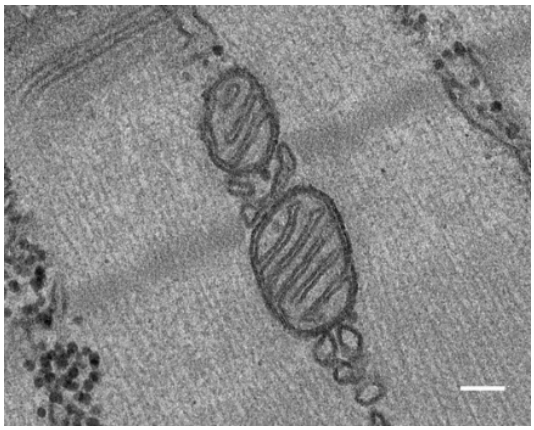
Postdoctoral position on mitochondrial efficiency in skeletal muscle

We are looking for a postdoctoral fellow to join our team *Biology of the NeuroMuscular System* headed by Fred Relaix at the IMRB, which offers an international environment with an easy access to core facilities and a strong network of multidisciplinary collaborations. Our lab is located in a brand-new building on the campus of the EnvA.

Keywords: mitochondrial diseases, mitochondrial membranes, respiratory coupling, metabolism, obesity, mouse genetics



Mitochondrial diseases form a large group of congenital diseases characterized by deficient mitochondrial efficiency that compromises the function of vital organs and locomotion. We have recently found that mutation of the *Hacd1* gene leads to a mitochondrial myopathy and identified that this gene is a key player of respiratory coupling in skeletal muscle, through the regulation of the lipid composition of mitochondrial membranes (Prola *et al., Science Advances*, 2021).
Unexpectedly, we found that this muscle-specific reduction in mitochondrial coupling leads to an elevated basal metabolism that protects *Hacd1* mutant mice against diet-induced obesity. This observation challenges the classical view in which a reduction in mitochondrial coupling efficiency is necessarily detrimental to health and we have first evidence that a fine tuning of HACD1 activity could confer a metabolic advantage yet preserving muscle function.
The project will thus aim at developing genetic strategies to improve both mitochondrial diseases and morbid obesity through the modulation of *Hacd1* expression. For this, you will set up an AAV-driven expression of *Hacd1* in two different mouse models of mitochondrial diseases. Reciprocally, you will test the capacity of *Hacd1* silencing at preventing and eventually curing diet-induced obesity by developing a conditional knockout or an antisense oligonucleotide strategy for *Hacd1* gene. Readouts of these strategies will include metabolic and locomotor assessments as well as histological and biochemical analyses.

Profile: You have a strong interest in mitochondria or muscle biology, and you have a solid expertise in mouse genetics or molecular biology. You work with rigor and creativity, and you are an appreciated teammate.

Position: The postdoctoral position is fully funded for one year by the *Association Française contre les Myopathies*, with the possibility to be extended for one or two years and with a starting date ideally in April 2022.

To apply, please send a cover letter, CV and contact information for 2 references to fanny.storck@vet-alfort.fr