New findings better elucidate TRAF7 syndrome, a neurological and developmental disease

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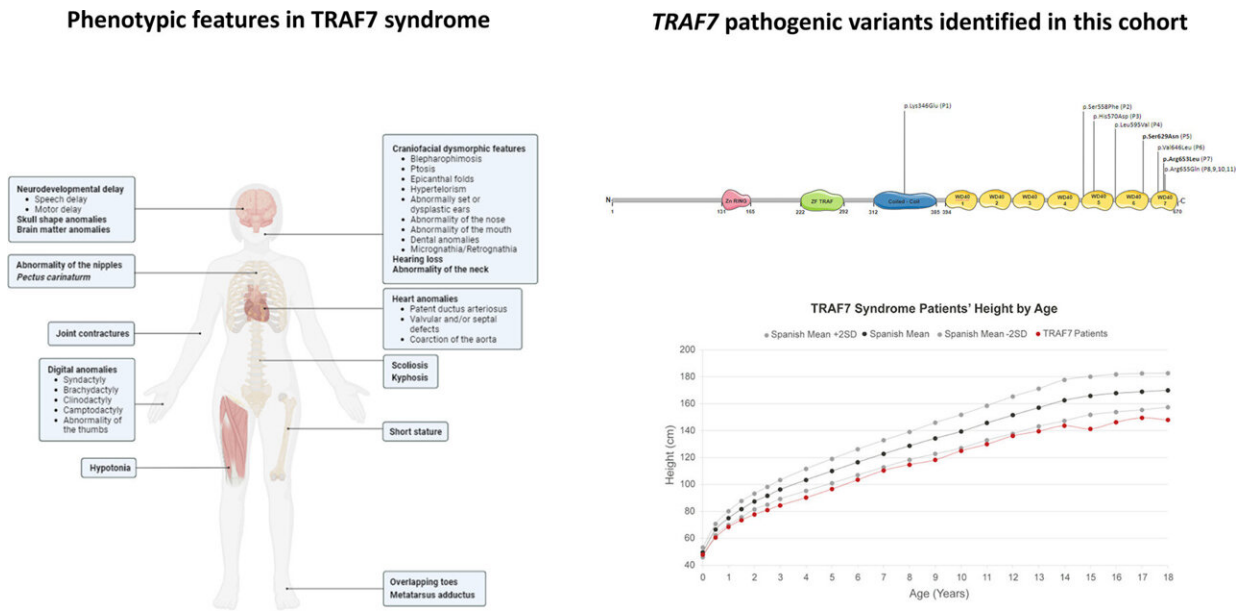

Credit: *Pediatric Neurology* (2024). DOI: 10.1016/j.pediatrneurol.2024.03.008

TRAF7 syndrome, or CAFDADD syndrome, is a neurological and developmental disease that causes a wide variety of clinical manifestations, such as cardiac, facial and digital abnormalities and developmental delay.

Now, a study published in *Pediatric Neurology* provides a better

understanding of the clinical, genetic and functional characteristics of CAFDADD syndrome, which is caused by the TRAF7 gene. The paper will contribute to a better understanding of this disease and the improvement of medical care and clinical management of patients.

The study was co-led by teams from the Faculty of Biology and the Institute of Biomedicine (IBUB) of the University of Barcelona, the Sant Joan de Déu Research Institute (IRSJD) and the 12 de Octubre University Hospital (Madrid), which are also members of the Rare Diseases Networking Biomedical Research Center (CIBERER).

TRAF7-related CAFDADD syndrome is caused by pathogenic germline variants in the TRAF7 gene encoding the TRAF7 protein. It was described in a previous study published in *Genetics in Medicine* in 2020 and led by the UB-IRSJD-CIBERER team in collaboration with experts from the National Institute of Health and Medical Research (INSERM, France).

From left to right, Mónica Centeno Pla, Aina Prat Planas, Juan Diego Gutiérrez Ávila, Susanna Balcells Comas and Raquel Rabionet Janssen, from the UB, the BUB, the IRSJD and the CIBERER. Credit: University of Barcelona

From clinical manifestations to oncological risk

The TRAF7 protein is a key component of several cell signaling pathways, including the NF-κB and MAPK pathways. It plays a critical role in cell apoptosis, proliferation, differentiation and survival. Altered variants in the TRAF7 gene cause dysfunctions in these signaling pathways and underlie several clinical features observed in CAFDADD syndrome, which can be quite variable and affect patients to varying degrees.

Hearing loss and short stature, present in all patients, are other main features highlighted in the new paper. Other less common but relevant manifestations, such as sleep disorder and autism, have also been addressed.

This paper analyzes in detail eleven new cases of this rare disease and presents a comprehensive review of the literature, including 58 previously reported cases. In particular, eight different dysfunctional missense variants have been identified and reveal aspects already known to be associated with TRAF7 syndrome, such as the existence of recurrent variants and the overlap between germline variants that give rise to TRAF7 syndrome versus tumor-associated somatic variants.

The findings of the study improve the understanding of the relationship between genetic variants and the clinical manifestations of CAFDADD

syndrome, with particular emphasis on the assessment of the potential oncological risk of patients.

The study notes the complexity and heterogeneity of TRAF7-related CAFDADD syndrome and emphasizes the importance of comprehensive, multidisciplinary clinical assessment for each patient.

The team also proposes evidence-based guidelines for the clinical management of patients with TRAF7-related CAFDADD syndrome, with recommendations for regular medical evaluations, specific therapeutic interventions and long-term follow-up to monitor disease progression and prevent possible complications.

More information: Carmen Palma-Milla et al, Expanding the Phenotypic Spectrum of TRAF7-Related Cardiac, Facial, and Digital Anomalies With Developmental Delay: Report of 11 New Cases and Literature Review, *Pediatric Neurology* (2024). DOI: 10.1016/j.pediatrneurol.2024.03.008

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