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► **To cite this version:**

Pauline Burger, Florent Colin, Axelle Strehle, Timothée Mazzucotelli, Nicole Collot, et al.. GenIDA, an international participatory database to better characterize comorbidities of genetic forms of intellectual disability: insights on Koolen-de Vries syndrome. *Genetics in Medicine Open*, 2023, 1 (Supplément 1), pp.100699. 10.1016/j.gimo.2023.100699 . hal-04089557

HAL Id: hal-04089557

<https://hal.science/hal-04089557v1>

Submitted on 4 May 2023

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Research Methods and Resources

Key: O is for Platforms; P is for Posters.

O46

GenIDA, an international participatory database to better characterize comorbidities of genetic forms of intellectual disability: insights on Koolen-de Vries syndrome

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Introduction: GenIDA (<https://genida.unistra.fr/>) is an international online research project initiated to better characterize the clinical manifestations and natural history of genetic forms of intellectual disability with or without ASD or epilepsy.

Methods: Clinical information reported and updated by the patient's family using a structured questionnaire is analyzed to identify new medically relevant information for families and professionals concerned with a given condition. The current questionnaire consists of 41 multiple-choice questions exploring physical parameters, cognitive and behavioral aspects, the presence or absence of neurological disorders or problems affecting major physiological functions (cardiac, renal, etc), etc. Five open-ended questions explore families' perception of the events that most affect their relative's health and quality of life, the secondary effects of treatments, etc.

Results: Currently, the questionnaire is available in 7 languages and has been completed for over 1670 patients from over 60 nationalities, the main cohorts being Koolen-de Vries/KdVS (n=249), and Kleefstra (n=191) syndromes. Other cohorts have experienced significant growth over the last year, including the MED13L (n=45), KBG (n=48) and DDX3X (n=50) syndromes.

Analysis of the data collected for 237 individuals with KdVS was conducted and showed no significant differences between patients with KdVS caused by a deletion of 17q21.31 that includes the *KANSL1* gene and those with a heterozygous intragenic pathogenic variant in *KANSL1*. GenIDA findings on KdVS were consistent with the existing literature and revealed a previously unreported susceptibility of these patients to respiratory problems including recurrent pneumonia, and childhood asthma. The frequency of epilepsy reported in GenIDA is consistent with data from the medical literature, but GenIDA data analysis provided further information on the nature of the seizures associated with KdVS, as well as information on the efficacy and possible adverse effects of the anti-epileptic treatments used to treat these disorders.

Two incidental studies conducted by collaborators using the GenIDA platform to rapidly reach out concerned people with KdVS likely to participate, have then emerged:

(i) an international retrospective cohort study including 54 participants aimed to characterize the prevalence, clinical and radiological characteristics of musculoskeletal problems in people with KdVS, as GenIDA results indicated the occurrence of scoliosis and abnormal thoracic kyphosis in more than 27% of these individuals (compared with a prevalence of 2-4% in the general population). It showed that scoliosis is common among the respondents (56%) with a clear increase of the prevalence with age.

(ii) another study including 67 GenIDA participants with KdVS was conducted to deepen insight on known ophthalmological manifestations of KdVS (occurrence and frequency of ocular and oculofacial malformations) while uncovering novel ocular associations. It indicated that KdVS is associated with various ophthalmic manifestations such as amblyopia, strabismus, refractive errors, and upper eyelid ptosis, while retinal abnormalities and nasolacrimal disorders were described for the first time in KdVS.

Comparative results on Kleefstra, KBG, DDX3X and MED13L cohorts regarding notably sleep and epilepsy aspects will also be presented.

Conclusion: These results validate the interest of our participatory approach: through their direct involvement, families can reveal aspects of the pathology that were previously underestimated, and thus lead to the implementation of incidental studies on specific aspects of rare forms of ID.

<https://doi.org/10.1016/j.gimo.2023.100699>