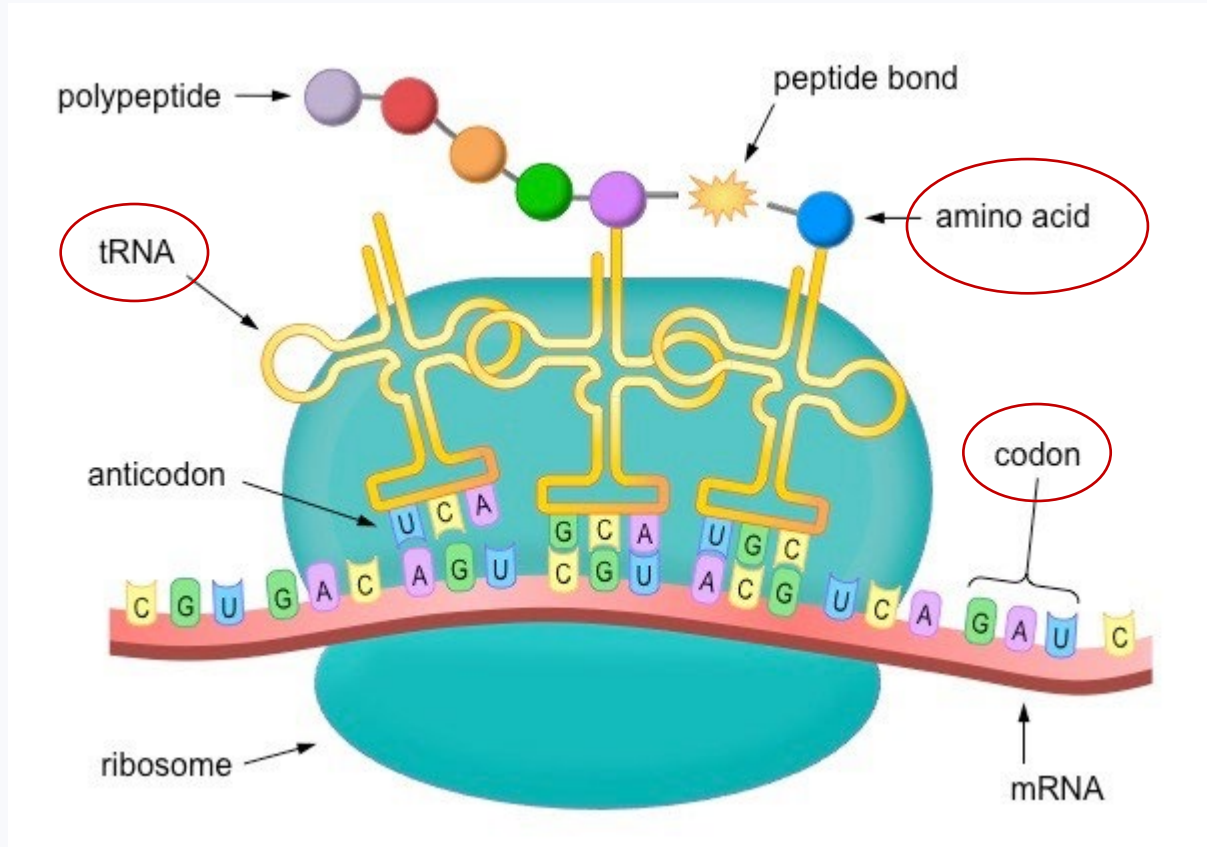


*Onco-proteomes
establishment rely on
tRNAs fitness*

Rapino et al., Nature com. 2021;
Rapino et al., Nature 2018;
Rapino et al., Trends in Cancer 2017;
Ladang, Rapino et al., J. Exp. Med. 2015

mRNA translation can be highly optimized: central role of tRNAs

mRNA translation



tRNA:

- 270 tRNA in human
- 150 enzymes for modification of tRNAs

MORE THAN 700 DIFFERENT TYPES OF tRNA

mRNA codons:

- 61 codons

Amino acids

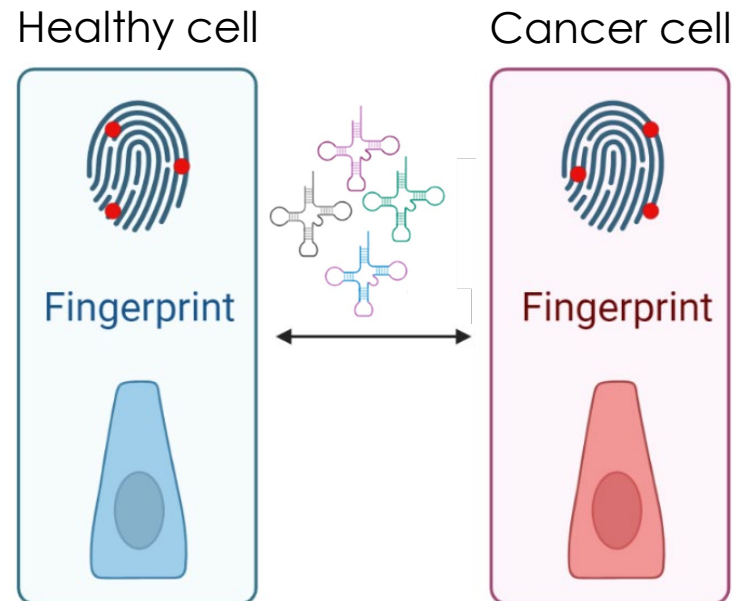
- 20 amino acids -> generate ALL proteins

tRNAs are essential for
**OPTIMIZATION OF mRNA
TRANSLATION**



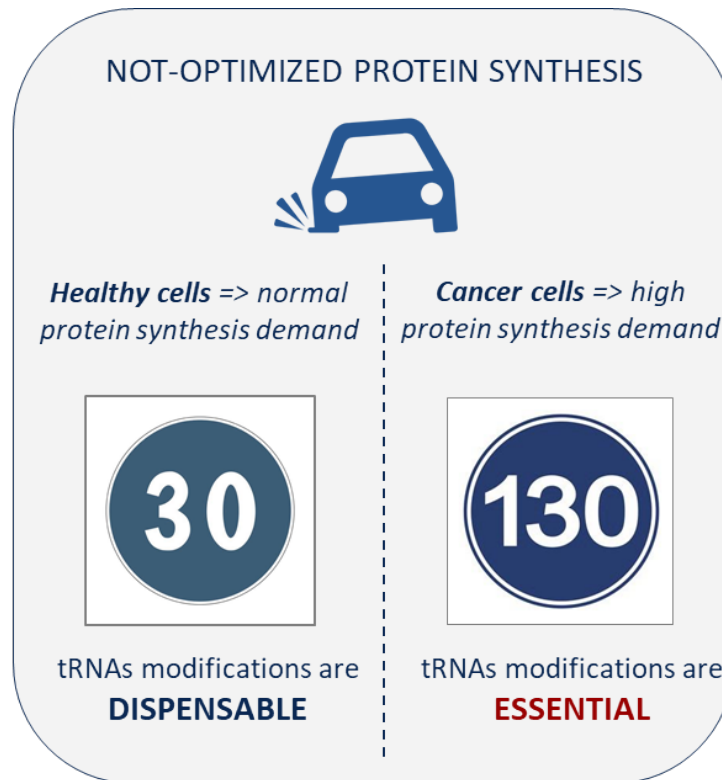


tRNA biology contributes to cell heterogeneity and can be important in determine **cell fate** in health and **disease**





tRNA biology contributes to cell heterogeneity and can be important in determine **cell fate** in health and **disease**

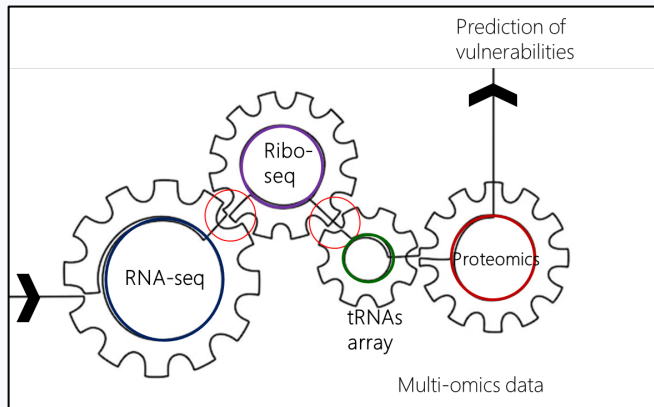


Integrative projects: understanding complex biology

Generate tRNA centric technologies

- ONT tRNA detection in blood
- tRNA silencing -> CRISPR-Cas9
-> shRNA screen
- tRNA-enzymes drop out screens

Implement predictive bionformatics pipelines



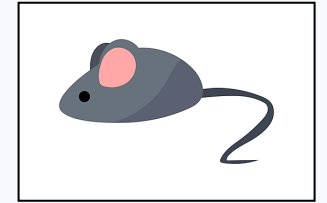
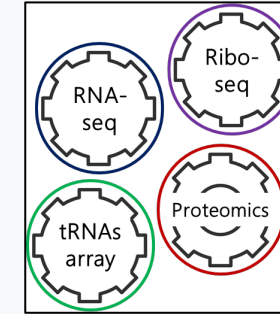
Healthy cell



Cancer cell

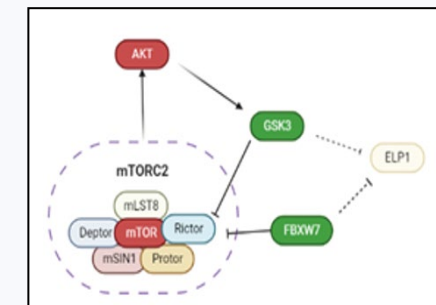


Identify tRNA functional targets



New mouse models

Dissect molecular regulation of tRNA dynamics



Collaboration Pierre Close lab

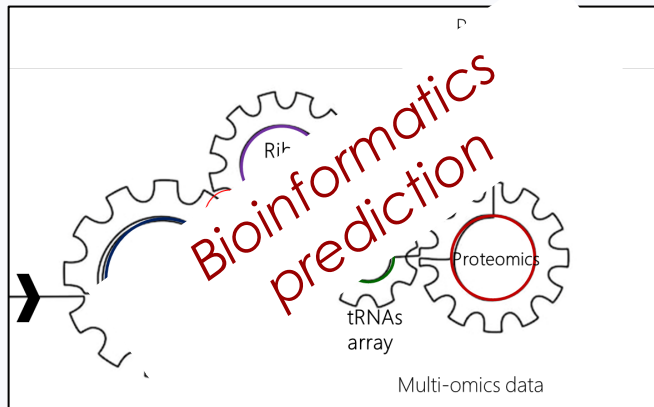
Integrative projects: from research to biotech

Generate tRNA centric technologies

- ONT tRNA detection
- tRNA silencing CRISPR-Cas9 -> shRNA screen
- tRNA enzymes drop out screens

Target identification

Implement predictive bioinformatics pipelines



Healthy cell



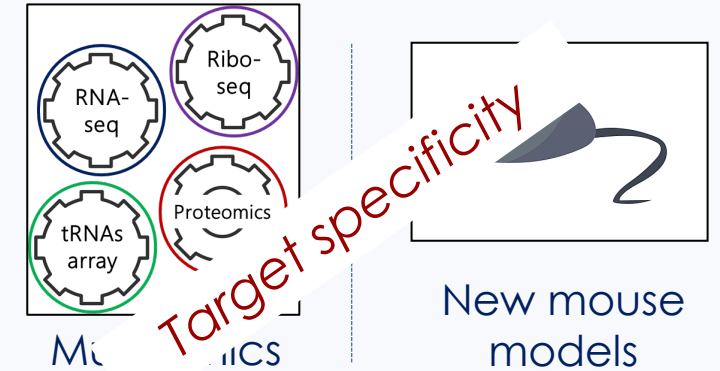
Cancer cell



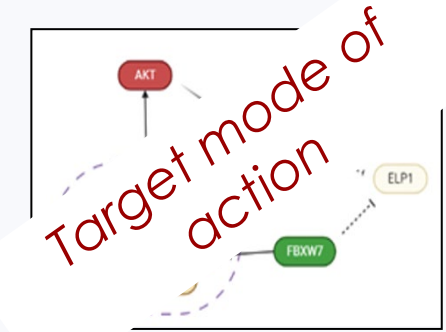
POTENTIAL THERAPEUTIC TARGETS



Identify tRNA functional targets



Dissect molecular regulation of tRNA dynamics



Collaboration Pierre Close lab

THERAtFRAME: new drugs targeting tRNA biology

DISCOVERY OF NEW CANCER TARGETS

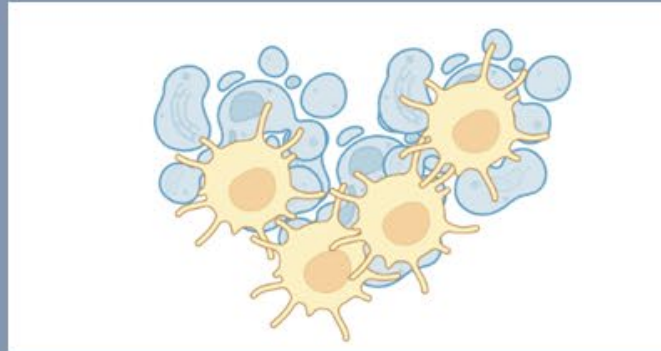


Underexplored target space
(>140 tRNA modifying enzymes)

Multiple cancers

Fundamental
research

NEW MODE OF ACTION



First-in-class therapeutics

Refractory cancers

Immune-oncology

Fundamental research
+
Industrial expertise

NEW TECHNOLOGIES TO DISCOVER DRUGS IN ONCOLOGY



Unique tRNA-centric
models & assays

Non canonical biomarkers

Industrial expertise