Rare Diseases 360°
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# "Les petits MecP2" and STOP orphan, an innovative model toward the discovery of new treatment for MECP2 duplication syndrome

*"It was in October 2015, at the age of 18 months and after more than a year of questioning about the reasons for the delay of acquisition of my eldest son that the diagnosis fell ... **Mecp2 gene duplication syndrome**.*

*His disease has a name and it should have been source of answers and perhaps even solutions. Not at all, it raised even more questions and uncertainties.*
*I discovered a medical publication published in November 2015 in Nature, demonstrating the reversibility of this anomaly.*
*I made the choice of doing my best for improving the living conditions of my child and others, by federating families around a project of research on MeCP2 duplication syndrome.*
*Les Petits MeCP2 was born on February 2016. In November, the hasard made me encountering Terence Beghyn, founder of Apteeus. In June 2017, a research program began on the MeCP2 duplication syndrome.*
*I remain convinced that science will provide answers. The mobilization of families through the association will drastically speed them up."*

**Laurent DeClimmer, President of the association.**

PARCE QU'ENSEMBLE NOUS SOMMES PLUS FORTS!

APTEEUS
engaging patients in discovery

APTEEUS is a biotech company exploiting the potential of all approved drugs to improve life of patient suffering from an orphan disease. Our objective is to reduce time and cost of drug discovery in the field.

By screening *in vitro* all available drugs directly on patient cells, we aimed at identifying new treatment opportunities that will benefit patients in a short-term.

Why do we commit the patient in search of his treatment?

The best model of a disease and often the sole one remains the patient himself. By working on its unmodified cells in culture, we ensure that the functional defect that we measure is the cause of its symptoms. The results we get are then very relevant to the clinic.

Why are we testing all drugs from the World Pharmacopoeia?

Drug repurposing consists in using an existing drug in a new indication. This is supported by common physiopathology between diseases and drug polypharmacology. It is a faster and less risky process than developing a new drug, since millions of people have already been treated.

**STOP Orphan strives to provide access to Apteeus cutting-edge technologies through partnerships, and gives you the opportunity to engage into drug discovery efforts on a disease that affects you.**

## STOP Orphan

Virtuous collaboration to leave no-one behind


**Step1: Eligibility study**
Delivery of a full review on the disease, its drugability and its compatibility with Apteeus technology. An *ad hoc* scientific and medical committee will participate in the elaboration of a precise workplan, defining scientific and decisional milestones.

**Step2: Implementation of the patient-based screening assay**
Operations begin with biopsies and biological samples cryopreservation. The screening assay is developed and validated.

**Step3: Drug screening**
APTEEUS original drug collection is tested and individual pharmacogrammes® are generated. Molecules that correct the defect are fully characterized. The best candidate is selected. Its compatibility with a clinical use and its pharmaceutical development is considered.

**Involvment** — Technology, Cells, Network, Knowledge

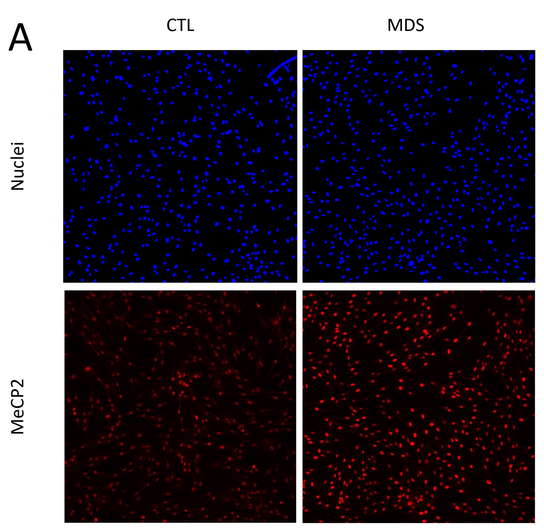
**Collaboration** — **STOP Orphan** — The process is 18 to 24-month long

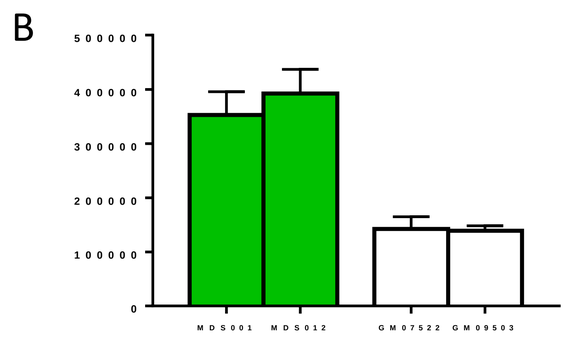
**Impact** — Biobanking, Screening assay, Visibility, Publications, **Drug Candidate**, Better knowledge, understanding and diagnosis, New therapeutic targets

## STOP Orphan for MecP2 duplication syndrome

**Step 1 :** Previous studies 1/ confirm the dominant role of increased MecP2 dosage in MeCP2 duplication syndrome (MDS) phenotype and its reversibility, 2/ suggest that even partial rescue of MeCP2 overexpression may be sufficient to alleviate symptoms (on animal model), 3/ shows that small drugs reduce MeCP2 expression in vitro.
The development of an assay based on MeCP2 expression level in cultured fibroblasts was validated by the scientific committee.

**Step 2 :** We miniaturized an immunostaining of MeCP2 assay in fibroblasts (in red on Figure). The level of MecP2 staining in patient fibroblast is twice the one of control fibroblasts. The assay is being validated for screening.




**MeCP2 expression in skin fibroblast .** A. Nuclear staining (in blue) and immunostaining of MecP2 protein (in red) in fibroblasts from patient (MDS001) and control (CTL) of MecP2. B. Integrated density level of immunostaining MeCP2 for two patients compared to two controls.

Apteeus partners & sponsors : Inserm, Institut Pasteur de Lille, Université de Lille 2 Droit et Santé, eurasanté, bpifrance

Les Petits MeCP2 partners & sponsors : ville de Lille, Carrefour market, Crédit Agricole Nord de France, Lutti, Fondation Tao Tape à l'oeil, Santélys