Identifying a genetic cause for a severe speech and language disorder reveals molecular processes underlying a uniquely human trait

**WHAT WAS KNOWN**
- Children with developmental language disorders have difficulty acquiring speech and language despite being of normal intelligence and showing no obvious sensory or neurological impairment
- Twin studies implicate a genetic cause but family pedigrees often show a complex pattern of inheritance
- No underlying gene that could point to the involvement of a particular molecular pathway had previously been identified

**WHAT WE DID**
- Mapped the defect in a rare family, KE, with a dominantly inherited speech disorder over three generations, to a locus on the long arm of chromosome 7
- Identified an unrelated patient, CS, with a strikingly similar speech and language disorder who had a chromosome translocation at the same locus
- Sequenced this region in KE family members to uncover any point mutations

**WHAT THIS ADDS**
- Meticulous genetic mapping in CS localised a translocation breakpoint to a 200bp region of the FOXP2 gene, one of a family of transcription factors
- Sequencing this gene in the KE family identified a G to A mutation in affected but not unaffected family members or controls
- The mutation causes a switch from a highly conserved arginine residue to histidine in the ‘forkhead’ binding domain of the FOXP2 protein
- Suggests that inactivation of FOXP2 during embryogenesis leads to abnormal development of neural structures that are key for speech and language development
- FOXP2 is the first gene to be implicated in the molecular pathways underlying language, a unique and complex human trait

**REFERENCES**

A forkhead-domain gene is mutated in a severe speech and language disorder.