FOCUS

N° 01 - April 2023

NOVEMBER 25, 2022

1ST INTERNATIONAL DAY FOR FAMILIES, CLINICIANS AND RESEARCHERS AROUND THE *MYT1L* GENE

- **99 present** at the Rouen University Hospital
- **Nearly 60 connected via ZOOM at the height of the day**
- **26 families gathered for the day,** 18 of whom were able to take advantage of an extended exchange time in Rouen with the family day on Saturday
- **15 MYT1L syndrome patients sharing moments** around music, dance and visual arts
- **Nearly 390 connections to the Replays in French and English** on the Youtube channels of the Extra-Vaillants MYT1L and the ANDDi-Rares health network

Sincere thanks to all the speakers, to the developmental anomalies reference centre of the ROUEN University Hospital, to the ANDDi-Rares health network, to the generous artists (Sonia Le Corre, Marion Lebarbier Goujard Centre Art'Damann, Bérénice Palier les Bleus de l'Être), to the volunteer students of the BTS social and family economy of the Flaubert High School, to our donors. Thank you for believing in us and making this day possible.
Thank you to all of you, strangers, families, friends, associations, communication agencies, companies, hoteliers, entrepreneurs .... without whom this day would not have been possible.
Thank you to all the participants for being curious and attentive to the Valiants.

A special thought for Dr Juliette Coursimault, Dr Anne-Marie Guerrot, Dr François Lecoquierre, for Gwendoline Giot and the AnDDi-Rares health network who made possible the live and replayed transcription in English.





Since then, OUR ACTIONS

- **Workshops** on rare diseases with the 2nd years of the Rouen Faculty of Medicine - January

- **Operation "Creative pancakes".** Eight Valiant families took part, with the result being good humour, beautiful photos, and for the champions, a diploma and two pastry accessories as a reward. To be found on the MYT1L Extra-Vaillants website on the "champions' corner" page - February

- **International Rare Diseases Day.** The Valiants from France and abroad have mobilized to illustrate "STRONG AND PROUD". 21 magnificent Valiants to be found on the homepage or the champions' corner of the association's website - February

- **The Extra-Vaillants MYT1L** were also present **for the Rare Disease Day organized by the Rouen and Caen University Hospital** - March

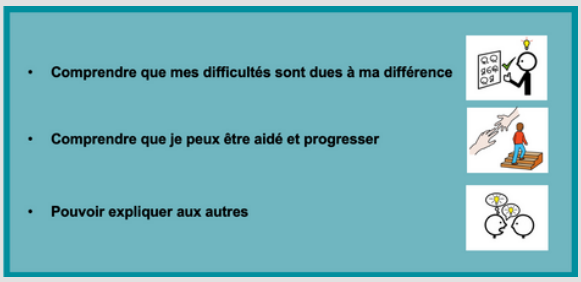
- **Departmental Day on Early Childhood and Disability organised by the PRH 76:** from the first identification of difficulties in children to the diagnostic process. More than 30 professionals from all walks of life, associations, testify. We were there - March
- All the contents and links of this day can be found on the association's website: www.extra-vaillants-myt1l.com on the "events" page (only in french)
  - the actors of the identification
  - the tools of detection
  - diagnosis
  - first level actors
  - second-level actors
  - the diagnosis... and afterwards?
  - an example of inter-service partnership: towards simplifying the pathway?
  - resources of common law at the service of families
  - support for parents and support for professionals, enhancing parental knowledge and increasing the power to act
- Discover other themes around childhood or disability on **Colloque TV**.(only in french)

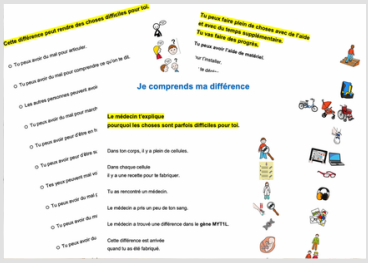
Click on the underlined words to activate the links

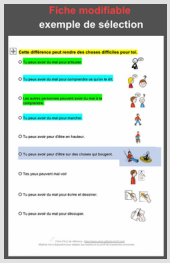
Depuis, LES PROJETS

- **Référent MDPH (specific to France)**

Within the association, Stéphanie will accompany you. You can reach her by e-mail at the following address: coordinateur.myt1l.mdph@gmail.com
January







- **FALC: "I understand my difference"**

AWith the help of professionals and associations from the AnDDi-Rares and DéfiScience health networks, a FALC tool "I understand my difference" for people with MYT1L syndrome has been developed.

The document is mainly aimed at children and adolescents. This is now the median age of diagnosis. It was tested with 11 families who validated its usefulness and stressed that a manipulable format would be more appropriate.

To guarantee the quality of interaction and understanding, the aim is to develop tools that can be manipulated in play or in digital use.

These complementary tools must meet the needs of MYT1L patients, including those in the most complex situations. This component is **the subject of collaborative work over 2023.**

!! Already available on the association's website: https://www.extra-vaillants-myt1l.com/falc ((even if the pictures are in french, ALL THE FILES ARE IN ENGLISH) **- January**

- **FALC (Easy to read and understand) reference document**
- **Modifiable FALC (Easy to read and understand) document**

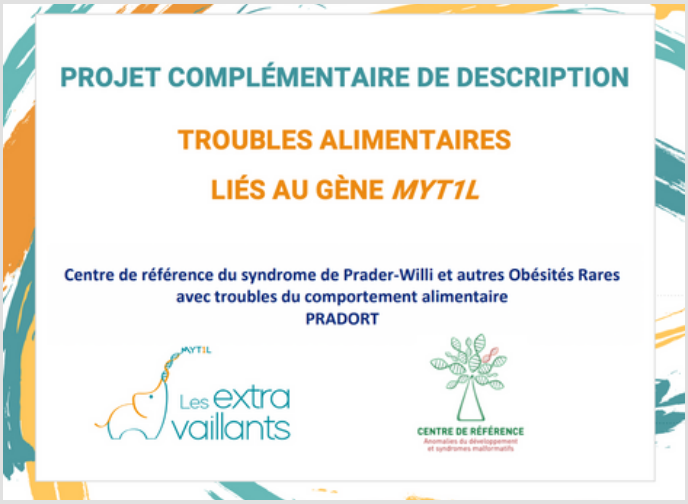
- **Transition from paediatrics to the adult sector**

The Rare Disease Network Transition Working Group, led by the NeuroSphinx Network, and the Transition Spaces are organising the second Adult Transition Conference in June 2023. We will be there.

Upstream, until 12 May 2023,
a survey is being circulated to patients, parents and/or carers. Link to the survey on the homepage of the association (www.extra-vaillants-myt1l.com) -
French patients

PARTICIPATE! Your opinions, expectations and experiences count.

Click on the underlined words to activate the links



• Complementary project on Eating Disorders

This complementary project is a continuation of the clinical-biological study conducted in 2020.

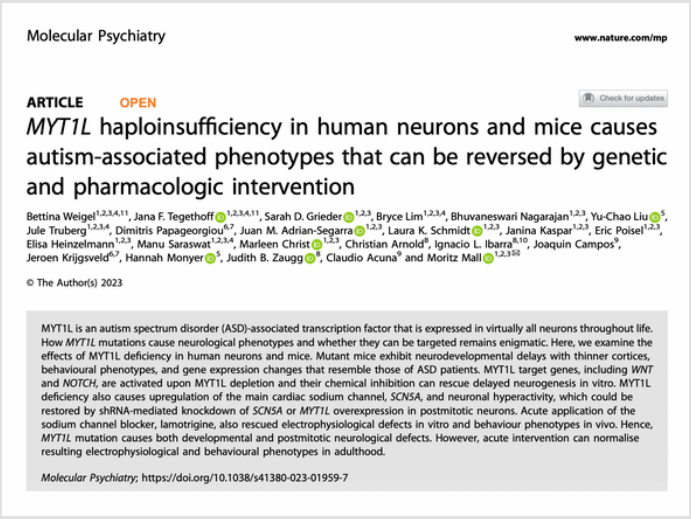
This project is a collaboration between the developmental anomalies reference centre of the Rouen University Hospital, and Pr Poitou Bernert and Pr Dubern, endocrinologists specialising in genetic obesity in adults and children, practising at the Pitié Salpêtrière Hospital and the Trousseau Hospital and attached to the PRADORT reference centre.

This project aims to shed light on the eating disorders of people with MYT1L syndrome, both **ADULTS and CHILDREN.** This is **not a project restricted to weight disorders, it also concerns oral and eating disorders, their manifestations and consequences.**
For people abroad who were not part of the first phase of the study, we are trying to see if participation is possible in this second phase.
If you have not been contacted by your geneticist, please contact the association: extravaillants@gmail.com.

• Collaboration with Dr Mall

On 14 February this year, Dr. Mall's team published this report:
"MYT1L haploinsufficiency in human neurons and mice causes autism-associated phenotypes that can be reversed by genetic and pharmacologic intervention ».

This study highlights the interesting effect of a molecule called Lamotrigine on the behaviour of mice with an anomaly in the *MYT1L* gene. It should be noted that the therapeutic trials were only carried out in mice. There are still many stages to go before we know whether it could work on humans.


Molecular Psychiatry www.nature.com/mp

ARTICLE OPEN

MYT1L haploinsufficiency in human neurons and mice causes autism-associated phenotypes that can be reversed by genetic and pharmacologic intervention

Bettina Weigel[1,2,3,4,11], Jana F. Tegethoff[1,2,3,4,11], Sarah D. Grieder[1,2,3], Bryce Lim[1,2,3,4], Bhuvaneswari Nagarajan[1,2,3], Yu-Chao Liu[5], Jule Truberg[1,2,3,4], Dimitris Papageorgiou[6,7], Juan M. Adrian-Segarra[1,2,3], Laura K. Schmidt[1,2,3], Janina Kaspar[1,2,3], Eric Poisel[1,2,3], Elisa Heinzelmann[1,2,3], Manu Saraswat[1,2,3,4], Marleen Christ[1,2,3], Christian Arnold[8], Ignacio L. Ibarra[8,10], Joaquin Campos[9], Jeroen Krijgsveld[6,7], Hannah Monyer[5], Judith B. Zaugg[8], Claudio Acuna[9] and Moritz Mall[1,2,3]✉

MYT1L is an autism spectrum disorder (ASD)-associated transcription factor that is expressed in virtually all neurons throughout life. How *MYT1L* mutations cause neurological phenotypes and whether they can be targeted remains enigmatic. Here, we examine the effects of MYT1L deficiency in human neurons and mice. Mutant mice exhibit neurodevelopmental delays with thinner cortices, behavioural phenotypes, and gene expression changes that resemble those of ASD patients. MYT1L target genes, including *WNT* and *NOTCH*, are activated upon MYT1L depletion and their chemical inhibition can rescue delayed neurogenesis in vitro. MYT1L deficiency also causes upregulation of the main cardiac sodium channel, *SCN5A*, and neuronal hyperactivity, which could be restored by shRNA-mediated knockdown of *SCN5A* or *MYT1L* overexpression in postmitotic neurons. Acute application of the sodium channel blocker, lamotrigine, also rescued electrophysiological defects in vitro and behaviour phenotypes in vivo. Hence, *MYT1L* mutation causes both developmental and postmitotic neurological defects. However, acute intervention can normalise resulting electrophysiological and behavioural phenotypes in adulthood.

Molecular Psychiatry; https://doi.org/10.1038/s41380-023-01959-7

The existence of the drug on the market, its already effective use in neurology and psychiatry are important factors that will save time in the plans to study the transition from mice to humans in order to define the real efficacy, the necessary dosage and the side effects for MYT1L patients.

It is likely that a new study will be conducted by Dr Mall's team in the near future. We should know more by the summer (feasibility, timetable, cost, coordination with the Rouen geneticists and the association...). This opportunity should accelerate the clinical study on behavioural disorders that we have been talking about since the beginning of our collaboration with Dr Coursimault and Dr Guerrot.

NB: FIND THIS ARTICLE AND OTHER PUBLICATIONS ABOUT MYT1L IN "PUBLICATIONS" ON THE ASSOCIATION'S WEBSITE.

- **NOTE:** Steps to obtain recognition of the TND linked to the MYT1L gene are underway with ORPHANET. A PNDS project (National Diagnosis and Care Protocols) specific to the disease is being considered and is awaiting preliminary agreement.

Click on the underlined words to activate the links

INFOS AND AGENDA

INFORMATION

- **FIND DYNAMIC INFORMATION on the FACEBOOK page of the Extra-Vaillants MYT1L: https://en.extra-vaillants-myt1l.com/**
  - resources: themes (autism, ID...), recommendations (notably the HAS), relay information...
  - events: specific days, news from the AnDDI-Rares health network, the Alliance Maladies Rares, rare disease expertise platforms, etc.
  - training courses that are open to you!
  - studies and surveys because your experiences and expectations count
  - regional action relays

- **FIND some of the e-RDVs of the AnDDI-Rares health network on the network's YouTube channel.**
  - e-RDV n°7: How to reconcile personal and professional life?
  - e-RDV n°6 : Transition from the paediatric sector to the adult sector
  - e-RDV n°5 : Talking about emotional and sexual life with your child
  - e-VR n°4: Neuropsychological assessment
  - e-RDV n°3: Communication and ID and if we innovate?

- **DISCOVER or have a look again at the contents of the association's website and YouTube channel.**

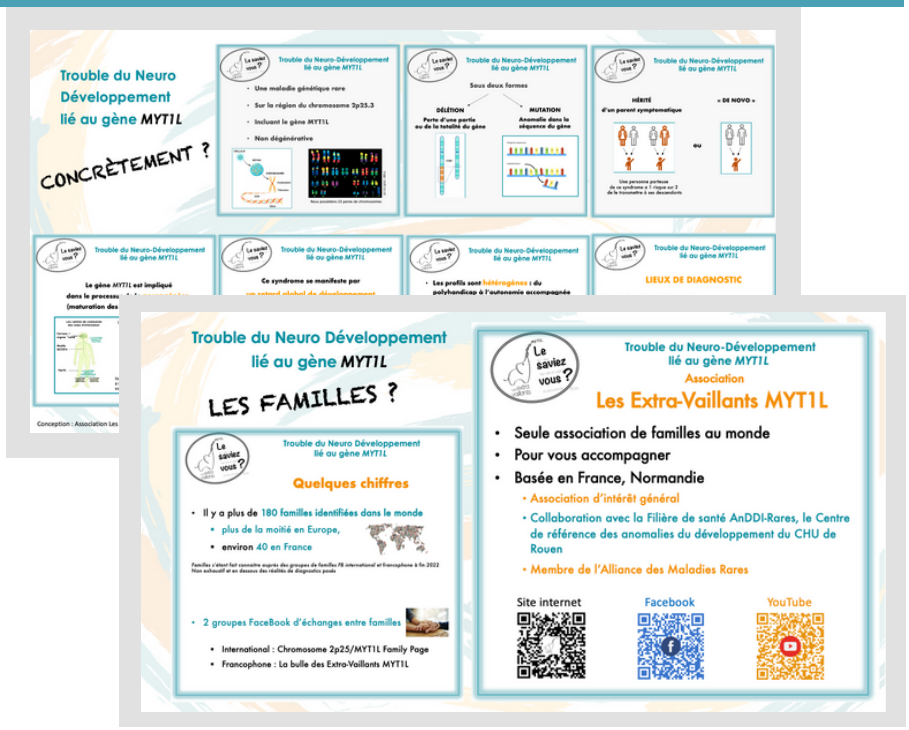
Site internet | Facebook | YouTube

AGENDA for the first half of 2023

- **11 May:** Day of the associations of the AnDDI-Rares network
- **2 and 3 June:** Annual Congress of the Rare Diseases Alliance
- **22 June:** 2nd Adult Transition Conference
- **27 June:** Annual scientific symposium of the Rare Diseases Foundation

Click on the underlined words to activate the links

COMMUNICATION SUPPORTS



We are carrying on our work of informing the public about the Neurodevelopmental Disorder linked to the *MYT1L* gene, as well as our referral to the health and medico-social sectors.
DO NOT hesitate to pass on this information!
If you need informations, please send your requests to: extravaillants@gmail.com
You can download the materials free of charge from the association's website: https://www.extra-vaillants-myt1l.com/myt1l

Site internet

Help us to MOBILIZE around MYT1L Extra-Vaillants
either by encouraging to JOIN,
or by encouraging DONATIONS (financial, in-kind or skills)
Association recognized as being of general interest and therefore tax deductible (10€ in donations cost 3,4€) - for France

Why join us ?

to make visible
to give emphasis
to make it possible

Association reconnue d'intérêt général
Adhésion déductible des impôts / - 66% pour les particuliers

- **For each Valiant wherever they are (>180 world) and the families**
- **For the 44 French-speaking families who have contacted the association**
- **For the 31 countries connected to the association's website to find information**
- **For the more than 2000 visits to the website in 15 months**
- **For all the professionals involved with Les Vaillants (health, medical and social services, culture, sport, etc.)**
- **For the 38 current members and our donors**

Click on the underlined words to activate the links

If you need help : Aline, Delphine, Katia,
Sandra, Simon, Stéphanie et Valérie (president)

extravaillants@gmail.com
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THANK YOU for believing in us!

FERRERO
O·P·I
BORNEO COMMUNICATION
Mercure HOTELS Mercure Rouen Centre Cathédrale
SPIN MASTER
BRIDGESTONE
AVENIR FOCUS
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un horizon pour Hélias
Sonia Le Corre
Bérénice Palier
les BLEUS de l'ÊTRE
Marion Barbier Goujard
LA CABANE Ateliers artistiques itinérants
Particuliers
Familles
Amis
Passion Sable
Société DELVOY A.
Société SA-BAT
LE XXI RESTAURANT

THANK YOU!
We are moving forward!

Qui voit l'invisible, réalise l'impossible !

WHO SEES THE INVISIBLE REALIZES THE IMPOSSIBLE

MYT1L

#MoiAUSSI