



Simons Variation in Individuals Project

Simons VIP HNRNPH2 Family Meeting

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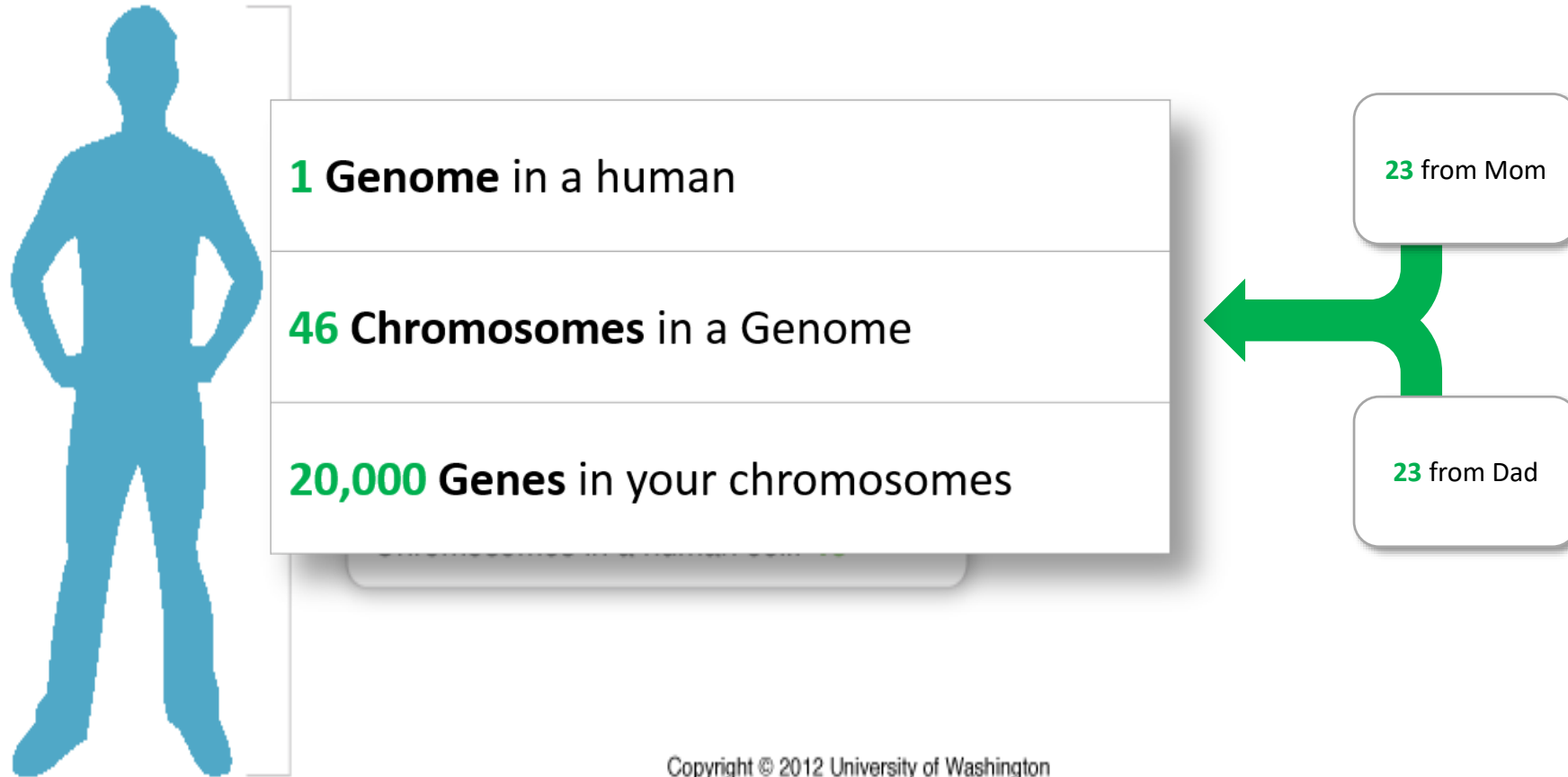
July 26, 2018



Genetics

- Caused by changes in the HNRNPH2 gene
- All reported cases are *de novo*
 - Recurrence risk if ~1%

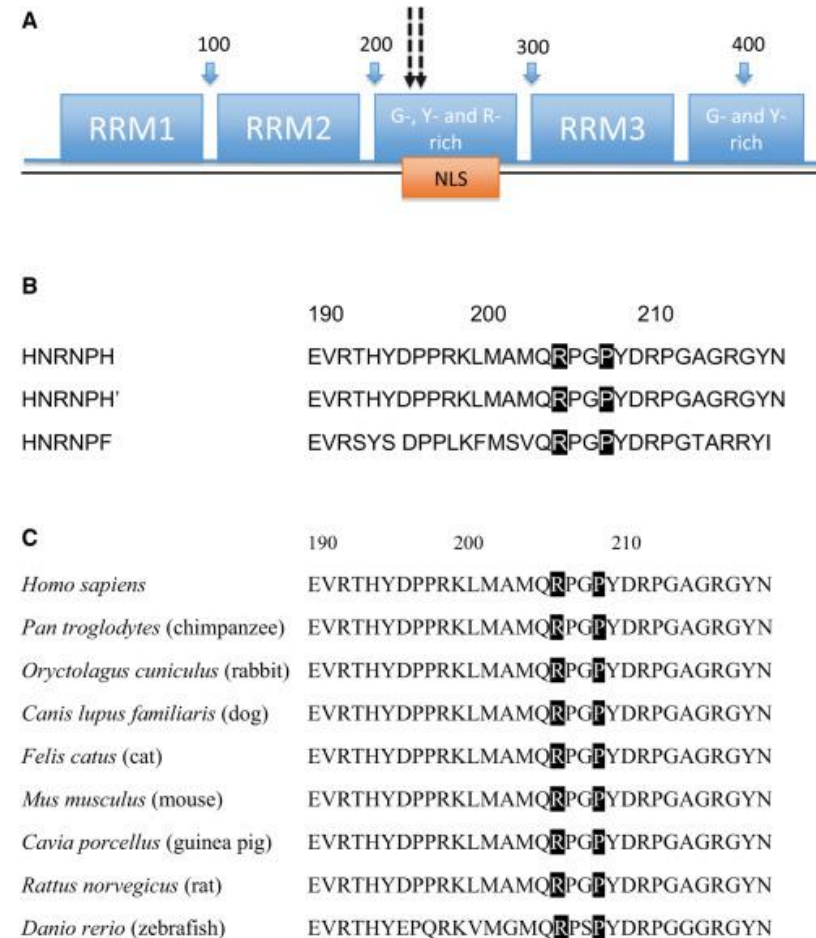
Our Genome



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The gene *HNRNPH2*

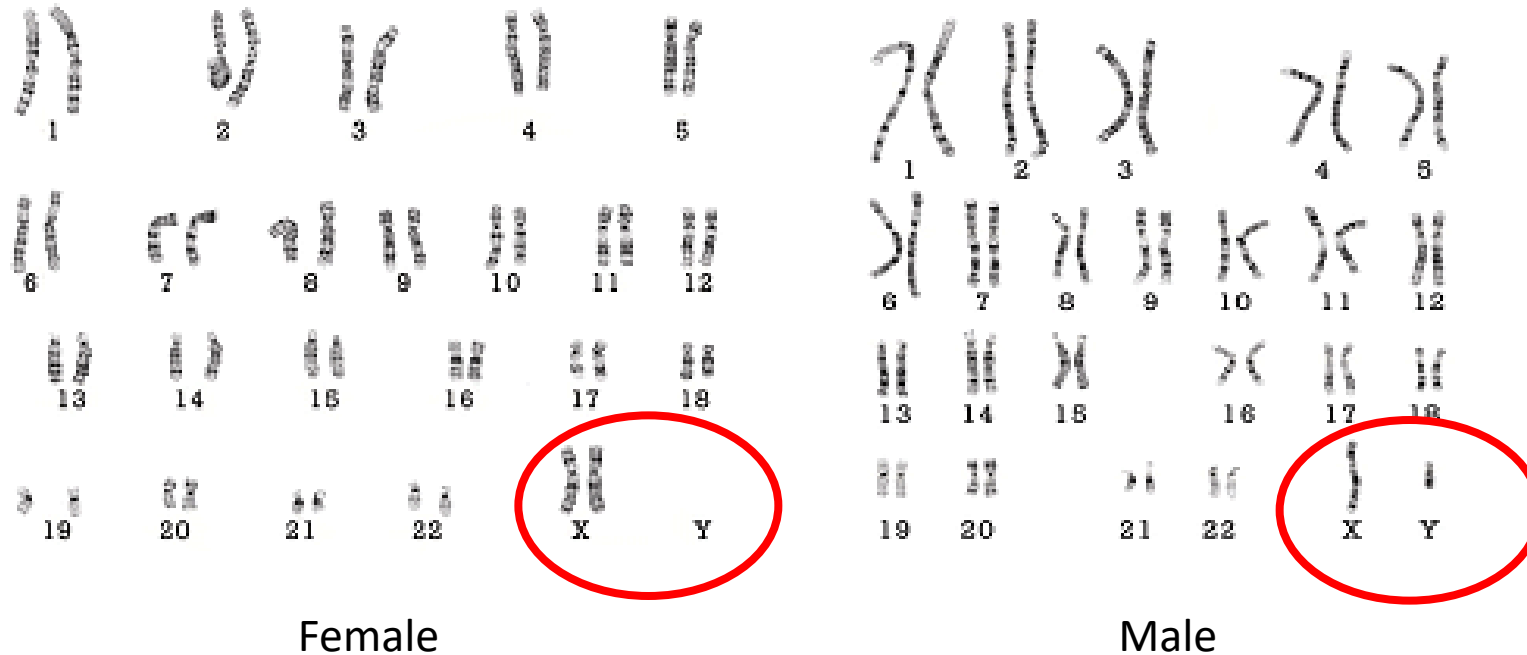
- Gene called Heterogeneous nuclear ribonucleotide binding protein H2 (*HNRNPH2*)
- Gene makes protein called HNRNPH2
- Gene on the X chromosome



Genetic mutations in HNRNPH2 are de novo. When do de novo mutations occur?

- In the egg
- In the sperm
- At or shortly after conception
- No way to know
- Recurrence risk of 1% in future pregnancies

Chromosomes in male and females



Simons VIP Individuals with HNRNPH2 Mutation

- Total number of registered, consented, participating families, $n = 10$
- Total number of participants with medical history data, $n = 9$
 - 9 female, 0 male
 - Ages 3 – 36 years

Variants in HNRNPH2 Mutations Observed (10 individuals)

Protein Change	
Arg206Trp	9
Arg206Gln	1

Common Developmental and Behavioral Diagnoses

Condition	Number of Children
Intellectual disability	5
Autism spectrum disorder	4
Developmental delay	4
Language or speech disorder or delay (without intellectual disability)	4
Anxiety	3

N = 9

Parent report of medical history

(9 individuals, ages 3 – 36 years)

Newborn Issues

Medical Condition	Number of Children
Lethargic	5
Poor suck	4
Feeding difficulties	4
Breathing difficulties	2
Resuscitation	1
Problems with tone	3

Hearing and Vision

Condition	Number of Children
Strabismus (cross eyed)	5
Vision correction	4
Nearsighted	4
Astigmatism (imperfect eye curvature)	1
Depth perception	1
Hearing aids	1

Neurological Issues

Medical Condition	Number of Children
Low muscle tone	9
Movement abnormalities	4
Microcephaly (head smaller than average)	3
Clumsy	2
High muscle tone	1

Neurological Issues

Medical Condition	Number of Children
Seizures	2
Grand mal	2
Petit mal	1

Gastrointestinal Issues

Medical Condition	Number of Children
Reflux (heartburn)	1

Endocrine Issues

Medical Condition	Number of Children
Difficulty gaining weight	4
Short stature	2

Bone Issues

Medical Condition	Number of Children
Scoliosis (curved spine)	2
Mild kyphosis (rounding of back)	1

Surgeries

Medical Condition	Number of Children
Surgery to correct foot positioning	1
Tendon release	1
Scoliosis repair	1
Ear tubes	1
Dental surgery	1
Hip dysplasia	1
Broken clavicle repair	1
Feeding tube	1

Current Medication Use

(SVIP Medications Interview, 9 individuals)

Conditions	Number of Children
Behavior (including anxiety, antidepressants, sedatives, antipsychotics)	4
Gastrointestinal	3
Seizures	1

Milestones

Milestone	
Average age for walking (4 individuals)	4.3 years
Age range for walking	2.75 – >7 years
Average age for first words (4 individuals)	19 months
Age range for first words	12 months – 25 months
Average age bladder & bowel trained (2 individuals)	>7 years
Age range for bladder or bowel training	>7 years

Summary-mostly neurological symptoms

- Developmental delay or intellectual impairment
- Language delays
- Motor delays
- Hypotonia
- Autism/autistic behaviors

- No regression