

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



Craniofacial abnormalities, hypersociability and visuospatial defects of Williams syndrome

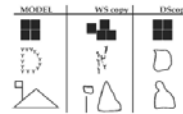
hypersociability



*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".*

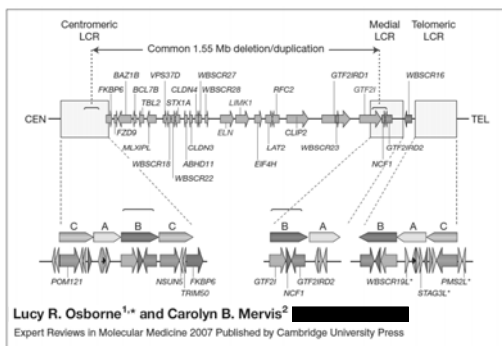


*In the grocery store it would take me hours to get my shopping done as my daughter would say hi and ask questions to every person we passed.*



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



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.

WILD-TYPE      TRANSGENIC

SLOW

IIA

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.

	wild type		transgenic	
	MyHC I	MyHC IIa	MyHC I	MyHC IIa
2d				
1w				
2w				
4w				
6w				

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

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