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Tori 17







Dad Clinical Geneticist Researcher



Why am I at a 1p36 conference?



Dad Clinical Geneticist Researcher



Why am I at a 1p36 conference? Answer your questions

# Question #1

Why does my son/daughter have medical problems?

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Why does my son/daughter have medical problems?

Children with 1p36 deletions have an <u>imbalance</u> in their genetic material.









Why does my son/daughter have medical problems? Children with 1p36 deletions have an <u>imbalance</u> in their genetic material.



# Question #1

Why does my son/daughter have medical problems?

Children with 1p36 deletions have an <u>imbalance</u> in their genetic material.



Ingredients Flour White sugar Brown sugar Eggs Butter Vanilla Baking soda Chocolate chips

Why does my son/daughter have medical problems?

Children with 1p36 deletions have an <u>imbalance</u> in their genetic material.



Ingredients Water Proteins Fats Minerals Carbohydrates DNA

# Question #1

Why does my son/daughter have medical problems?

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Ingredients Water Proteins Fats Minerals Carbohydrates DNA

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Ingredients Water Proteins Fats Minerals Carbohydrates DNA

#### Question #1

Why does my son/daughter have medical problems?

Children with 1p36 deletions have an <u>imbalance</u> in their genetic material.



Ingredients Water Proteins Fats Minerals Carbohydrates DNA 645 Genes

# Question #2

Why do some children with 1p36 deletions have more medical problems than others?

# Question #2

Why do some children with 1p36 deletions have more medical problems than others? 1p36 deletions can be of different sizes and affect different genes.

#### 1p36 Deletions



#### 1p36 Deletions



# 1p36 Deletions



# 1p36 Deletions

1p36 Deletions



#### 1p36 Deletions





Why do some children with 1p36 deletions have more medical problems than others? 1p36 deletions can be of different sizes and affect different genes.



Other genetic differences not associated with a 1p36 deletion

#### Question #2

Why do some children with 1p36 deletions have more medical problems than others? 1p36 deletions can be of different sizes and affect different genes.



Other genetic differences not associated with a 1p36 deletion (Genetic background)

# Question #2

Why do some children with 1p36 deletions have more medical problems than others? 1p36 deletions can be of different sizes and affect different genes.

Genetic background.

# Question #2

Why do some children with 1p36 deletions have more medical problems than others? 1p36 deletions can be of different sizes and affect different genes. Genetic background.

Every child with a 1p36 deletion is unique!

Why do some children with 1p36 deletions have more medical problems than others? 1p36 deletions can be of different sizes and affect different genes. Genetic background.

Every child with a 1p36 deletion is unique! They are genetically unique!

#### Question #3

How do doctors know which region of 1p36 is deleted?

Question #3

How do doctors know which region of 1p36 is deleted? Microarray analysis.



#### Microarray Analysis



Blood sample White blood cells

#### **Microarray Analysis**



Blood sample White blood cells Extract DNA





























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# Is each medical problem caused by deletion of a specific gene?

Is each medical problem caused by deletion of a specific gene? Good question!

#### 1p36 Deletions



#### 1p36 Deletions

**Terminal deletions** 



#### 1p36 Deletions

#### **Terminal deletions**

- Eye/vision problems
- Postnatal growth deficiency
- Cognitive impairment
- Brain anomalies
- Delayed motor development
- Facial Clefting
- Hearing loss
- Cardiovascular malformations
- Cardiomyopathy
- Renal anomalies







**Renal anomalies** 

# 1p36 Deletions

Interstitial deletions

- Eye/vision problem
- Postnatal growth deficier
- Cognitive impairment
- Brain anomalies
- Delayed motor development
- Facial Clefting
- Hearing loss

Cardiovascular malformationsCardiomyopathy

Renal anomalie



#### 1p36 Deletions

#### 1p36 Deletions

- Isolated
- Microarray data
- Cardiovascular malformations
- Cardiomyopathy



p36.33

p36.31

p36.22

p36.21



# 1p36 Deletions

1p36 Deletions

- Isolated
- Microarray data
- Cardiovascular malformations

Cardiomyopathy

Data Sources

- Patients recruited to 1p36 study
- Patients referred to Baylor for CMA
- DECIPHER database
- Literature search



p36.33

p36.31

p36.22

p36.21



#### 1p36 Deletions

#### 1p36 Deletions

- Isolated
- Microarray data
- Cardiovascular malformations

#### Cardiomyopathy

#### Data Sources

- Patients recruited to 1p36 study
- Patients referred to Baylor for CMA
- DECIPHER database
- Literature search
- Surprisingly few cases

#### **Cardiovascular Malformations**



#### **Cardiovascular Malformations**



Five non-overlapping critical regions

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#### **Cardiovascular Malformations**







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#### target genes







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"Cardiac" "Heart" "Cardio"



"Cardiac" "Heart" "Cardio"

# Cardiovascular Malformations



Five non-overlapping critical regions



Five non-overlapping critical regions = Candidate genes



# Cardiomyopathy



Two non-overlapping critical regions



#### Two non-overlapping critical regions

# Question #4

Is each medical problem caused by deletion of a specific gene? Good question!

Some medical problems may be caused by loss of a single gene.

Is each medical problem caused by deletion of a specific gene? Good question! Some medical problems may be caused by loss of a single gene. Other medical problems may be caused by loss of several genes.

#### Question #4

Is each medical problem caused by deletion of a specific gene?

Good question!

Some medical problems may be caused by loss of a single gene.

Other medical problems may be caused by loss of several genes.

The same medical problem can be caused by different genes in different people.

#### Question #5

How does knowing the genes involved help people?

#### Question #5

How does knowing the genes involved help people? Help doctors make good medical decisions.

#### Question #5

How does knowing the genes involved help people? Help doctors make good medical decisions.

Child with 1p36 deletion. Should we screen for cardiomyopathy?









# How does knowing the genes involved help people?

Help doctors make good medical decisions. Identifying the genes involved is the first step to developing new treatments.

# Question #5

# How does knowing the genes involved help people?

Help doctors make good medical decisions. Identifying the genes involved is the first step to developing new treatments.

The second step is learning what these genes do in the body and how they do it.

#### How do scientists learn what each gene does?

#### Question #6

How do scientists learn what each gene does? Sometimes we learn from individuals with mutations in a specific gene.



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How do scientists learn what each gene does? Sometimes we learn from individuals with mutations in a specific gene.

#### Question #6

How do scientists learn what each gene does? Sometimes we learn from individuals with mutations in a specific gene. Sometime we learn from animal models.



**Blind Mice** 



#### **Blind Mice**





#### **Blind Mice**



#### **Blind Mice**



# 1p36 Deletions

#### Interstitial deletions

- Eye/vision problems
- Postnatal growth deficiency
- Cognitive impairment
- Brain anomalies
- Delayed motor development
- Facial Clefting
- Hearing loss
- Cardiovascular malformations
- Cardiomyopathy
- Renal anomalies



#### **Cardiovascular Malformations**



#### **RERE-Deficient Mice**



#### **RERE-Deficient Mice**



 $\implies$  Descending aorta

#### **RERE-Deficient Mice**



➡ Descending aorta
➡ Ascending aorta

#### **RERE-Deficient Mice**





#### **RERE-Deficient Mice**



⇒ Descending aorta
 → Ascending aorta
 → Ventricular septum

#### **RERE-Deficient Mice**



⇒ Descending aorta
 → Ascending aorta
 → Ventricular septum

#### **RERE-Deficient Mice**



⇒ Descending aorta (right sided aorta)
 → Ascending aorta
 → Ventricular septum

#### **RERE-Deficient Mice**



⇒ Descending aorta (right sided aorta)
 → Ascending aorta
 → Ventricular septum

#### **RERE-Deficient Mice**



⇒ Descending aorta (right sided aorta)
 → Ascending aorta (double outlet right ventricle)
 → Ventricular septum

#### **RERE-Deficient Mice**





➡ Descending aorta (right sided aorta)
→ Ascending aorta (double outlet right ventricle)

➡ Ventricular septum

#### **RERE-Deficient Mice**



⇒ Descending aorta (right sided aorta)
 → Ascending aorta (double outlet right ventricle)
 → Ventricular septum

#### **RERE-Deficient Mice**



⇒ Descending aorta (right sided aorta) Ascending aorta (double outlet right ventricle) → Ventricular septum (ventricular septal defect)

#### 1p36 Deletions

#### Interstitial deletions

- . **Eye/vision problems**
- Postnatal growth deficiency
- Cognitive impairment
- Brain anomalies
- Facial Clefting
- Hearing loss
- **Cardiovascular malformations**
- Cardiomyopathy
- **Renal anomalies**





#### **RERE-Deficient Mice**



#### **RERE-Deficient Mice**



Cardiac fibrosis

# 1p36 Deletions

#### Interstitial deletions

- **Eye/vision problems**
- Postnatal growth deficiency
- Cognitive impairment •
- **Brain anomalies**
- Delayed motor development
- Facial Clefting
- **Hearing loss**
- **Cardiovascular malformations**
- Cardiomyopathy
- **Renal anomalies** •



**Postnatal Growth Deficiency?** 











**Cleft Palate?** 



#### **Cleft Palate?**



#### **Hearing Loss?**



#### **Renal Problems?**



#### **Renal Problems?**



#### **Renal Problems?**



# 1p36 Deletions

#### **RERE-deficiency**

- Eye/vision problems
- Postnatal growth deficiency
- Cognitive impairment
- Brain anomalies
- Delayed motor development
- Facial Clefting
- Hearing loss
- Cardiovascular malformations
- Cardiomyopathy
- Renal anomalies



Does RERE cause 1p36 deletion syndrome?

Question #7

Does *RERE* cause 1p36 deletion syndrome? No. Not all 1p36 deletions include *RERE*.

Question #7

**Does RERE cause 1p36 deletion syndrome?** No. Not all 1p36 deletions include *RERE*. Deletion of *RERE* may be <u>sufficient</u> to cause some problems and may <u>contribute</u> to others.

#### Question #8

Is there hope for a cure? Is there hope for new treatments?

#### Question #8

Is there hope for a cure? Is there hope for new treatments? A cure would be very difficult.

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Is there hope for a cure? Is there hope for new treatments? A cure would be very difficult. New treatments may be possible.

Is there hope for a cure? Is there hope for new treatments? A cure would be very difficult. New treatments may be possible. Identifying the genes involved is the first step to developing new treatments. The second step is learning what these genes do in the body and how they do it.

#### Question #8

Is there hope for a cure? Is there hope for new treatments? A cure would be very difficult. New treatments may be possible.

Identifying the genes involved is the first step to developing new treatments.

The second step is learning what these genes do in the body and <u>how they do it</u>.

#### **RERE-Deficient Mice**



Cardiac fibrosis

#### **RERE and Vitamin A**



#### Vitamin A as a Therapy?



Cardiac fibrosis

WARNING ! DO NOT TAKE VITAMINE A Unless directed to do so by your physician!

Vitamin A as a Therapy?



#### WARNING ! DO NOT TAKE VITAMINE A!

Vitamin A is a <u>TERATOGEN</u> meaning that if a pregnant mother takes to much it can cause birth defects! Vitamin A can also be <u>TOXIC</u>! If you take too much it can kill you! If Vitamin A <u>EVER</u> becomes a therapy, the dosage taken will need to be determined by a physician! <u>DO NOT TAKE VITAMIN A OR GIVE VITAMIN A TO</u> YOUR CHILD unless directed to do so by a

physician!

#### Question #8

Is there hope for a cure? Is there hope for new treatments? A cure would be very difficult. New treatments may be possible. New therapies will need to take into account the genes involved.

#### Question #8

#### Question #9

Is there hope for a cure?

Is there hope for new treatments? A cure would be very difficult. New treatments may be possible. New therapies will need to take into account the genes involved. New therapies will take time to develop.

#### What can we do to help?

#### Question #9

What can we do to help? Encourage financial support for 1p36 research.

#### Question #9

What can we do to help? Encourage financial support for 1p36 research. Become involved in research projects.

What can we do to help? Encourage financial support for 1p36 research. Become involved in research projects.

#### Mapping projects

- Microarray test results
- Clinical summary
- Learn more e-mail me! dscott@bcm.edu



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Oleg Shchelochkov Wayne State University David Stockton



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