

GTF2IRD1 a gene involved in Williams-Beuren syndrome also has a role in muscle development



Craniofacial abnormalities, hypersociability and visuospatial defects of Williams syndrome



hypersociability

Socializes with anyone she meets. In church she recognizes a new member or someone visiting and says, "I don't know them - I need to know them".



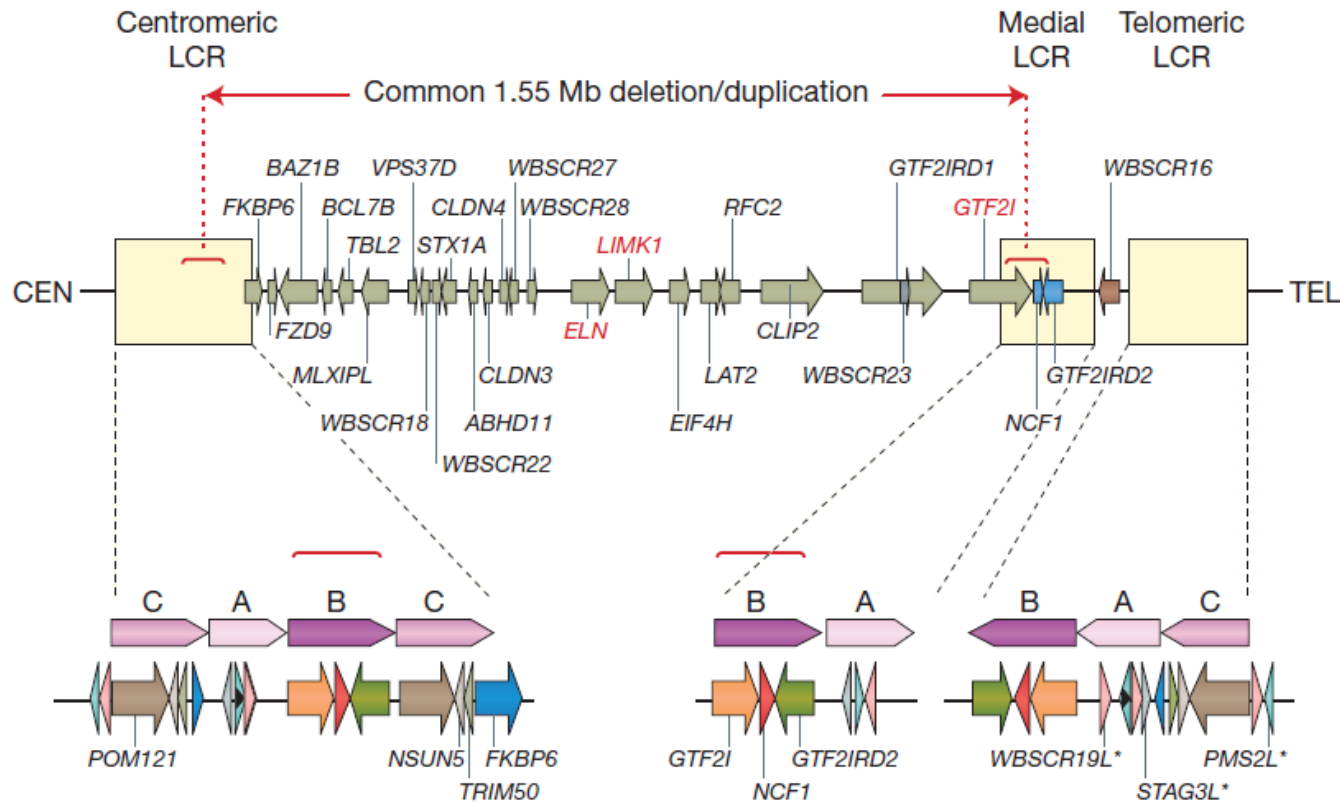
In the grocery store it would take me hours to get my shopping done as my daughter would say hi and ask questions to every person we passed.



MODEL	WS copy	DScopy

Delis hierarchical processing task
Subjects are asked to copy a large global figure made of smaller local forms. Karmiloff-Smith 2003

Williams syndrome is caused by a hemizygous microdeletion within Chr 7q11.23



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Human GTF2IRD1 protein

Found in the nucleus

Can bind to DNA

Was found to bind to the *TNNI1* upstream enhancer and is expressed during myogenesis – a possible protein X?

Human skeletal actin promoter and enhancer combined

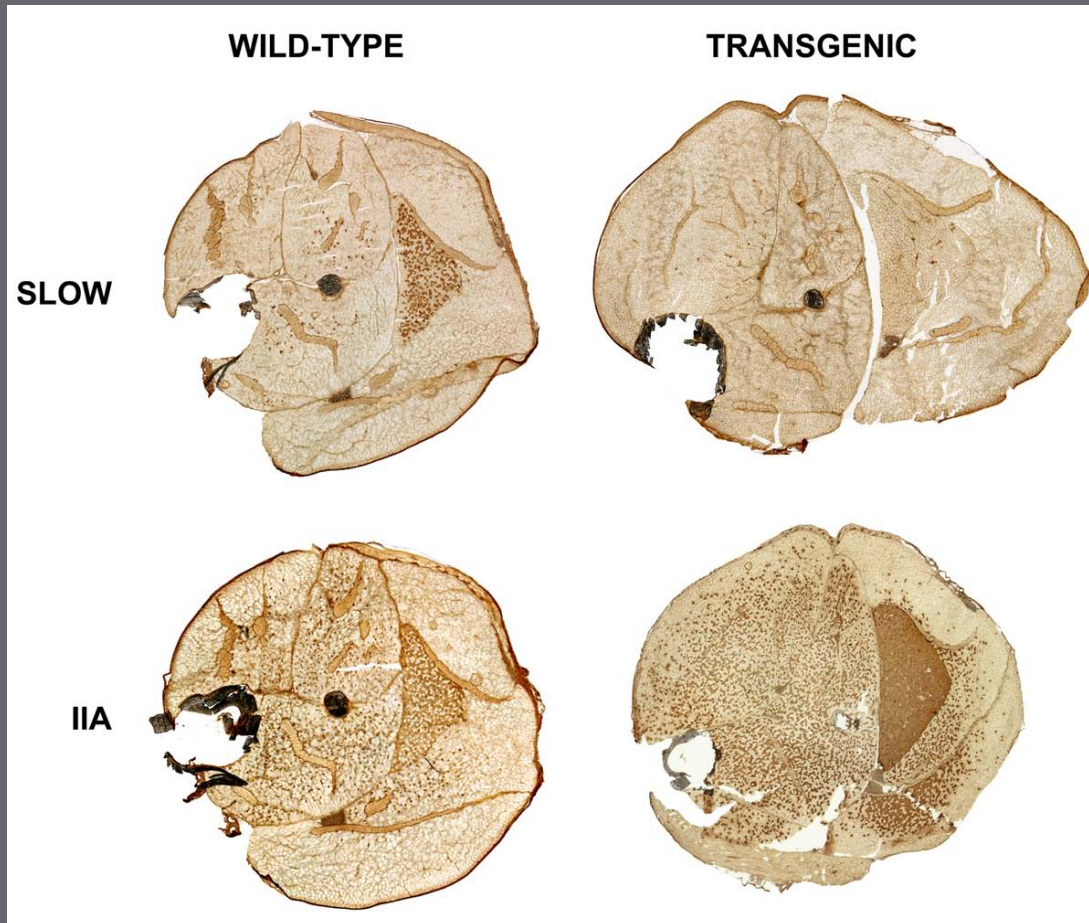
Human *GTF2IRD1* cDNA
i.e. makes a pre-spliced mRNA



Cloned in bacterial plasmid DNA



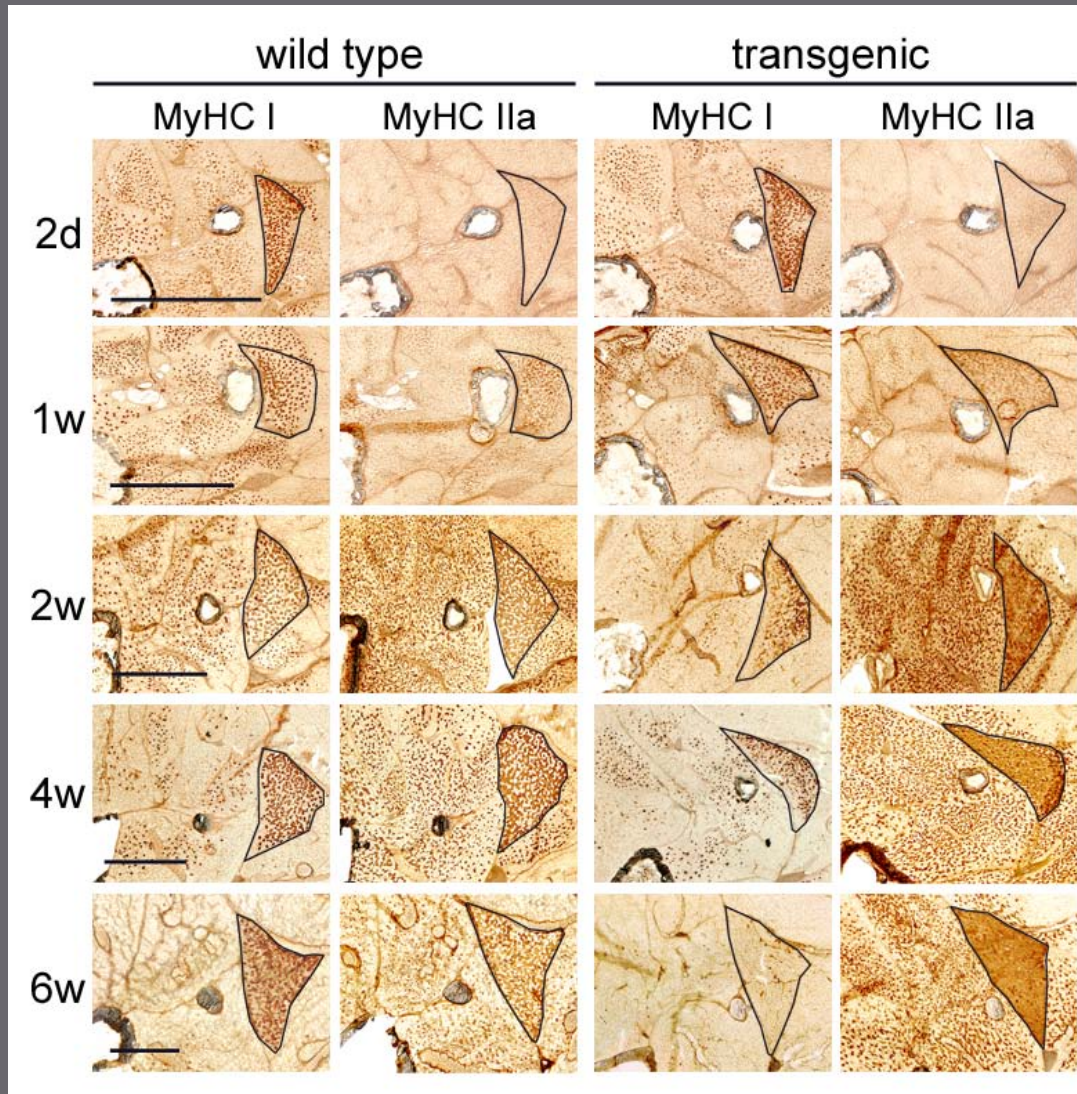
DNA microinjected into a fertilized mouse embryo to make a transgenic 'founder' mouse.



Transverse sections through the lower hind-limb of adult GTF2IRD1-transgenic and wild type mice - stained for MyHC type I/slow and MyHC2A.

1. Identify the muscle types
2. Describe what has happened to the muscle fibre types
3. Propose a theory for what might have caused the observed effect. Is there more than one possibility?

Examining the developing fibre types in *Gtf2ird1*-transgenic mice.



Transverse sections through the lower hind limb of transgenic and wild type mice from 2 days after birth to 6 weeks.

Questions

1. Has embryonic fibre type patterning been affected by the expression of the transgene?
2. What process would describe what is happening?
3. Refine the theory concerning the effect of *Gtf2ird1* on muscle development.
4. How would you prove that *Gtf2ird1* has an important role in fibre type differentiation?

Questions

1. Briefly; what is a myotube and how is it formed?
2. What changes would I expect to see in the muscle fibre types in my legs if I:
 - a) Suffered a spinal cord injury
 - b) Took up marathon running