Genetics of Hearing Loss

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Why do we care?
Hearing Loss

% hearing loss

1:1000
17:1000
314:1000
500:1000

Newborn 18 yrs 65 yrs 75 yrs

60%
Members of the Rock and Roll Hall of Fame
Why do we care?

- National level
  - Cost in lost productivity
  - Special education
  - Medical treatment for hearing loss

- Personal level
  - Communication
  - 8 to 10% read >4th grade level

Deaf Culture

- Members of the Deaf community (the Deaf)
- Deafness not a disability or a disease
- NOT hearing "impaired"
- NOT affected by hearing "loss"

- Deaf culture
  - Unique history
  - Language, American Sign Language (ASL)
  - Cultural norms

- 95% of deaf children have hearing parents
How does hearing work?

- Tympanic Membrane
- Ossicular Chain
- Cochlea
Organ of Corti

Basilar Membrane
Basilar Membrane

Basilar Membrane
High Frequency

Basilar Membrane

Low Frequency

Basilar Membrane
High Frequency

Low Frequency

Tectorial Membrane

Hair Cells

Basilar Membrane
What could go wrong?

- Just about anything
- Useful to think about three types of hearing loss
Three Types of Hearing Loss

- Conductive
- Sensorineural
- Mixed

Other Descriptors?

- Unilateral/bilateral
- Profound/severe/moderate/mild
- High frequency/low frequency
- Prelingual/postlingual
- Static/progressive/fluctuating
How many genes?

• With so many different ways to mess things up, how many genes probably cause hearing loss?
  • Hundreds?

Limiting Our Discussion

• Congenital hearing loss
• Hearing loss present at birth
• 1:1000 children born deaf
Children Congenital Deafness

Congenital Hearing Loss

50%
Environment
Disease/Idiopathic
Infections
High fever
Trauma
Medicines
Prematurity

50%
Genetic

1/20/2015
Congenital Hearing Loss

Children Congenital Deafness

- 50% Genetic
- 30% Syndromic
- Nonsyndromic 70%

Hearing Loss Syndromes

- Hearing loss syndromes: >400
- Hearing loss syndromes you should look for: 5
Hearing Loss Syndromes

Branchio-Oto-Renal Syndrome

Hearing Loss Syndromes

Jervell and Lange-Nielsen Syndrome
Hearing Loss Syndromes

Pendred Syndrome

Hearing Loss Syndromes

Usher Syndrome
Hearing Loss Syndromes

Waardenburg Syndrome

Hearing Loss Syndromes

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• Hearing loss syndromes you should look for: 5
  – Branchio-oto-renal syndrome
  – Jervell and Lange-Nielsen syndrome
  – Pendred syndrome
  – Usher syndrome
  – Waardenburg syndrome
Congenital Hearing Loss

All Children With Hearing Loss

50% Genetic Hereditary

30% Syndromic

Nonsyndromic 70%

Non-Syndromic Hearing Loss

• Many different inheritance patterns
  – Autosomal Recessive
  – Autosomal Dominant
  – X-Linked
  – Y-Linked

• All of these types look the same
• Take a family history
Non-Syndromic Hearing Loss

• Many different genes cause this disease
• Prediction: Each gene will be responsible for only a fraction of hearing loss

Fishing
THE BIG ONE

- Tunisia: recessive hearing loss: 13q
THE BIG ONE

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- Bedouin: recessive hearing loss: 13q

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Luck!

- Dermatologist
- Palmoplantar keratoderma (PPK)
- Family with both PPK and hearing loss
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• Palmoplantar keratoderma (PPK)
• Family with both PPK and hearing loss
• *GJB2, Connexin 26*
Connexin 26: 35delG Mutation

- Bedouin Family: Mutation 35delG
- 1/100 controls had a 35delG allele
- Could this mutation be that common?
- Screen 560 blood cards for 35delG
- 14 samples were positive
- Carrier rate 35delG: 2.5%
- Carrier rate for all Connexin 26 mutations: 3%
- Class 500 students = 15 carriers

Do the Math

Approximately 20% of congenital hearing loss

About 50% of Autosomal Recessive Non-Syndromic Hearing Loss
Do the Math

All children with autosomal recessive non-syndromic hearing loss should be screened!

Does Knowing the Gene Help?

• Connexin 26
• Autosomal recessive – counseling
• No concerns about other problems
• Intellectually normal
• Cochlear implants
NOT THE BIG ONE

USE A NET
Next Generation Sequencing

• Obtain sequencing information on many genes at once
• Panels—screen many hearing loss genes
• Whole exome—sequence the exons of all genes

What Can I Do?
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• Help children get initial and yearly hearing screens

• Help children get yearly eye exams
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• Encourage hearing aid use
• Encourage families with hearing loss to see a geneticist
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QUESTIONS?