

ANKRD11 And KBG Syndrome

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Mutations affecting the transcriptional regulator Ankyrin Repeat Domain 11 (ANKRD11) are mainly associated with the multisystem developmental disorder known as KBG syndrome, but have also been identified in individuals with Cornelia de Lange syndrome (CdLS) and other developmental disorders caused by variants affecting different chromatin regulators. The extensive functional overlap of these proteins results in shared phenotypical features, which complicate the assessment of the clinical diagnosis. Additionally, re-evaluation of individuals at a later age occasionally reveals that the initial phenotype has evolved toward clinical features more reminiscent of a developmental disorder different from the one that was initially diagnosed. For this reason, variants in ANKRD11 can be ascribed to a broader class of disorders that fall within the category of the so-called chromatinopathies. In this work, we report on the clinical characterization of 23 individuals with variants in ANKRD11. The subjects present primarily with developmental delay, intellectual disability and dysmorphic features, and all but two received an initial clinical diagnosis of either KBG syndrome or CdLS. The number and the severity of the clinical signs are overlapping but variable and result in a broad spectrum of phenotypes, which could be partially accounted for by the presence of additional molecular diagnoses and distinct pathogenic mechanisms.