THE GenIDA NEWSLETTER

Issue n°2 / July 2024

LATEST PUBLICATIONS

Forbes*, Morison* et al. (2024) Speech and Language in DDX3X-neurodevelopmental disorder: a call for early augmentative and alternative communication intervention. American Journal of Medical Genetics Part B: Neuropsychiatric Genetics, https://doi.org/10.1002/ajmg.b.32971

Ruault et al. (2024) Lessons from two series by physicians and caregivers' self-reported data in DDX3X-related disorders. Molecular Genetics & Genomic Medicine, https://doi.org/10.1002/mgg3.2363

EDITO

Summer is here, so it's time for a second issue of the GenIDA newsletter, to keep you informed of our progress.

The first half of the year has been a busy one, with the publication of two articles using data from the DDX3X cohort (see banner opposite), by the teams of Prof. David Geneviève (Montpellier) and Prof. Angela Morgan (Melbourne, Australia), and GenIDA's participation in the 12th *Assises de Génétique Humaine et Médicale* in Paris in January, where we shared our stand with the Association Coffin-Siris France. GenIDA took part in the annual meeting of the American College of Medical Genetics - ACMG, in Toronto in March and in the workshop of ERN-Ithaca, the European research network on rare neurodevelopmental diseases (https://ern-ithaca.eu/), in Lisbon in April. These were great opportunities for us to present our activities and some of our results in the form of posters (in particular the results of the DDX3X cohort) to an international audience. Finally, in June, GenIDA took part, as it does every year, in the ESHG-European Society of Human Genetics congress in Berlin, where we held the annual meeting of our international scientific advisory board (see article below).

Once again, we would like to take this opportunity to thank you, the patients and families taking part, for your involvement in GenIDA! We would also like to thank all the professionals who are working alongside us in the analysis of the data collected. We hope you have a great summer, and look forward to seeing you in September to discover our new web interface.

The GenIDA team

A big thank you to all of you, patients and families, for your ever-growing involvement in GenIDA, and a great summer to you all!

GenIDA … AS CLOSE TO PATIENTS AS POSSIBLE

Recruiting more and more patients is essential if we are to obtain reliable medical data on the various pathologies listed in GenIDA. This is why we are mobilising on several fronts. In January, Benjamin Durand and Sarah Baer, members of our Scientific Advisory Board, presented the project to the French families of the recently created Wiedemann-Steiner French association. In April, we discussed the steps to be taken to develop the GRIN cohort, with the vice-president of GRIN Europe, and the SETBP1 one, with the president of the SETBP1 association UNIQUES ENSEMBLE, and presented GenIDA to the scientific council of the European 22q11 association and at the 'Collaboration between patients and researchers' day. We also exchanged views with CASK families in France (replay available from the association) in June and in the UK in July,

with the aim of collecting ever more data to improve care for these patients. We also created the GenIDA_project account on Instagram in May. All these efforts are bearing fruit: we're approaching 2,000 participants!

7th MEETING OF OUR INTERNATIONAL SCIENTIFIC COUNCIL

The conference of the European Society of Human Genetics, held in Berlin from 1 to 4 June, provided an opportunity to organise the annual meeting of our international Scientific Advisory Board and to review with our collaborators the progress made by GenIDA since last year in terms of recruiting new participants and ongoing studies in specific cohorts (see article below). Also on the agenda was an update on the ongoing redesign of the GenIDA website. In particular, we have asked some members of the Scientific Advisory Board to take part in the test phase of the web interface aimed at professionals during the summer of 2024 (see below).

Meeting of the GenIDA Scientific Council, Berlin, 2 June 2024.
From left to right : Standing - Angela Morgan, Melbourne, AU ; Aafke Engwerda, Groningen, NL ; David Koolen, Nijmegen, NL ; Bert de Vries, Nijmegen, NL ; Saskia Koene, Nijmegen, NL ; Ece Gepni, Istanbul, TR ; Sylvie Odent, Rennes, FR ; Thomas Smol, Lille, FR ; Delphine Héron, Paris, FR ; Damien Sanlaville, Lyon, FR ; Julien Thevenon, Grenoble, FR ; Klea Vyshka, Paris, FR ; Marc Abramowicz, Genève, CH.
Sitting - Charlotte Ockeloen, Nijmegen, NL ; Pauline Burger & Jean-Louis Mandel (GenIDA), Strasbourg, FR ; Sarah Baer, Strasbourg, FR ; Benjamin Durand, Strasbourg, FR. Absentes sur la photo - Tijtske Kleefstra, Rotterdam, NL ; Francesca Matteoli, Lausanne, CH ; Alessandra Renieri, Sienne, IT.

REDESIGN OF THE WEBSITE

As announced in the previous issue of this newsletter, GenIDA's web interface is currently being redesigned by a team of 3 IT specialists, who are working hard to provide you with the best possible user experience. The site's content and functions have been redesigned to make it easier to use, both for participants and for professionals (for data analysis). A modern design and dynamic visual elements will ensure fluid navigation and make the information more accessible to everyone. The site and consent form will now be fully translated and available in several languages. Adding questionnaires and exporting the data collected will be simplified. The new site will also be compatible with smartphones.

Data migration to the test version to validate the process is scheduled for August. The full beta version of the site will be tested in September, with the final migration of the system scheduled for the end of October 2024.

RNU4-2, AN IMPORTANT NEW GENE LINKED TO INTELLECTUAL DISABILITY

A very recent study has revealed that mutations in the RNU4-2 gene, coding for a small RNA, are involved in a genetic form of neurodevelopmental disorder. Published by Chen et al (2024, medRxiv preprint, then this 11 July in Nature), this study identified 115 patients, mainly in the UK and the US, 80% of whom have the same specific mutation in this gene. This is a very important discovery, as the individuals affected had no genetic diagnosis until now, as diagnostic strategies such as gene panels or exomes were unable to detect mutations in this gene. These mutations were identified by sequencing the entire genome in trio (child and parents). However, the small size of the RNU4-2 gene and the limited number of mutations will soon enable a simple test to be developed to identify these mutations, which are thought to affect around 0.4% of people with intellectual disabilities.

In France, the community of geneticists and the AnDDI-Rares and DéfiScience rare diseases networks quickly mobilised, identifying and validating around a hundred cases. A call for collaboration for an in-depth study in France has been launched, and GenIDA has joined the initiative to collect health data to gain a better understanding of the clinical manifestations, quality of life and response to symptomatic treatments at an international scale. Eight families have already completed the questionnaire as of 13 July.

2024 PROJECTS

Specific studies on the POGZ, KBG and MYTL1 cohorts are currently underway; we will share the results as soon as possible (if you are concerned and interested, contact us to find out more). A cross-cohort study on vestibular disorders was also put online in January in the form of an additional short questionnaire available in French and English.

Setting up GenIDA interoperability with ILIAD: Since March, we have been collecting your individual consents to set up GenIDA's interoperability with the various registries included in ILIAD, the meta-registry developed by ERN-Ithaca. Such an operation requires the creation of a unique SPIDER identification number for each patient registered in GenIDA, which will make this interoperability possible, while still guaranteeing the anonymity of your data. If you have not already done so, you can still give your consent by completing this short survey (please answer as many times as you have relatives registered in GenIDA):
https://www.evalandgo.com/f/126847/4pWKEgDJyaij6n3Dokf5Bp

DO NOT FORGET ...

- To spread the word about GenIDA, our flyer is always available on request in electronic format (French, English, German, Dutch, Italian, Portuguese, Greek, Bulgarian, Romanian and Spanish) or can be downloaded directly from our website.
- If you have the opportunity, encourage other families concerned to take part in the project.
- To update your answers to the health questionnaire by logging back on to our website.

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