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## Exome sequencing identifies a branch point variant in Aarskog-Scott syndrome.

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**Abstract:** Aarskog-Scott syndrome (ASS) is a rare disorder with characteristic facial, skeletal, and genital abnormalities. Mutations in the FGD1 gene (Xp11.21) are responsible for ASS. However, mutation detection rates are low. Here, we report a family with ASS where conventional Sanger sequencing failed to detect a pathogenic change in FGD1. To identify the causative gene, we performed whole-exome sequencing in two patients. An initial analysis did not reveal a likely candidate gene. After relaxing our filtering criteria, accepting larger intronic segments, we unexpectedly identified a branch point (BP) variant in FGD1. Analysis of patient-derived RNA showed complete skipping of exon 13, leading to premature translation termination. The BP variant detected is one of very few reported so far proven to affect splicing. Our results show that besides digging deeper to reveal nonobvious variants, isolation and analysis of RNA provides a valuable but under-appreciated tool to resolve cases with unknown genetic defects.