



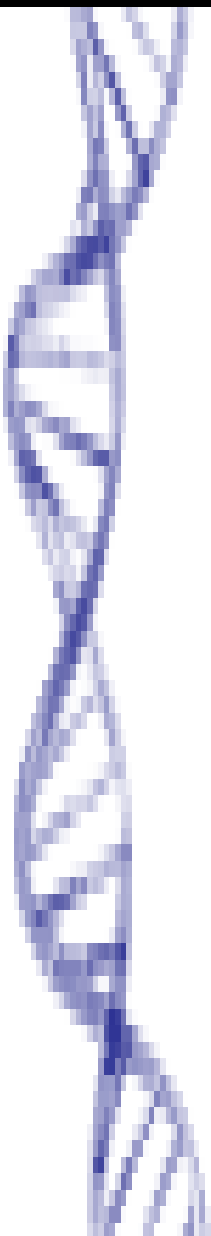
Approach to Understanding the Genetics of VACTERL Association

Ben Solomon, MD
June 27, 2009

Outline

- Our Research
- Genetics 301
- Progress Report





I. Our Research

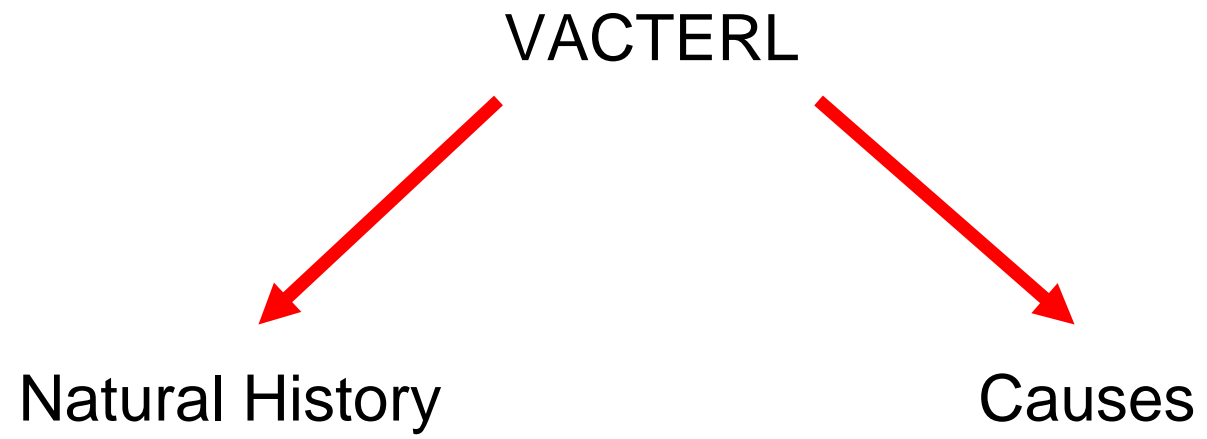
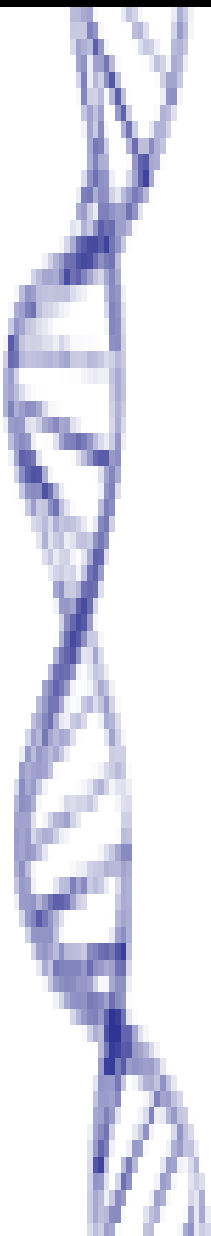


Our Research: Motivations

- Variable diagnostic criteria
- No uniform plan for work-up or treatment
- Little is known about causes and long-term outcomes
- More knowledge = Better health

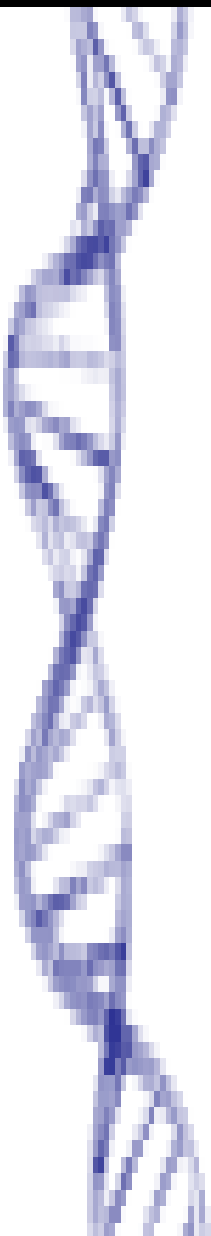


Our Research: Goals



Why do we want to know what causes VACTERL?

- More information for clinicians and patients
- Knowing what to look out for
- (Eventually) condition-specific treatments

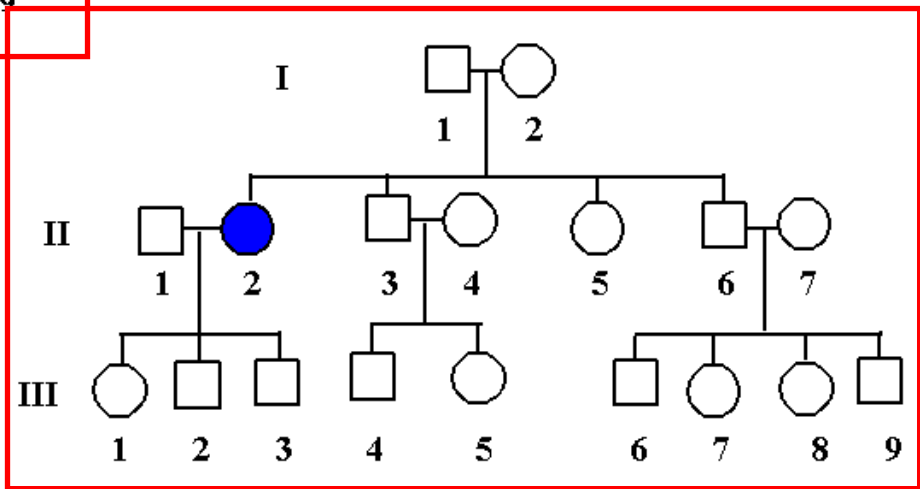
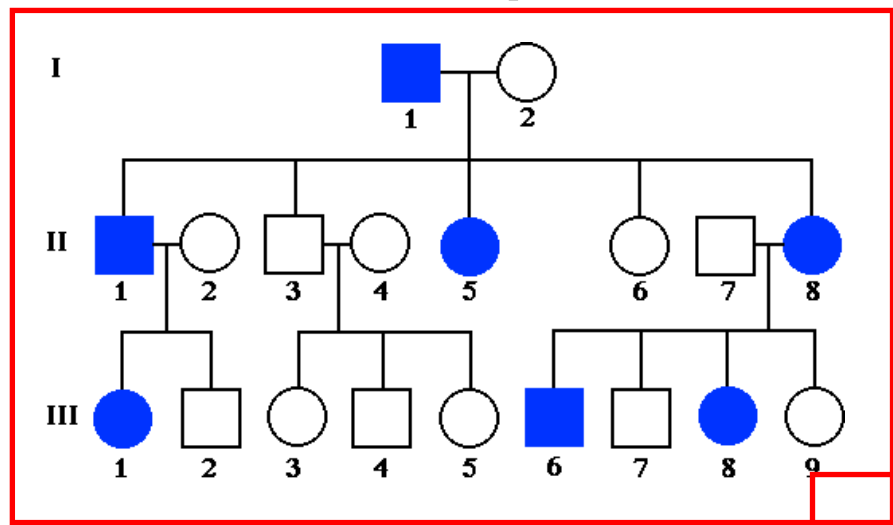


A vertical blue DNA double helix structure on the left side of the slide.

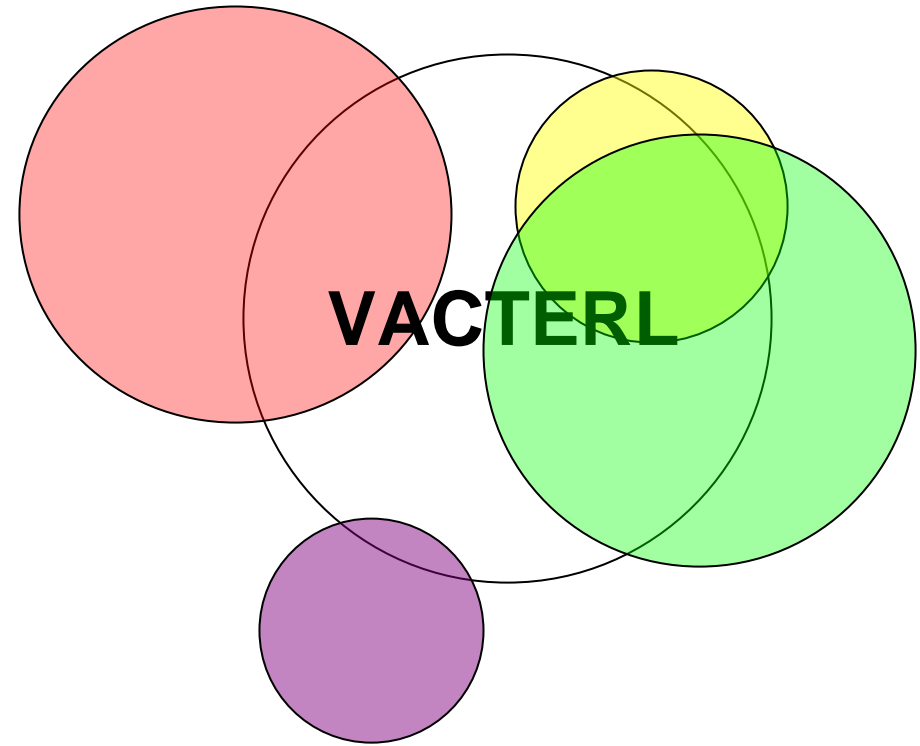
Why is VACTERL so challenging to understand?

Challenges:

? "Sporadic" Inheritance



Challenges: Many Overlapping Conditions



Challenges: Many Causes



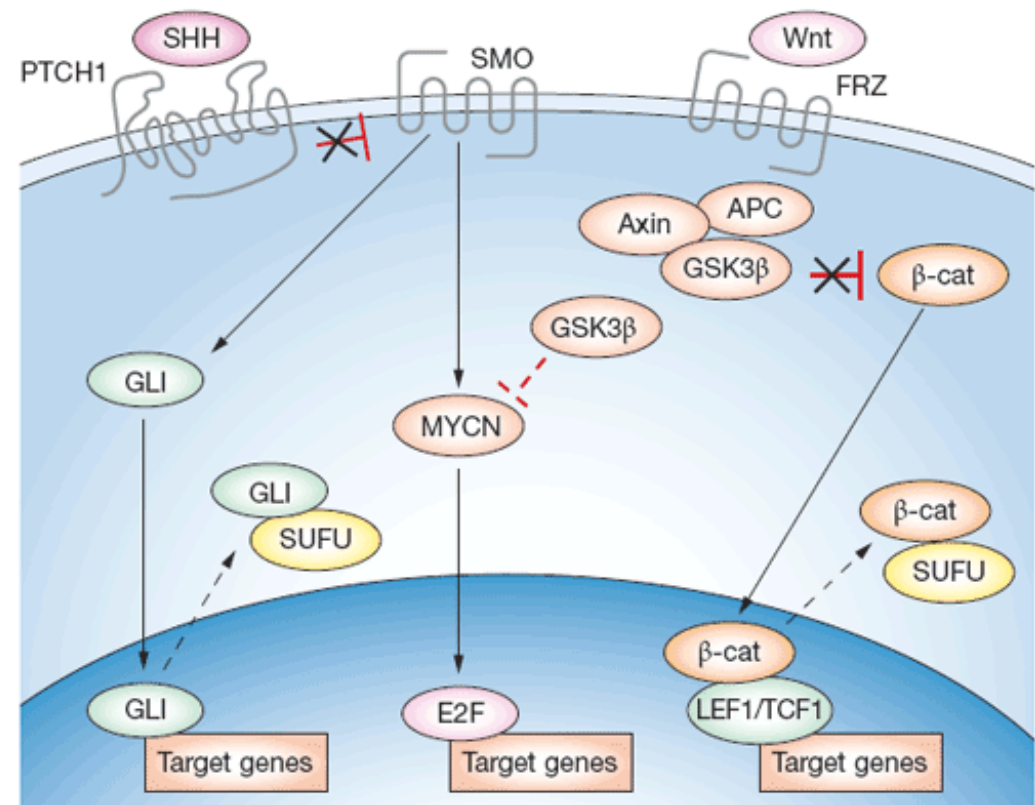
Challenges: Many Causes



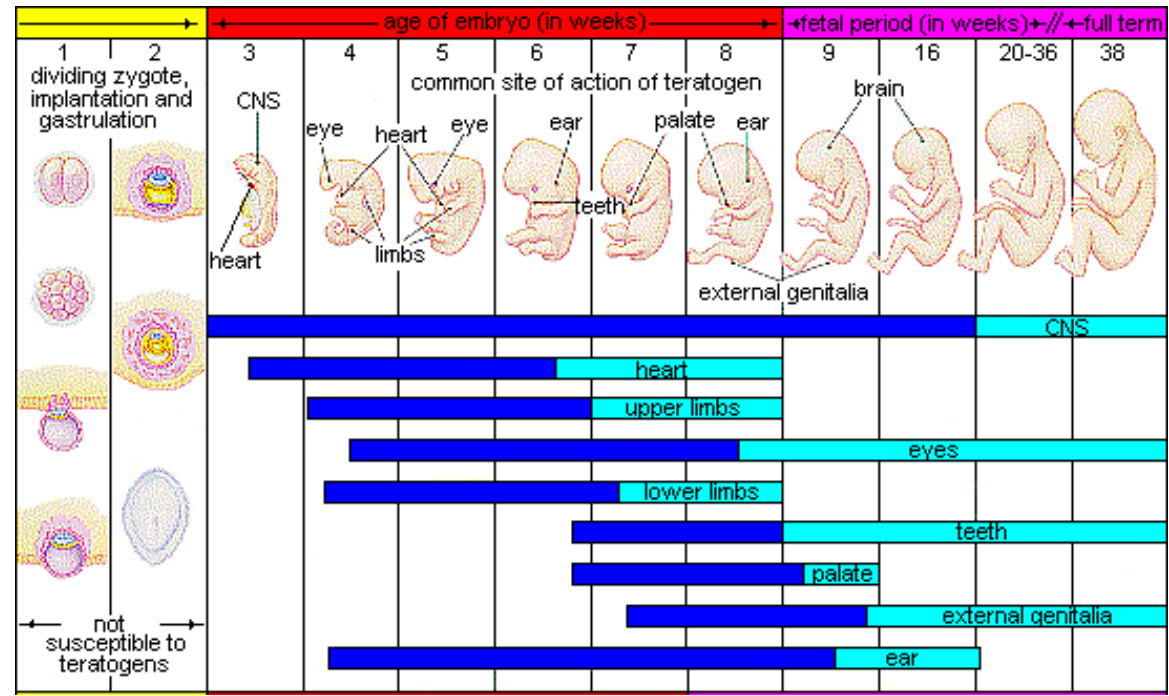
Pathways: The “Domino” Theory



Pathways: The “Domino” Theory



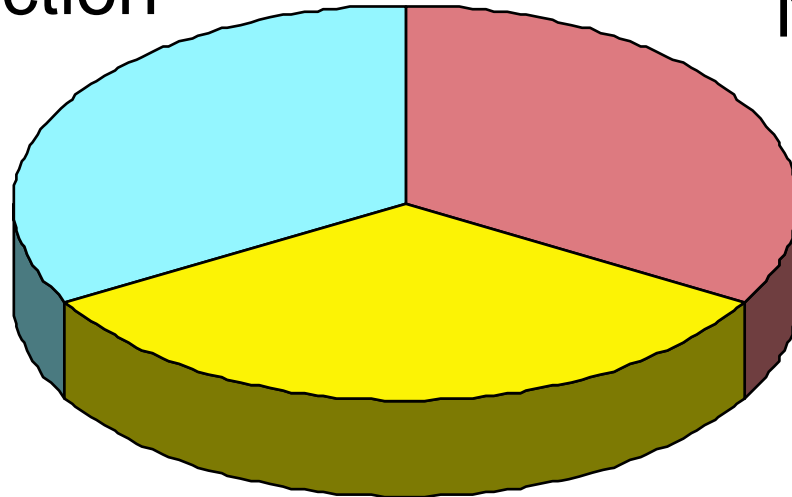
“Primary Polytopic Fields”



Our Research: What We Do

Data
Collection

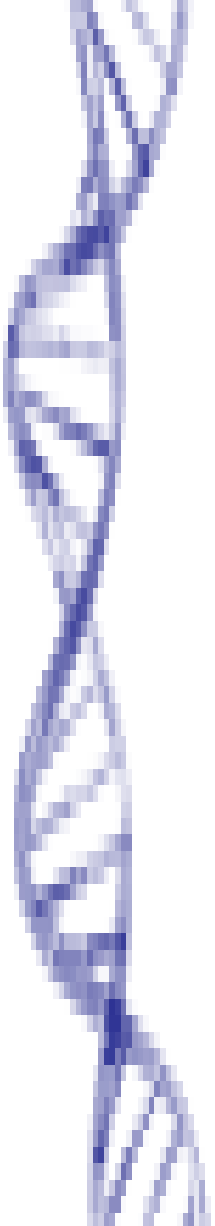
NIH Visit



DNA
Studies

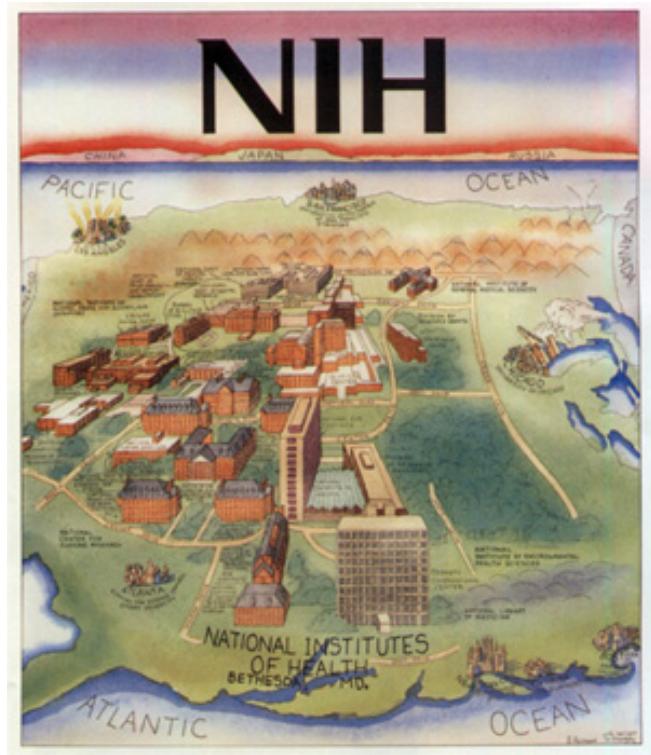
Data Collection

- Phone/e-mail/mail
- Standardized questionnaire
- Medical records, images, etc.
- Initial goal = 50-100 families



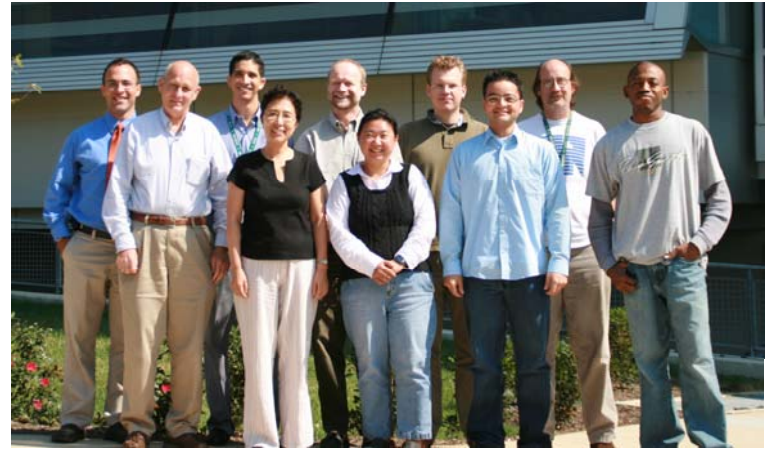
NIH Visit

- Bethesda, MD (near Washington, DC)
- 3-5 days
- We pay for flights, lodging, food, etc.
- No charge for any medical tests, consultations, etc.
- Confidential (including insurance!)



NIH Visit

- History & Physical
- Genetic Counseling
- Ophthalmology (eye doctor)
- X-rays, echocardiogram, ultrasound
- Blood draw/urine collection
- Other consultations as necessary



DNA Research

- Now: only samples from people who come to the NIH
- Within a few months: samples sent to our lab from clinicians or families
- Collaborations





II. Genetics 301

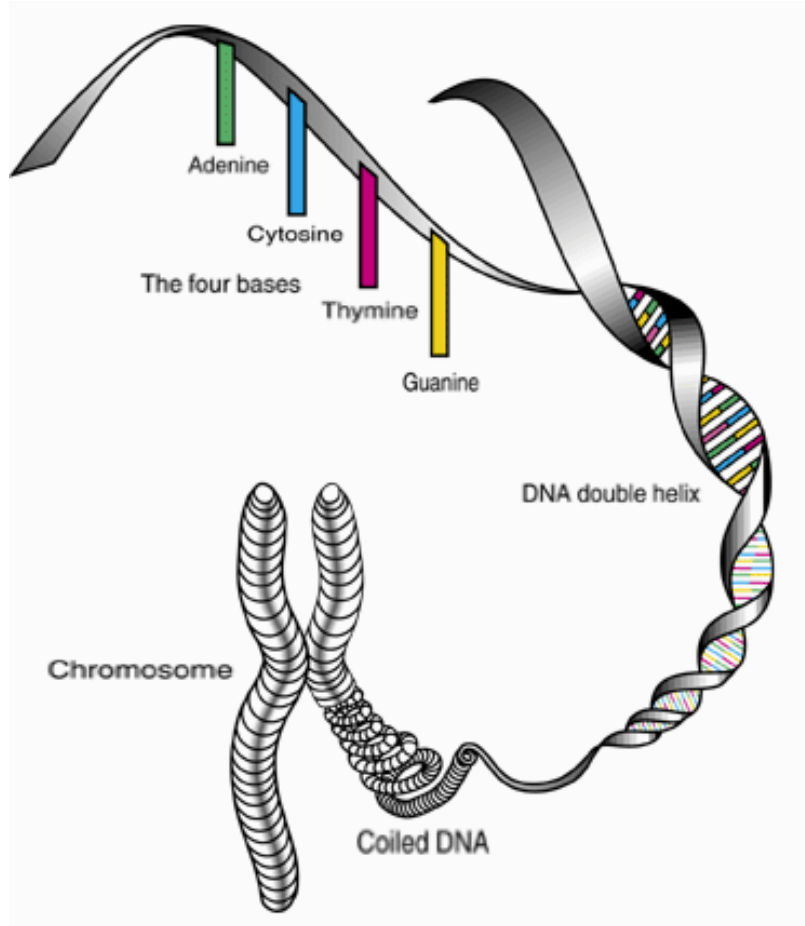


Genetics 301: Seeing a Geneticist

- History
- Physical Examination
- Testing
- Genetic Counseling



Genetics 301: Definitions



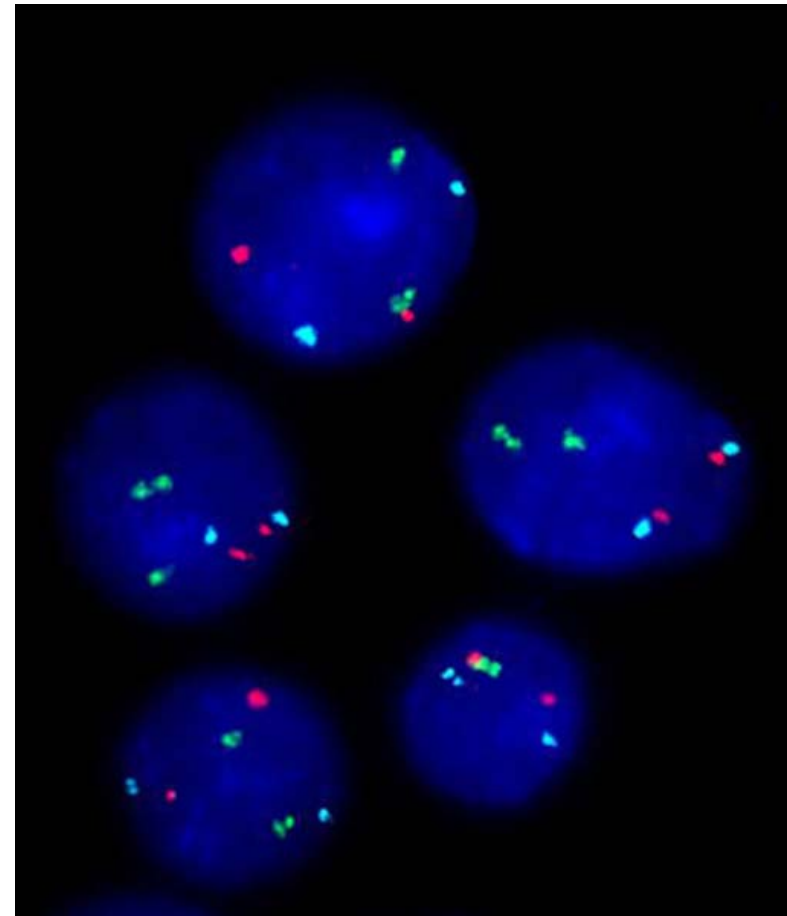
Genetics 301: Tests

- Karyotype/
Chromosome
Analysis
- Looks under
microscope at
all genetic
information



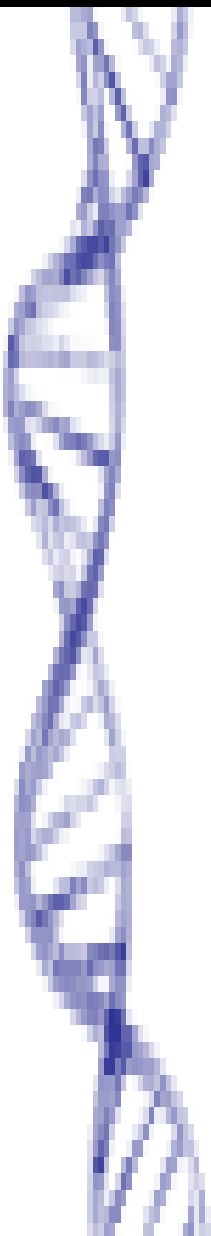
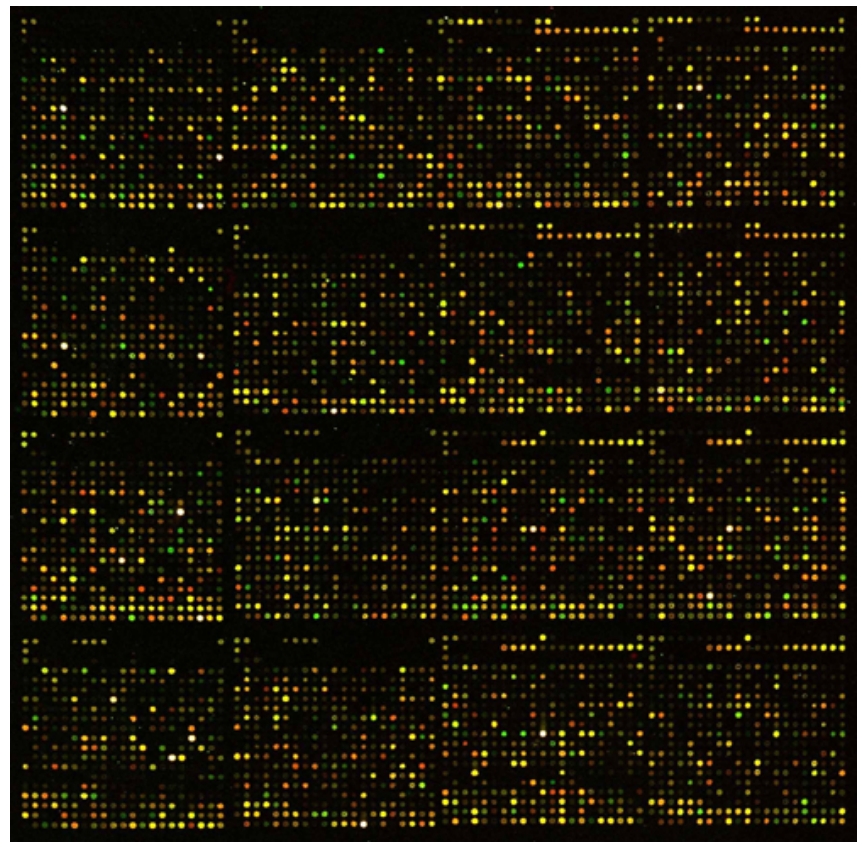
Genetics 301: Tests

- FISH Testing
- Looks for specific pieces of extra or missing genetic material



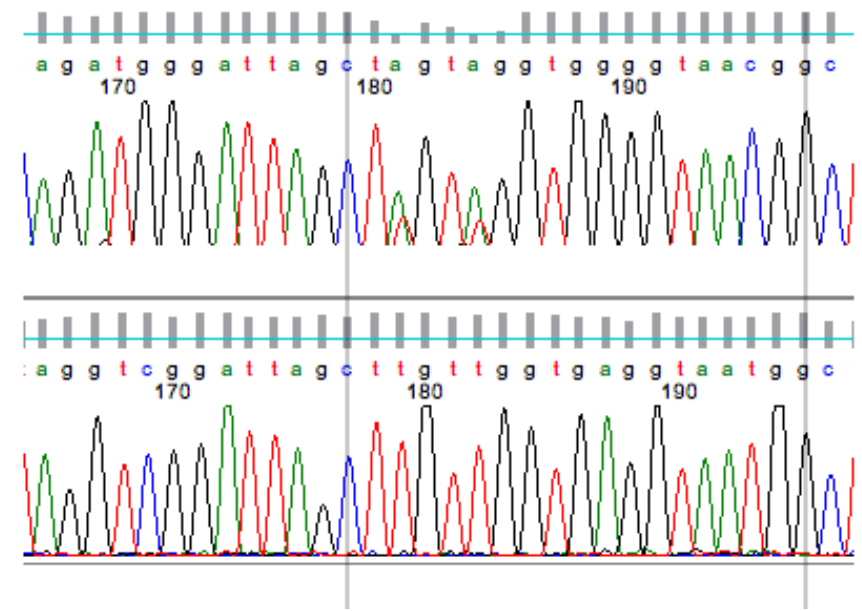
Genetics 301: Tests

- Microarray
- Looks for extra or missing genetic material



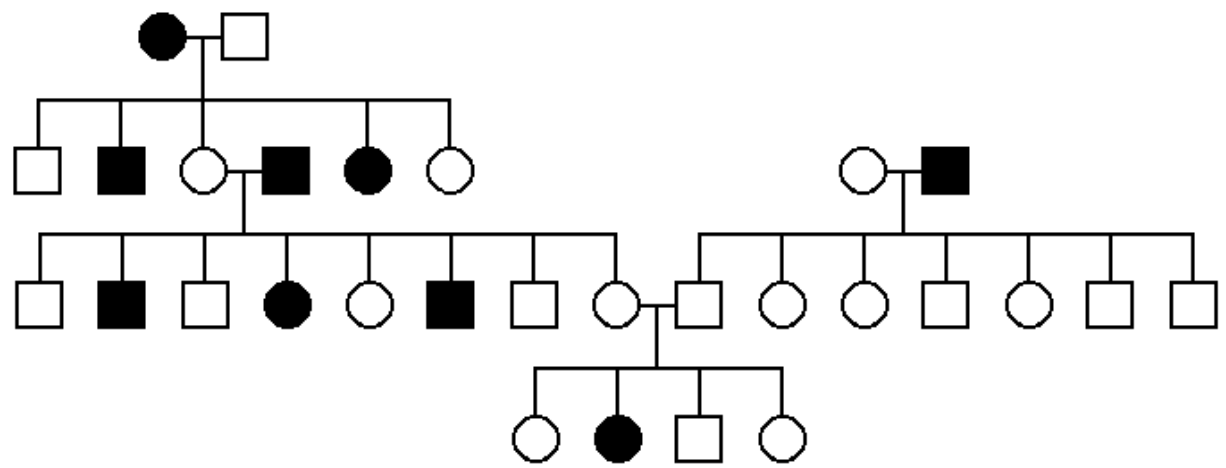
Genetics 301: Tests

- Specific gene testing
- Looks for tiny changes in one gene
- Labor-intensive



Genetics 301: Tests

- Research tests
- Example: Linkage analysis





III. Progress Report

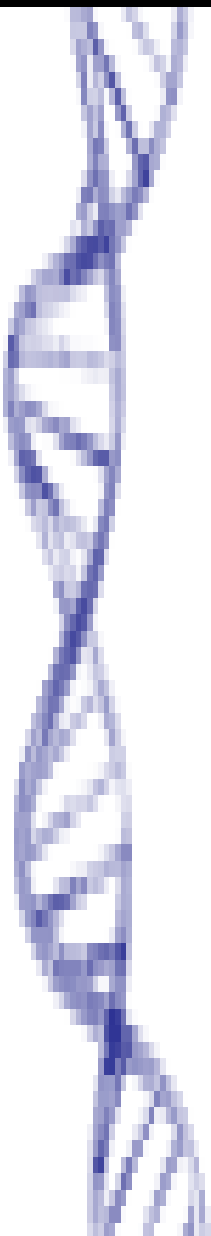


Progress Report

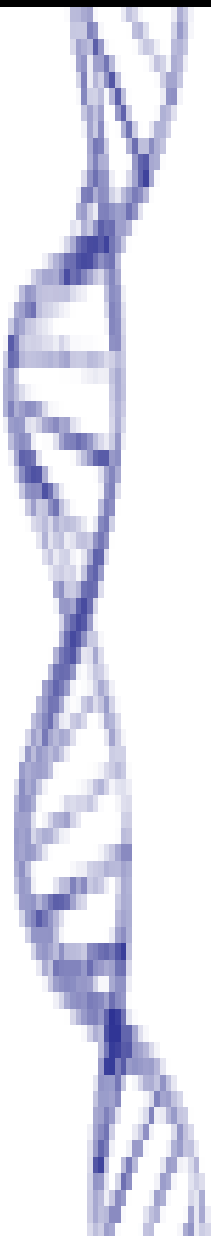
- Data Collection: ~40 families
- NIH Visits: 12
- DNA Research: Target gene sequencing started, microarrays about to start

Progress Report

- Participants range from newborns to over 60 years old
- Huge range of testing, treatment, etc.
- ~10% with multiple family members with features of VACTERL



NIH O8-HG-0224



	V	A	C	TE	R	L	Other
1*	+			+			
2*				+			
3	+		+				
4	+	+			+		
5	+	+	+		+		2-vessel cord
6	+	+	+		+	+	2-vessel cord, tracheal ring
7	+	+	+				Tracheal ring
8*				+			Hydrocephalus
9*						+	Genital abnl
10*			+				
11*	+		+	+	+		Absent R lung
12		+	+				
13		+	+	+	+		
14	+	+		+	+	+	Hydrocephalus, hypospadias
15	+	+	+				Single umbilical artery, hydrocephalus
16	+	+	+	+			Clinodactyly
17	+		+	+	+		Hypothyroidism
18	+	+	+		+		
19*	+		+		+		Tremor
20*			+	+			Tremor
21	+			+			Cystic hygroma, hypospadias
22	+		+	+	+	+	
23				+	+	+	Craniosynostosis
24	+	+	+	+	+	+	
25	+	+	+	+			Seizures (no DD)



Preliminary Data



	Quest	NIH	Literature
V	19	68	58
A	33	48	57
C	62	68	78
TE	38	56	67
R	24	48	63
L	39	24	15
Other	33	40	75

My 2 Cents...

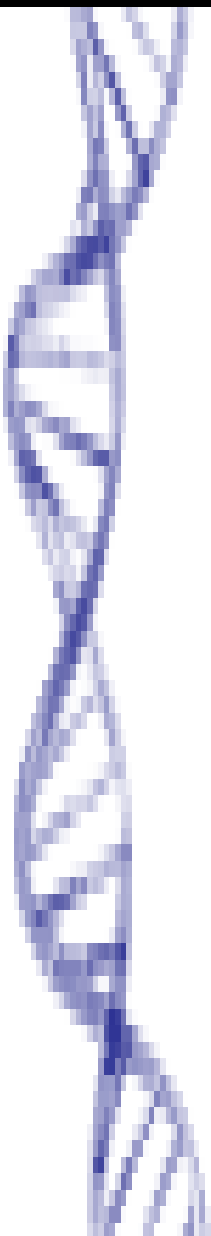
- Everyone should meet with a clinical geneticist
- For prenatal testing, a karyotype should be offered
- For postnatal testing, specific testing can be done to test for VACTERL-like conditions
- Karyotype can be offered in “VACTERL-plus” situations
- If your questions aren’t being addressed, **KEEP ASKING!!**



We Need Your Help!

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Thank You!

Questions?

