Team MITO : Intercompartmental traffic of RNA & Mitochondrial Diseases

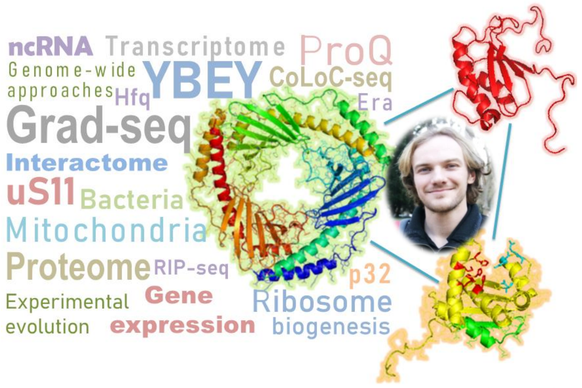
Université de Strasbourg

gmgm Génétique Moléculaire ▪ Génomique ▪ Microbiologie

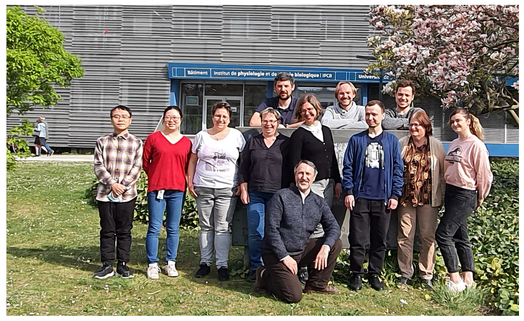
cnrs

MITO CROSS — Investissements d'avenir

Post-transcriptional networks & RNA-binding hubs
Genome-wide approaches

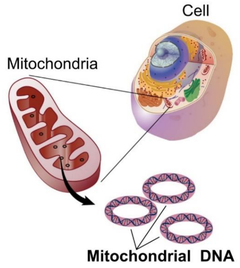


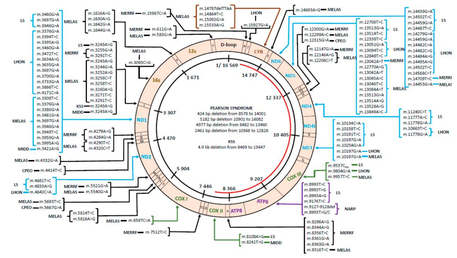
Alexandre Smirnov



IMC Bio

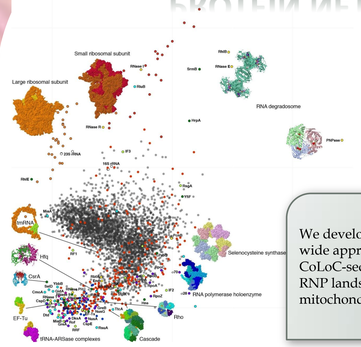
Mitochondrial DNA expression and editing.
Molecular mechanisms & therapy of mitochondrial diseases





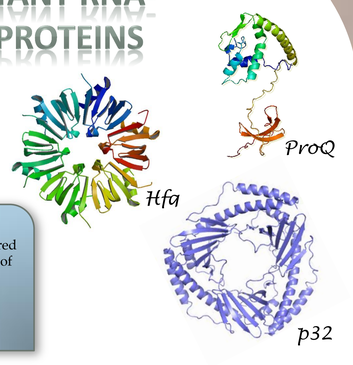
Nina Entelis & Ivan Tarassov

WE STUDY RNA & PROTEIN NETWORKS



We develop & use genome-wide approaches (Grad-seq, CoLoC-seq, RIP-seq) to chart RNP landscapes in bacteria & mitochondria

WE DISCOVER NEW RNAs & IMPORTANT RNA-BINDING PROTEINS



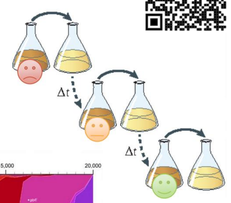
With Grad-seq, we discovered ProQ & an entire new class of bacterial noncoding RNAs. Even more surprises are to expect in mitochondria !

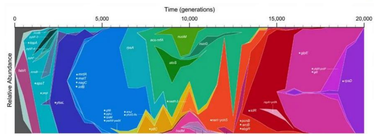
WE LEVERAGE THE DIVERSITY OF MODELS

We work with evolutionarily distant models (*E. coli*, human mitochodnria) to understand biology of deeply conserved proteins, such as YBEY, & pathways, such as ribosome assembly.

WE DO EXPERIMENTAL EVOLUTION

We study how important RNA-binding proteins (or their absence) affect & direct bacterial evolution by observing the process in real time in the lab!





WE COLLABORATE

ANR — Projet financé par l'ANR — Projet funded by the ANR

Investissements d'avenir

USIAS

WE PUBLISH

Liao Z, Schelcher C, Smirnov A (2021) **YbeY, *éminence grise* of ribosome biogenesis.** *Biochem Soc Trans*

Gerovac M, Vogel J, Smirnov A (2021) **The world of stable ribonucleoproteins and its mapping with Grad-seq and related approaches.** *Front Mol Biosci*

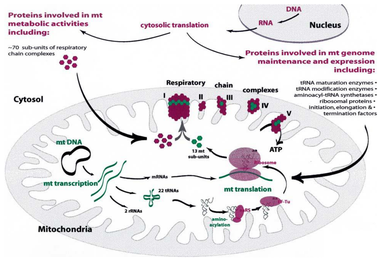
Summer S, Smirnova A, Gabriele A, Toth U, Fasemore AM, Förstner KU, Kuhn L, Chicher J, Hammann P, Mitulović G, Entelis N, Tarassov I, Rossmanith W, Smirnov A (2020) **YBEY is an essential biogenesis factor for mitochondrial ribosomes**. *Nucleic Acids Res*

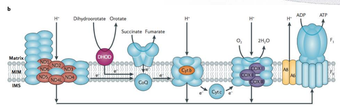
Smirnov A, Wang C, Drewry LL, Vogel J (2017) **Molecular mechanism of mRNA repression in trans by a ProQ-dependent small RNA.** *EMBO J* 36:1029-1045

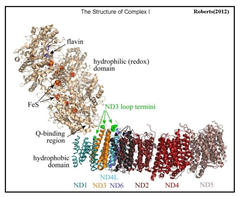
Smirnov A, Förstner KU, Holmqvist E, Otto A, Günster R, Becher D, Reinhardt R, Vogel J (2016) **Grad-seq guides the discovery of ProQ as a major small RNA-binding protein.** *Proc Natl Acad Sci USA* 113:11591-11596

More info here

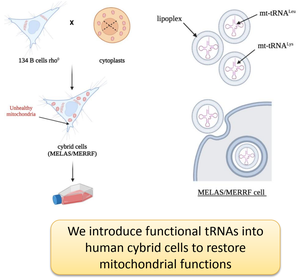
WE STUDY MOLECULAR MECHANISMS OF DISEASES AND DEVELOP INNOVATIVE THERAPIES





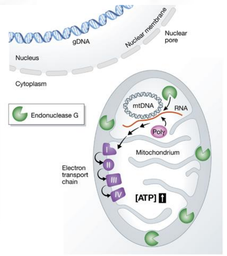


We aim to understand the molecular mechanisms of pathologies associated with mutation in the ND5 genes



We introduce functional tRNAs into human cybrid cells to restore mitochondrial functions

We aim to describe the molecular function of a nuclear - encoded mitochodnrial endonuclease EnoG



WE PUBLISH

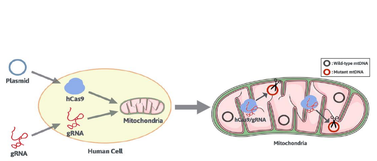
Shebanova, R. *et al.* Efficient target cleavage by Type V Cas12a effectors programmed with split CRISPR RNA. *Nucleic acids research*, doi:10.1093/nar/gkab1227 (2021).

Meschaninova, M. I., Entelis, N. S., Chernolovskaya, E. L. & Venyaminova, A. G. A Versatile Solid-Phase Approach to the Synthesis of Oligonucleotide Conjugates with Biodegradable Hydrazone Linker. *Molecules* **26**, doi:10.3390/molecules26082119 (2021).

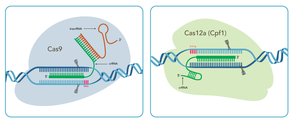
Dovydenko, I. *et al.* Lipophilic Conjugates for Carrier-Free Delivery of RNA Importable into Human Mitochondria. *Methods in molecular biology* **2277**, 49-67, doi:10.1007/978-1-0716-1270-5_4 (2021).

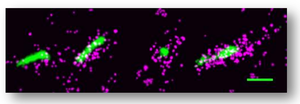
Jeandard, D. *et al.* Import of Non-Coding RNAs into Human Mitochondria: A Critical Review and Emerging Approaches. *Cells* **8**, doi:10.3390/cells8030286 (2019).

Loutre, R., Heckel, A. M., Smirnova, A., Entelis, N. & Tarassov, I. Can Mitochondrial DNA be CRISPRized: Pro and Contra. *IUBMB life* **70**, 1233-1239, doi:10.1002/iub.1919 (2018).

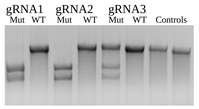


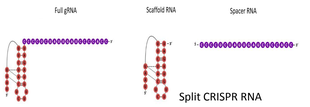
We develop a CRISPR-Cas system targeting human mitochondrial DNA bearing pathogenic mutations

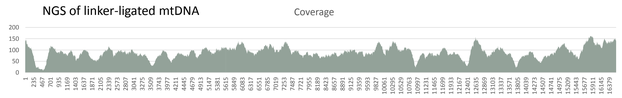




Localisation-precision super-resolutive images of the Cas9 and Twinkle-mEos2 (mitochondrial nucleoid)







WE COLLABORATE