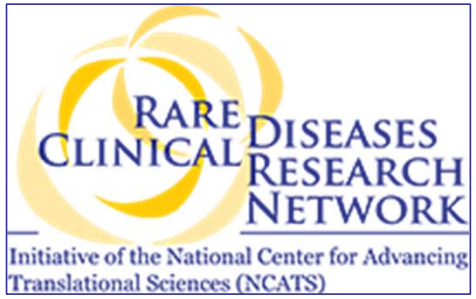
Primary Ciliary Dyskinesia: Overview and Update

Margaret W. Leigh, MD
Professor of Pediatrics
University of North Carolina at Chapel Hill

Genetic Diseases of Mucociliary Clearance Consortium

In



Funded by:

Financial Disclosures

- Vertex Pharmaceticals, INC
  - Research grant
- Parion Sciences, INC
  - Research grant
- Circassia Pharmaceuticals, INC
  - Research grant

Reference to unlabeled/unapproved use of drugs:

- None

Primary Ciliary Dyskinesia is a Rare Disease

NIH Office of Rare Diseases: affects <200,000 in US

~7,000 rare diseases affect 25-30 million in US

Primary Ciliary Dyskinesia is a Rare Disease

NIH Office of Rare Diseases: affects <200,000 in US

~7,000 rare diseases affect 25-30 million in US

Rare Lung Diseases	# in US
Cystic fibrosis (CF)	~35,000
Primary ciliary dyskinesia (PCD)	~17,000
Childhood interstitial lung diseases (chILD)	~10,000

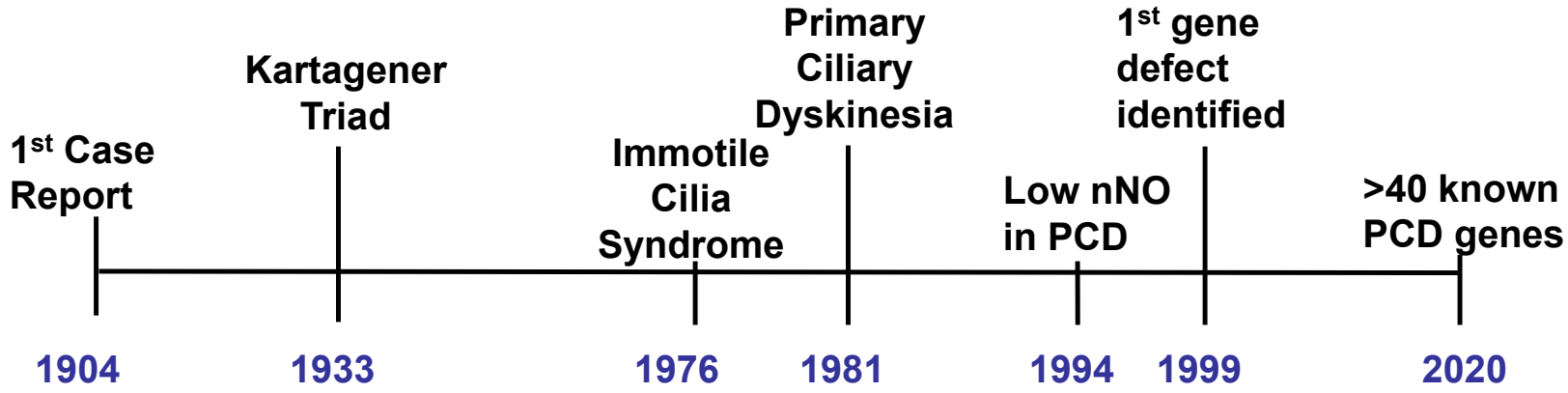
Primary Ciliary Dyskinesia is a Rare Disease

NIH Office of Rare Diseases: affects <200,000 in US

~7,000 rare diseases affect 25-30 million in US

Rare Lung Diseases	**# in US**
Cystic fibrosis (CF)	~35,000
Primary ciliary dyskinesia (PCD)	~17,000
Childhood interstitial lung diseases (chILD)	~10,000
Common Lung Disease	
Asthma	22,000,000

Primary Ciliary Dyskinesia Timeline: Advances with New Technology



Kartagener triad

- situs inversus
- chronic sinusitis
- bronchiectasis

Primary Ciliary Dyskinesia

- chronic oto-sino-pulmonary disease
- situs inversus totalis in ~ 50%
- male infertility (defective sperm motility)
- usually autosomal recessive

more recent observations:

-neonatal respiratory distress in ~85%

-heterotaxy (or situs ambiguus) in at least 10%

-congenital heart disease in at least 5%

Audience Response Question 1

You are counseling parents whose child has just been diagnosed with primary ciliary dyskinesia (PCD). What is the typical mode of inheritance for PCD?

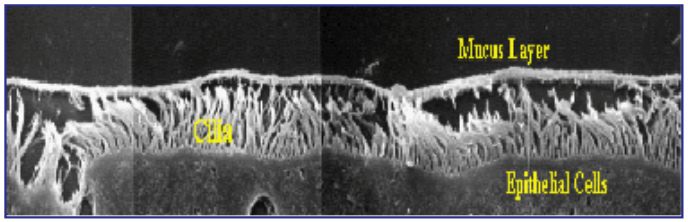
A. Autosomal dominant
B. X-linked
C. Autosomal recessive
D. Polygenic disorder (mutations in multiple different genes)
E. Chromosomal disorder

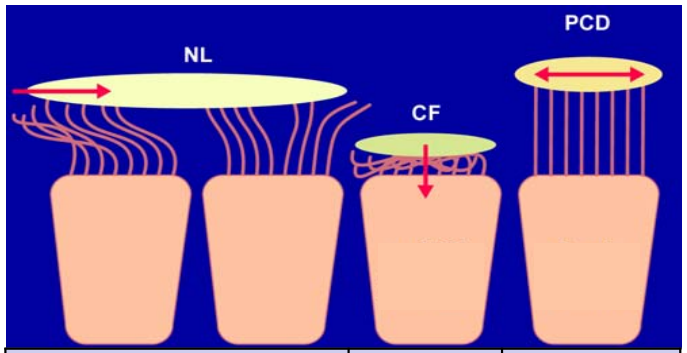
Audience Response Question 1

You are counseling parents whose child has just been diagnosed with primary ciliary dyskinesia (PCD). What is the typical mode of inheritance for PCD?

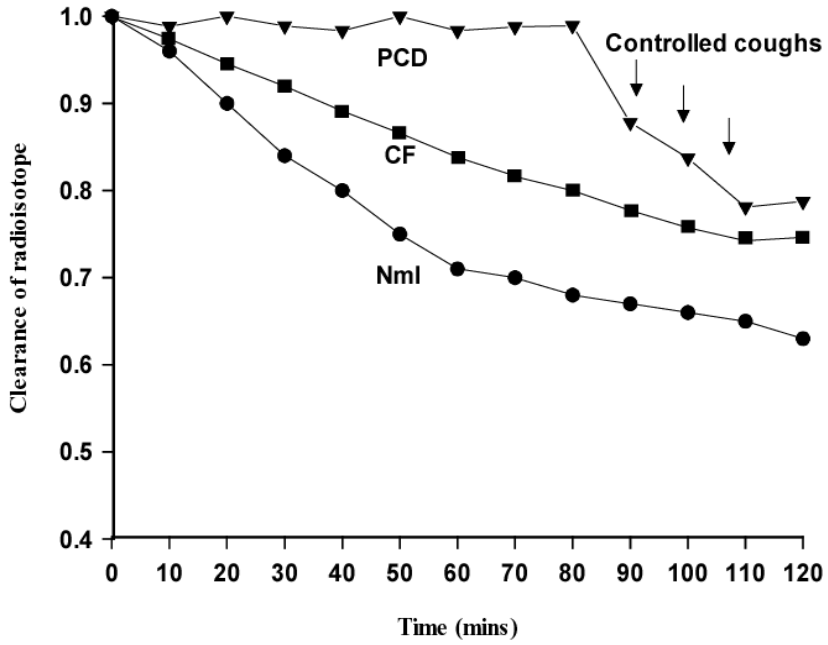
A. Autosomal dominant
B. X-linked
→ C. Autosomal recessive
D. Polygenic disorder (mutations in multiple different genes)
E. Chromosomal disorder

Airway Host Defense: Mucociliary and Cough Clearance





Normal	CF	PCD
MCC +	MCC -	MCC - -
CC +	CC -	CC ++



Phenotypic Clinical Features in PCD

Clinical feature	Pediatric (n=31, 8 mo-18 yr)	Adult (n=47, 19-73 yr)
Chronic cough	100%	100%
Chronic rhinitis/sinusitis	100%	100%
Chronic otitis media	100%	92%
Neonatal resp. distress	87%	65%
Bronchiectasis	61%	98%
Situs inversus	68%	46%

Noone PG et al: Am J Respir Crit Care Med 169:459–467, 2004

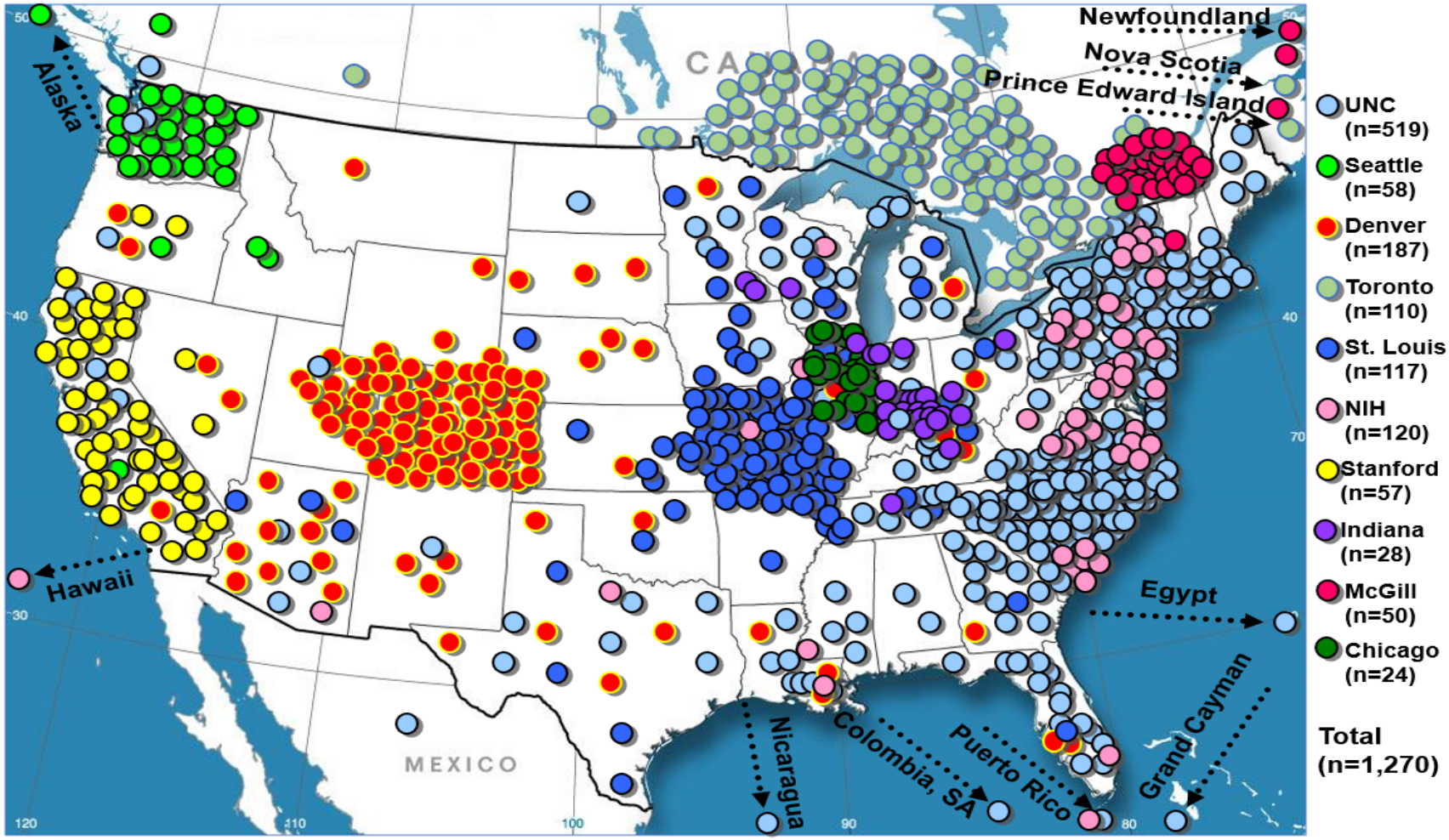
GDMCC:
Genetic Disorders of Mucociliary Clearance Consortium
PI: M Knowles (initiated 2004)

Specific Aims:

- Develop a clinical research network to study rare diseases of the airways, focusing on PCD
- Test for disease-causing mutations in PCD to develop genetic diagnostic approach
- Perform a longitudinal study in infants and children with PCD to define the clinical pathogenesis of airways disease by serial tracking of:
  - Standardized clinical history, respiratory cultures, pulmonary function tests and chest CT scans.

http://rarediseasesnetwork.epi.usf.edu/

Participants Evaluated by GDMCC (2004-2018)

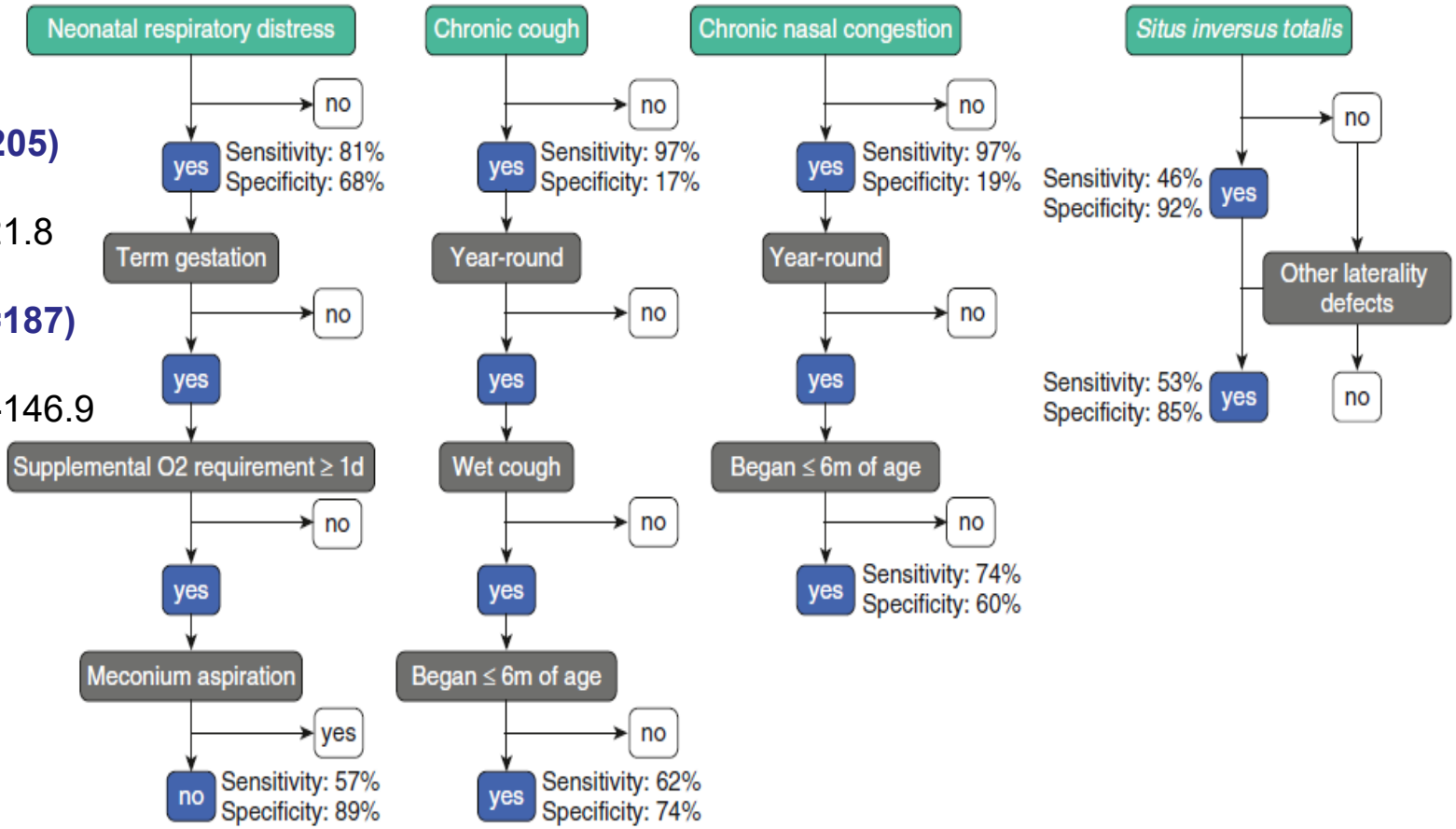


Criteria-defined clinical features in PCD

Participants <18 yo referred to GDMCC:

Confirmed PCD (n=205)
Age (yr) 7.8+/-5.4
nNO (nl/min) 20.9+/-21.8

Other/Undefined (n=187)
Age (yr) 7.0+/-4.5
nNO (nl/min) 258.3+/-146.9



1. Unexplained neonatal respiratory distress

2. Early onset, year-round wet cough

3. Early onset, year-round nasal congestion

4. Laterality defect

Leigh MW. Ann Am Thorac Soc 13:1305-13, 2016

Participants (<18 years of age) Fulfilling Criterion

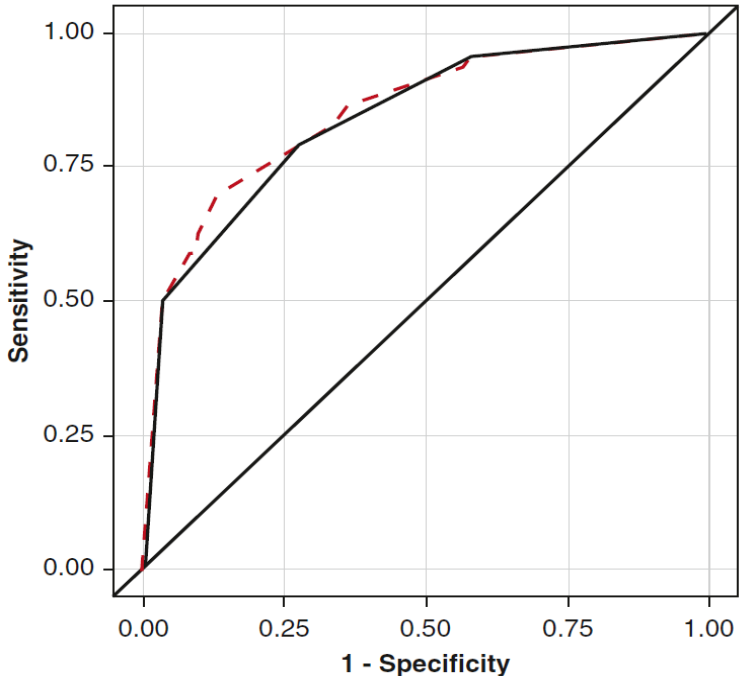
Criteria-defined clinical features	PCD (n=204)	Other disease or Undefined (n=185)	Adjusted Odds Ratio (95% Confidence intervals)*	P-value
Unexplained neonatal respiratory distress (#1)	116 (57%)	21 (11%)	6.6 (3.5,12.3	<0.0001
Early onset, year-round wet cough (#2)	128 (62%)	48 (26)	3.1 (1.7,5.5)	0.0001
Early onset nasal congestion (#3)	151 (74%)	74 (40%)	3.4 (1.9,6.3)	<0.0001
Laterality defect (#4)	109 (53%)	28 (15%)	7.7 (4.0,14.9)	<0.0001
Multiple ear infections in first 2 years of life (#5)	89 (43%)	66 (35%)	1.0 (0.6,1.8)	0.981

* after adjusting for age at enrollment

Leigh MW. Ann Am Thorac Soc 13:1305-13, 2016

Number of PCD clinical features: Sensitivity and specificity

Features	Sensitivity	Specificity
Number of general clinical features		
4	0.37	0.97
3	0.84	0.74
2	0.99	0.22
1	1.00	0.04
0	1.00	0.00
Number of criteria-defined clinical features		
4	0.21	0.99
3	0.50	0.96
2	0.80	0.72
1	0.96	0.41
0	1.00	0.00



Leigh MW. Ann Am Thorac Soc, 13:1305-13, 2016

Audience Response Question 2

Which of the following patients is MOST LIKELY to have primary ciliary dyskinesia?

A. 8 year old child with situs inversus totalis but no chronic respiratory symptoms.

B. 17 year old girl who developed chronic cough at 15 years of age and now has bronchiectasis on chest CT.

C. 3 year old child with year-round wet cough, year-round nasal congestion and history of neonatal respiratory distress despite term gestation.

D. 14 year old with history of chronic intermittent asthma and allergic rhinitis with recent sinus CT showing mucosal thickening of the right maxillary sinus.

Audience Response Question 2

Which of the following patients is MOST LIKELY to have primary ciliary dyskinesia?

A. 8 year old child with situs inversus totalis but no chronic respiratory symptoms.

B. 17 year old girl who developed chronic cough at 15 years of age and now has bronchiectasis on chest CT.

→ C. 3 year old child with year-round wet cough, year-round nasal congestion and history of neonatal respiratory distress despite term gestation.

D. 14 year old with history of chronic intermittent asthma and allergic rhinitis with recent sinus CT showing mucosal thickening of the right maxillary sinus.

What is the best way to diagnose PCD?

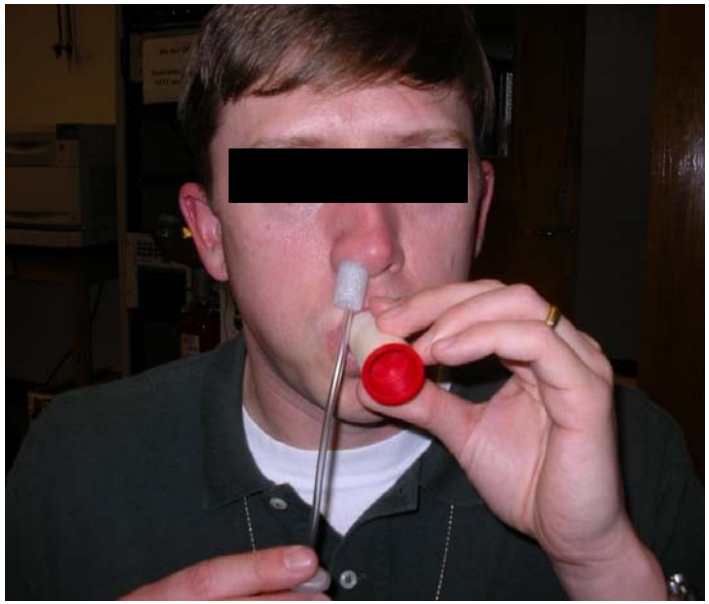
Panel of tests

- Clinical criteria
- Nasal nitric oxide measurement
- Ciliary biopsy for electron microscopy
- Genetic testing for mutations PCD genes
- Other testing
  - Ciliary biopsy w/ high speed videomicroscopy
  - Immunoflourescent analysis of ciliary biopsy
  - Mucociliary clearance studies

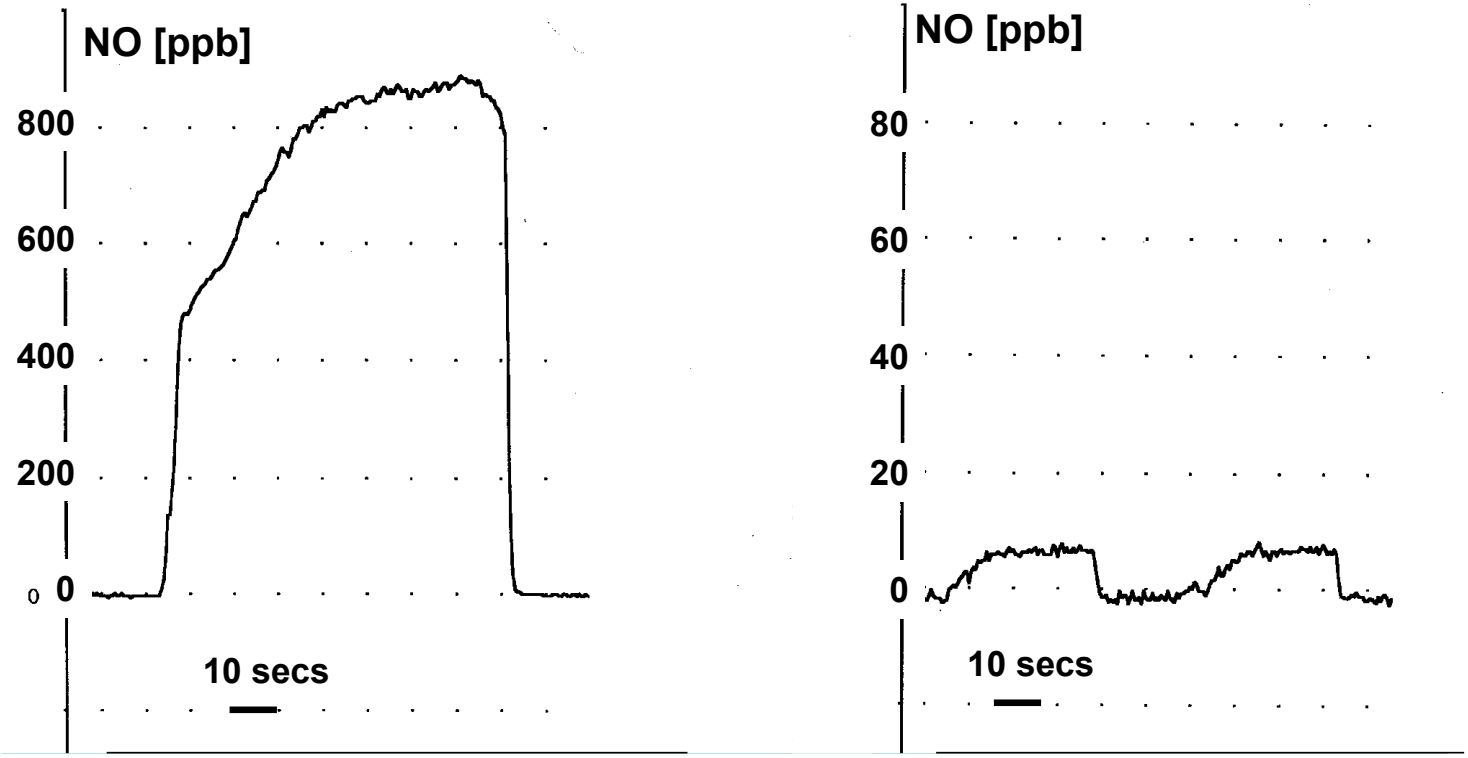
Shapiro AJ et al. : Diagnosis of Primary Ciliary Dyskinesia: An Official American Thoracic Society Clinical Practice Guideline. Am J Respir Crit Care Med. 187(12):e24-e39, 2018

Nasal Nitric Oxide Measurement

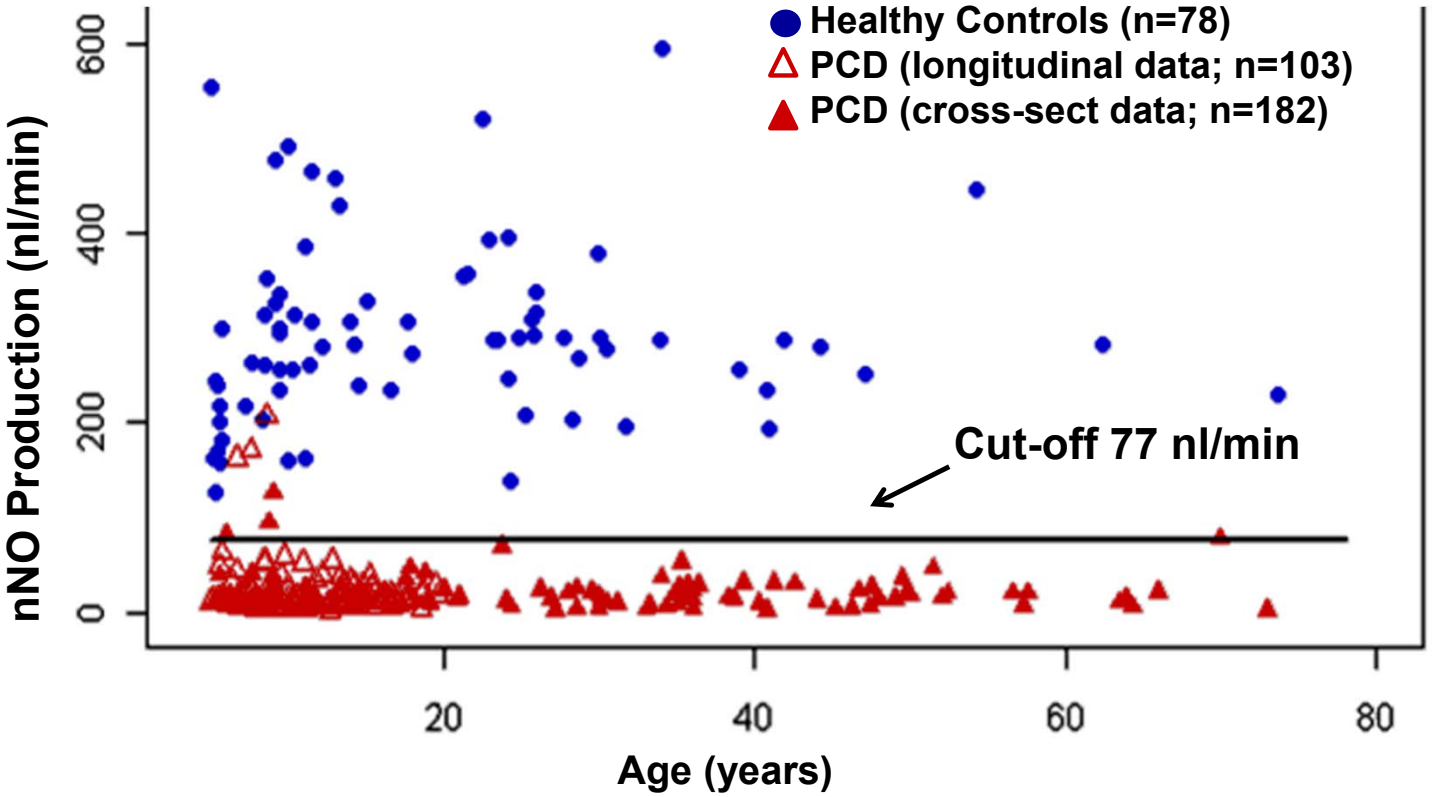
- Direct measurement of NO in gas phase
- On line detection of chemiluminescence by photomultiplier tube
- Sensitive (parts per trillion)
- Maneuvers to eliminate contamination with alveolar gases
  - Blowing against resistor



Nasal NO Plateau Tracings in Healthy Control and PCD

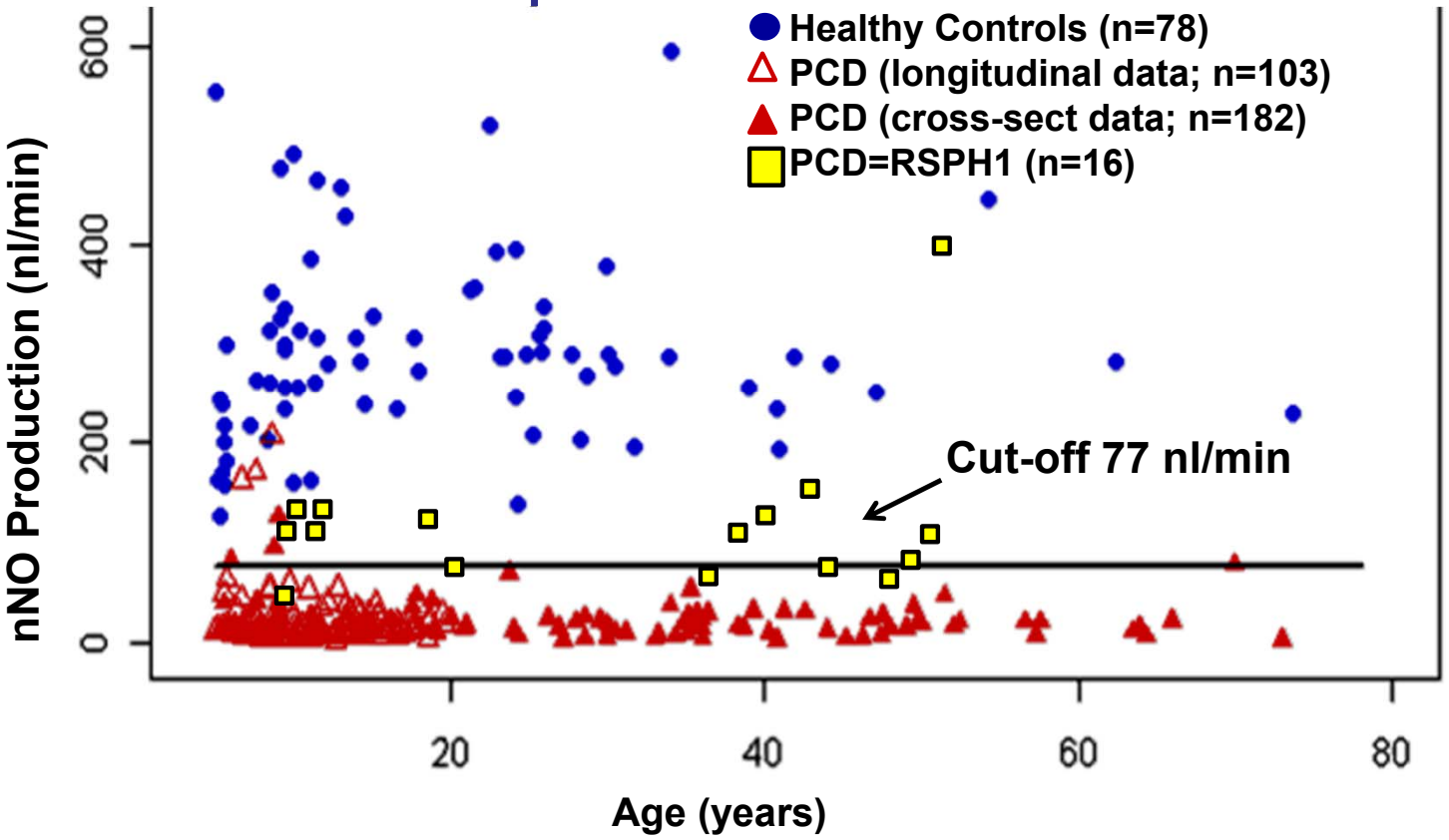


Nasal Nitric Oxide (nNO) is Low in PCD



Leigh MW et al, Ann ATS 2013:10:574-81

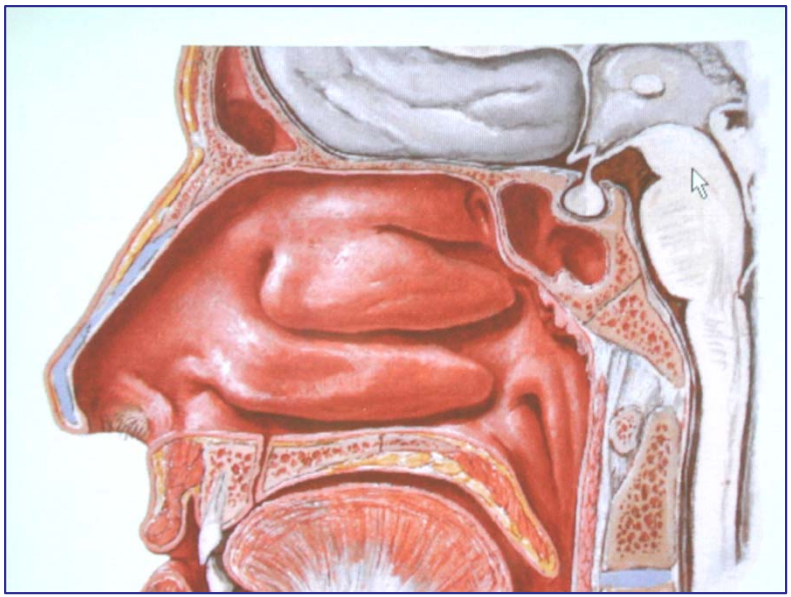
Nasal Nitric Oxide (nNO) is Low in PCD Exception: *RSPH1*



Knowles MR et al, AJRCCM 2014;189:707
Leigh MW et al, Ann ATS 2013:10:574-81

Examination of Ciliary Structure and Function

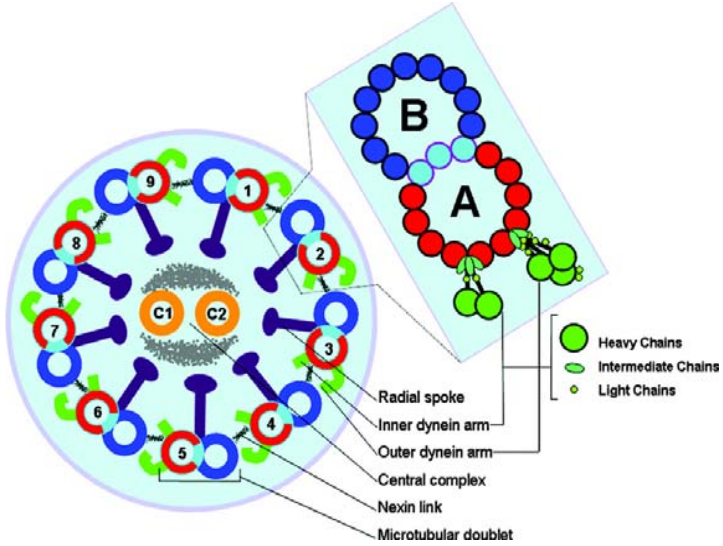
- Visualize turbinate with surgical otoscope
- Brush inferior surface of lower turbinate with biopsy brush or scrape with curette
- Immediately place sample in culture media to examine motility by high-speed videomicroscopy
- Process for electron microscopy to examine ciliary ultrastructure

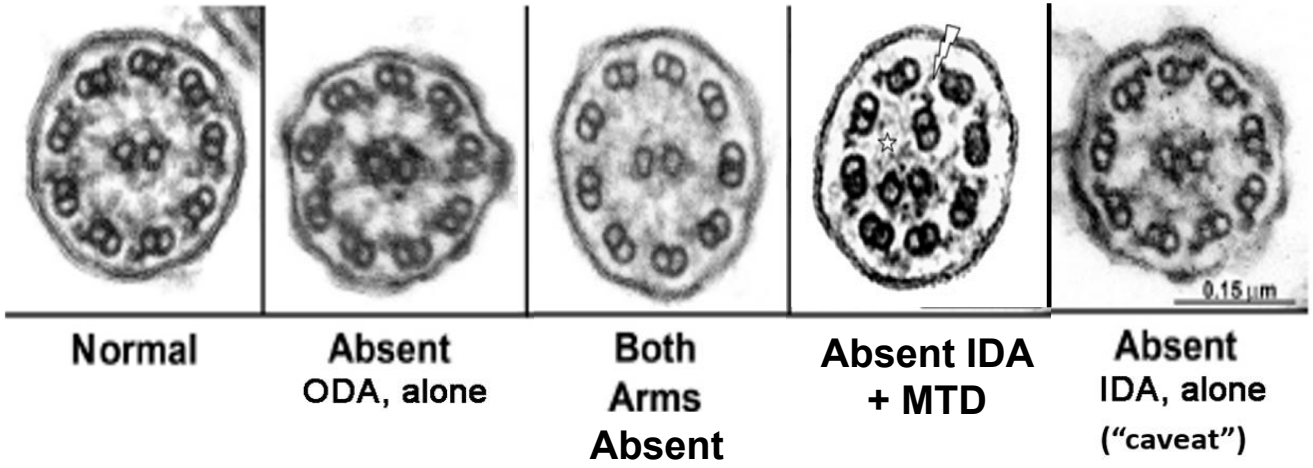


PCD: Ciliary Ultrastructural Defects

Dynein Arms Defects

- Absence/shortening ODA, alone
- Absence/shortening ODA+IDA
- Absent IDA+Microtubular Disorganization (MTD)
- Absence /shortening IDA, alone (?non-specific)



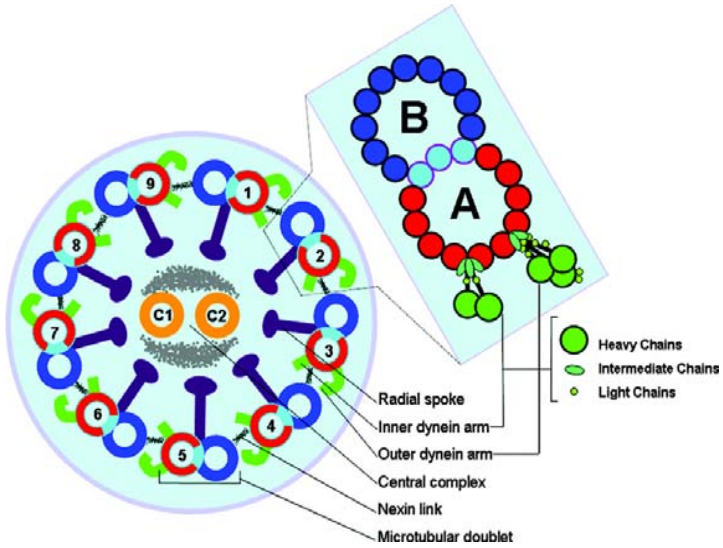


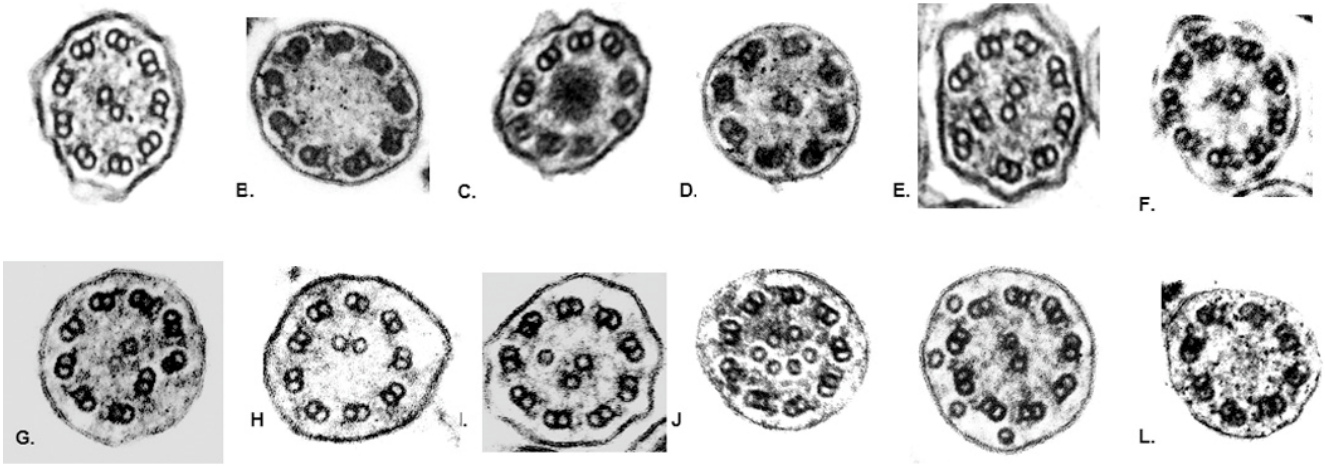
PCD: Ciliary Ultrastructural Defects

Central Complex Defects

(up to 90% appear normal)

- Absence of radial spoke (RS) or spoke head
- Absence of central pair with transposition of outer doublet to the center
- Associated genes:
  RSPH9, RSPH4A, RSPH1

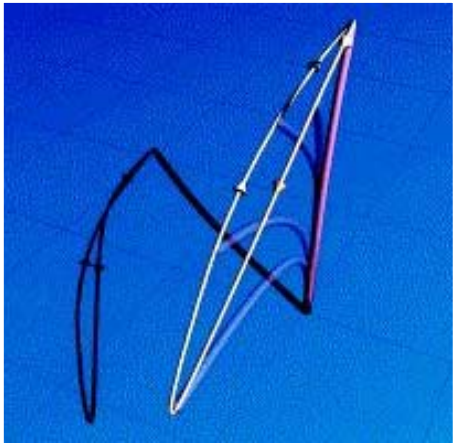


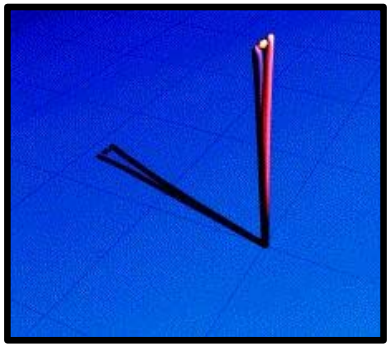


Daniels, ML, Human Mutat 2013

High-speed videomicroscopy: Ciliary beat patterns

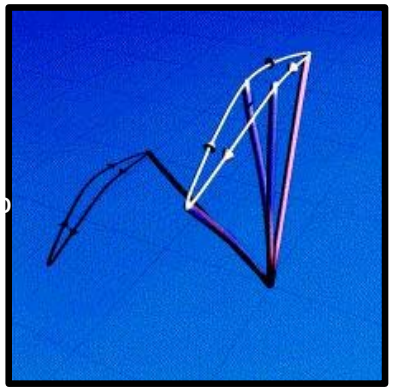
Normal
Planar motion w/ forward power stroke and backward recovery stroke
CBF 12.8 Hz
Immotility 0%

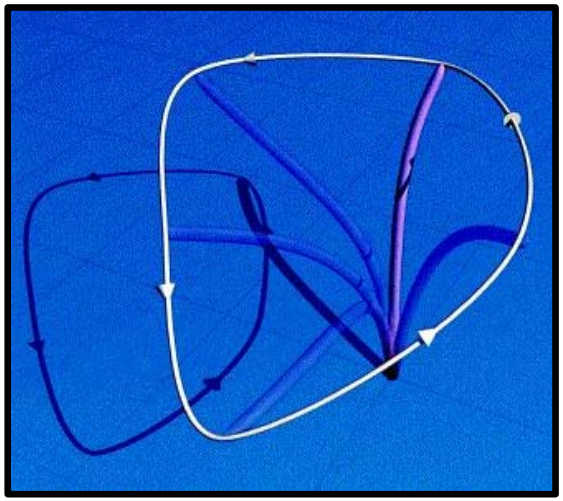




Virtually immotile
ODA+IDA defect
CBF 0.8 Hz
Immotility 79.8%

Stiff/dyskinetic
ODA defect
CBF 2.3 Hz
Immotility 55.0



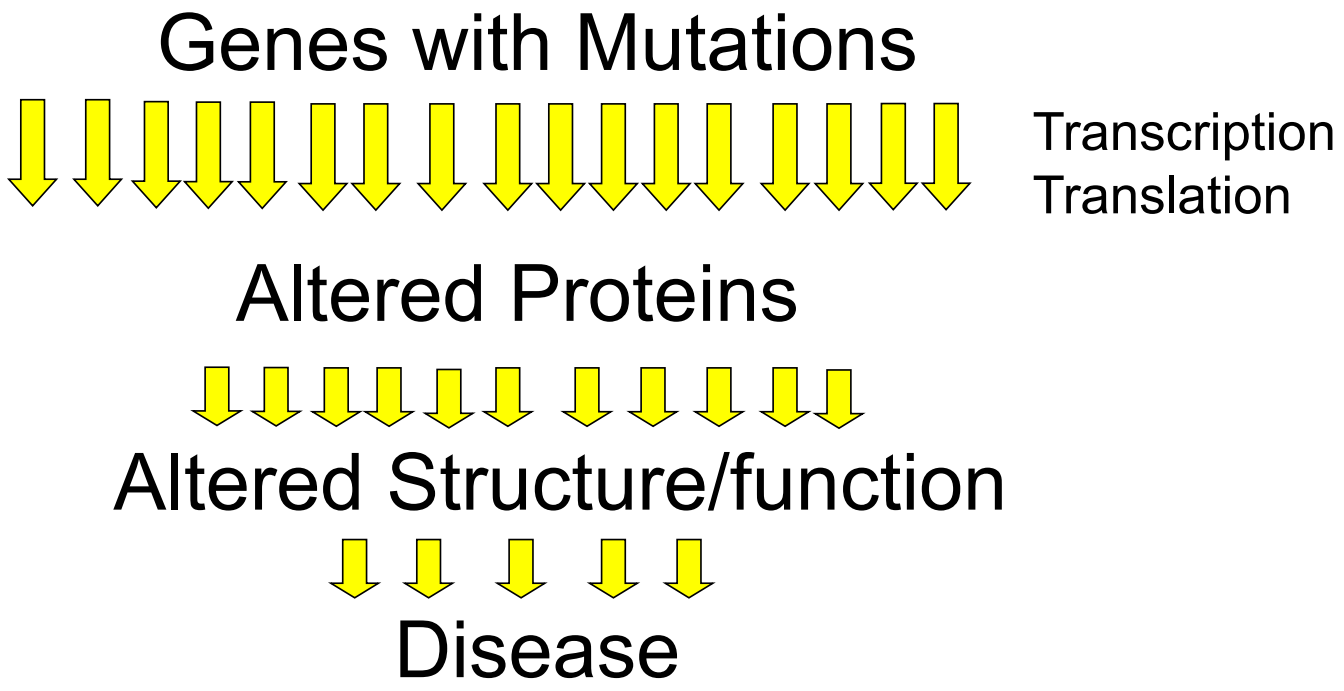


Circular
Absence of central pair
CBF 10.7 Hz
Immotility 0%

Chilvers, Am J Respir Crit Care Med. 2004;169:634-7

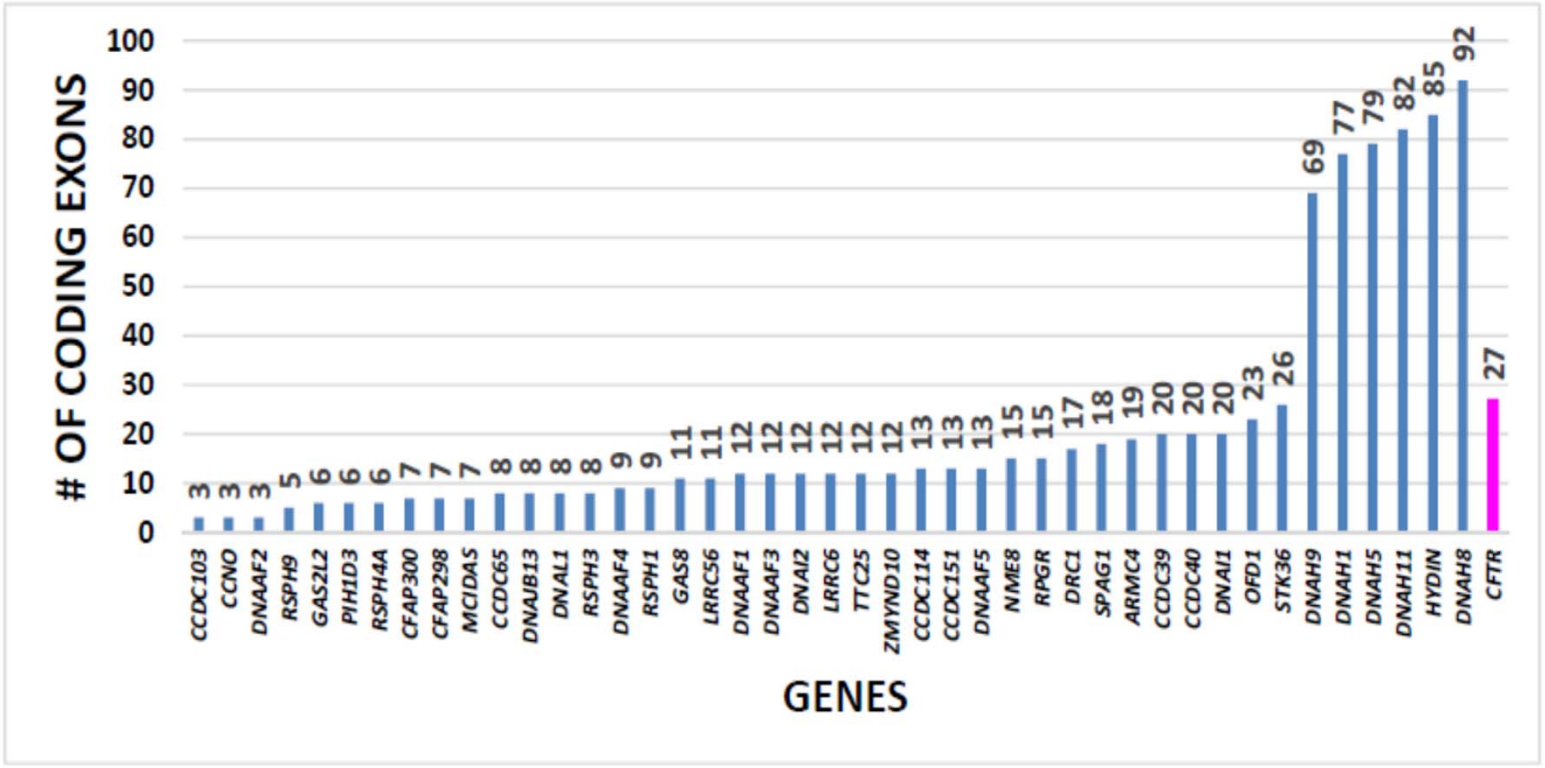
Genetic Testing for PCD is Complex

Multiple PCD genes; multiple pathogenic mutations for each PCD gene



PCD Molecular Genetic Testing

Challenging: Extensive genetic heterogeneity; 43 genes (911 coding exons); account for ~70% of PCD patients.

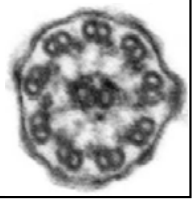


PCD Genotype - EM Phenotype

"Hallmark" EM Defects

ODA alone defects

*-DNAH5*** *-DNAI1**
-DNAI2 *-DNAL1*
-NME8 (TXNDC3)
-ARMC4 *-CCDC103*
-CCDC114 *-CCDC151*
-TTC25



ODA+IDA defects

-CCDC103 *-CFAP298 (C21orf59)*
-CFAP300 (C11orf70) *-DNAAF1 (LRRC50)*
-DNAAF2 (KTU) *-DNAAF3*
-DNAAF4 (DYX1C1) *-DNAAF5 (HEATR2*
-LRRC6
-PIH1D3 [x-linked]
-SPAG1
-ZMYND10

IDA defect + MTD

*-CCDC39**
*-CCDC40**

Other Defects

IDA alone defect

-TTC12

Oligocilia

-CCNO
-MCIDAS
-FOXJ1 [aut dominant]

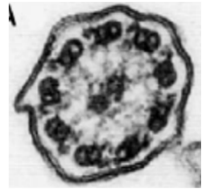
EM defect not defined

-DNAH1
-DNAH8

Most prevalent genes
* in 4-10% of PCD patients
** in >15% of PCD patients

Normal/Near Normal EM

ODA structural protein
*-DNAH11** *-DNAH9*
Central pair protein
-HYDIN *-CFAP221*
-STK36 *-SPEF2*
Nexin-link proteins
-CCDC164 (DRC1) *-GAS8 (DRC4)*
-CCDC65 (DRC2)
Radial spoke proteins
-RSPH1 *-RSPH3* *-RSPH4A*
-RSPH9 *-DNAJB13*
Basal body
-GAS2L2
IFT protein
-LRRC56
Protein kinase
-NEK10



PCD + other syndrome
Retinitis pigmentosa
RPGR [x-linked]
Oro-facial-digital Syndrome
OFD1 [x-linked]

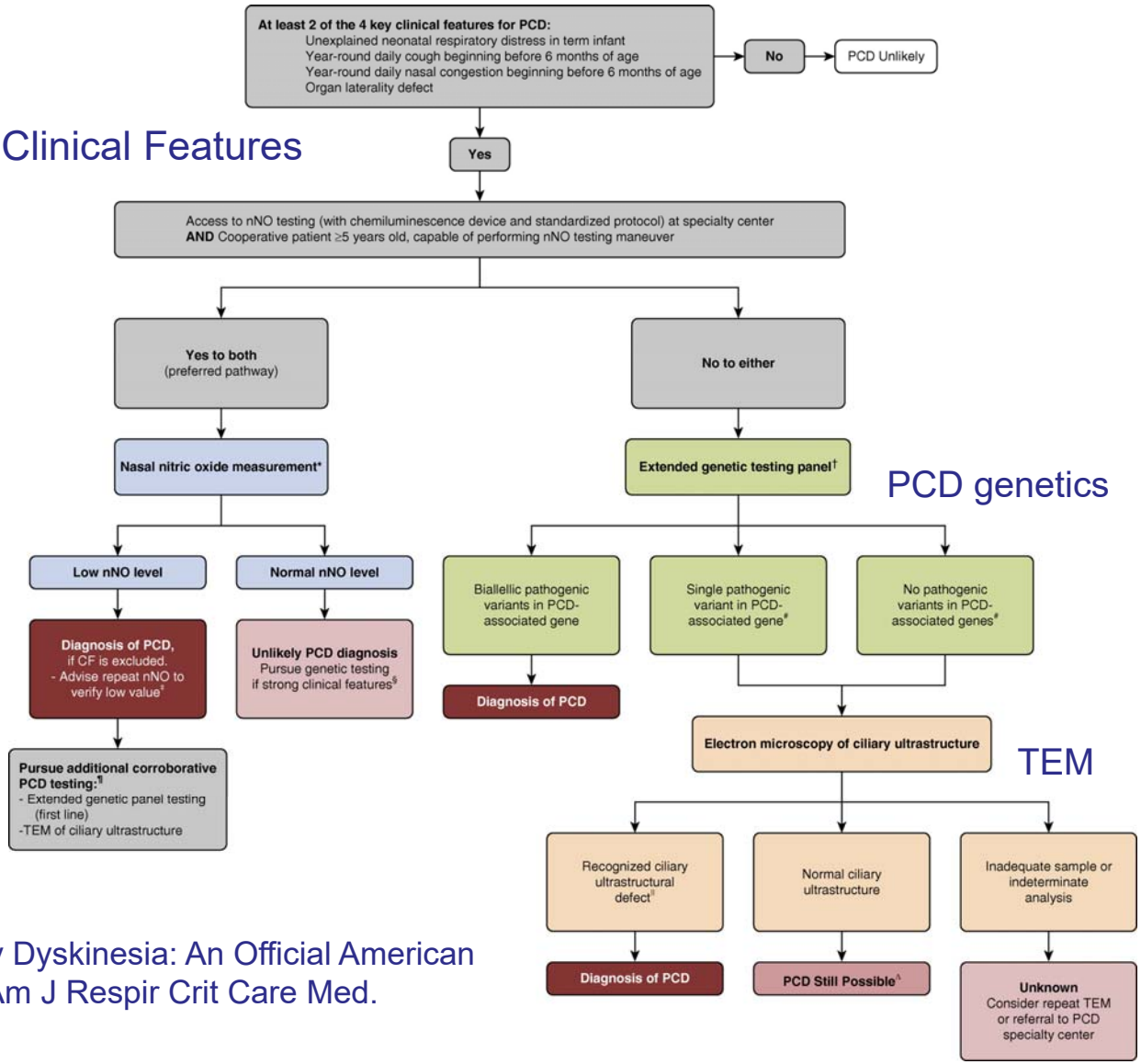
49 genes
2/6/2020

PCD Diagnostic Approach

Clinical Features

Nasal NO:
low in 97% PCD
r/o CF

PCD genetics
+ in 70% PCD
TEM
+ in 70% PCD

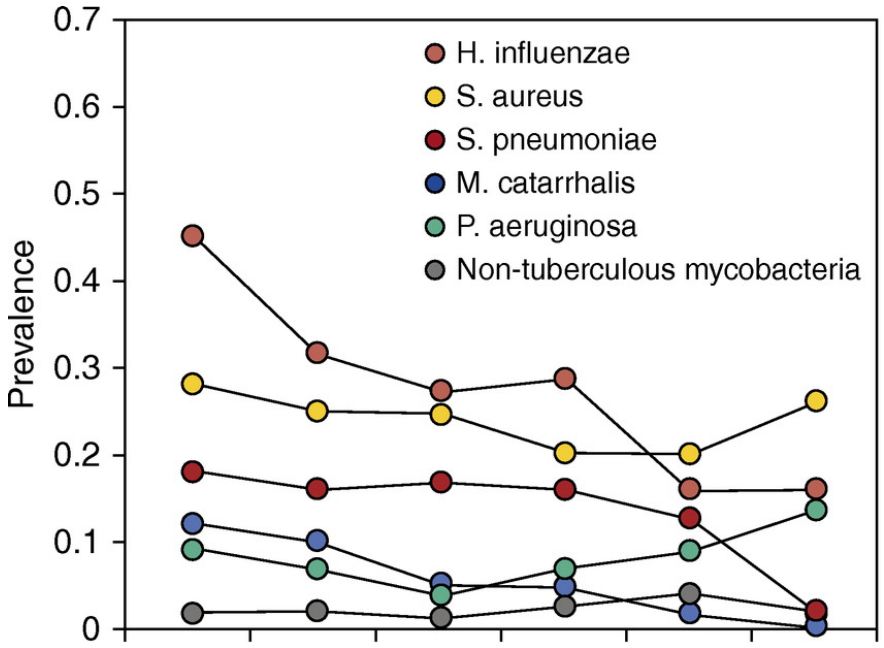


Shapiro AJ et al. : Diagnosis of Primary Ciliary Dyskinesia: An Official American Thoracic Society Clinical Practice Guideline. Am J Respir Crit Care Med. 187(12):e24-e39, 2018

Primary Ciliary Dyskinesia

Natural History of Lung Disease during Childhood

Respiratory Pathogens in PCD children:
Cross-sectional plot by age category



Age (years)	< 5	6–8	9–11	12–14	15–17	≥18
Number of subjects	52	68	77	60	44	22
Number of oropharyngeal cultures	106	54	25	14	12	5
Number of expectorated cultures	35	96	137	116	84	44

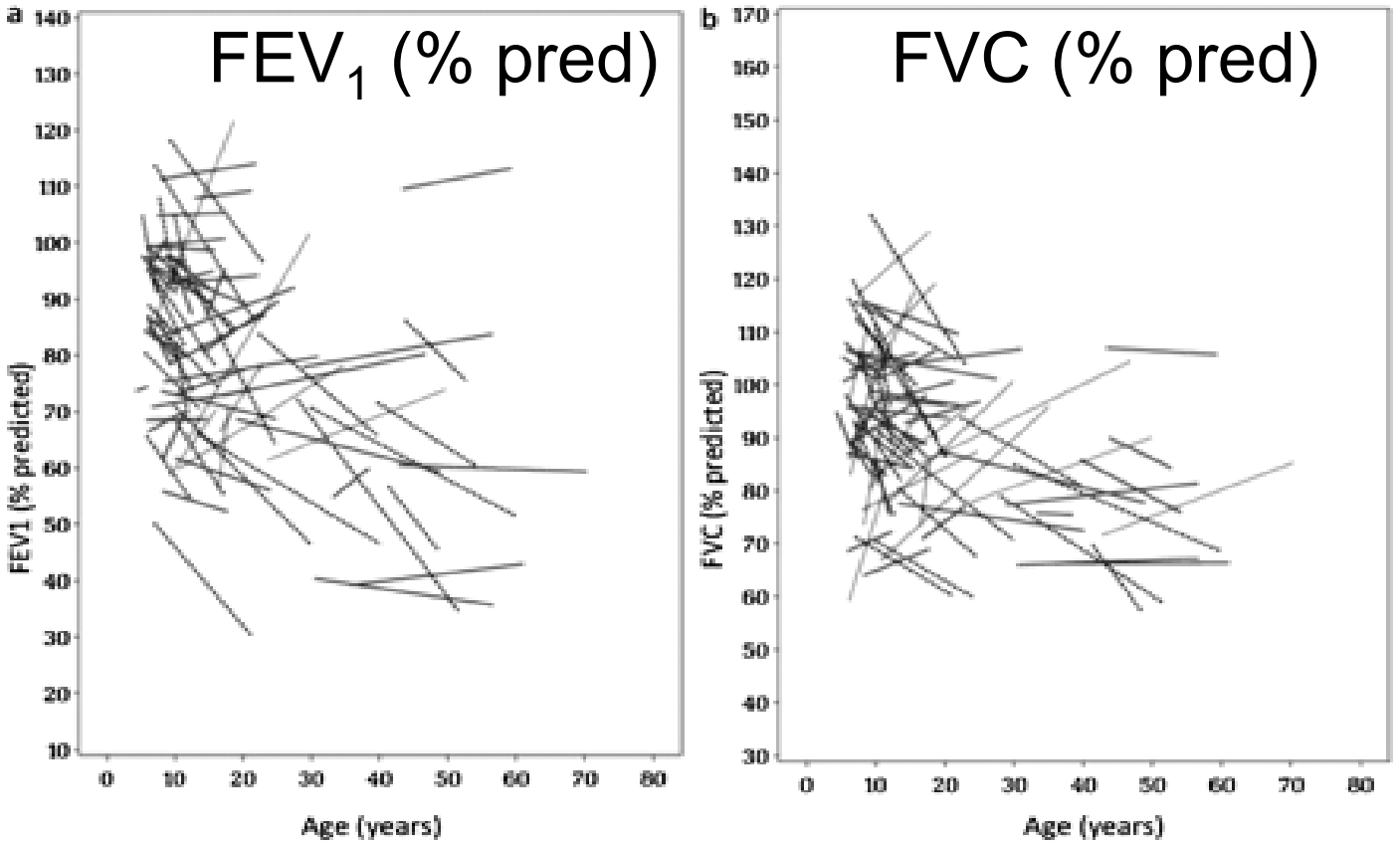
Participants ≤ 18 yrs at entry
- 137 with confirmed PCD
- 49% male; 82% Caucasian
- Age at enrollment 7.8 ± 4.6 yr
- Baseline plus 5 annual visits

Respiratory cultures
- at 728 of 732 visits
- 70.3% expectorated sputum
- 29.7% deep pharyngeal

Pseudomonas aeruginosa
- In 40/137 participants
- Mucoid in 4 participants
- Persistent in 13 participants

Davis SD et al. Am J Respir Crit Care Med 199:190-198, 2019

PCD: Longitudinal change in lung function: Wide range in severity and progression of lung disease

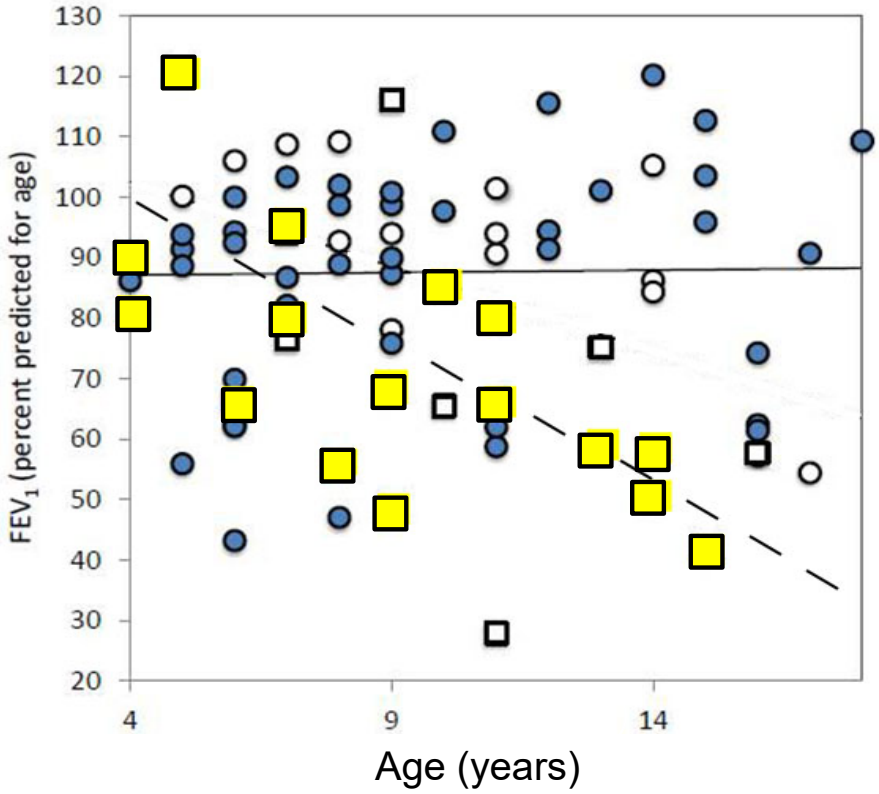


Linear regression of f/u years from 1st measured lung function

Marthin: *AJRCCM* 181:1262, 2010

PCD in Childhood: Lung Function vs Age:

Cross-sectional Analysis



Outer dynein arm defect

Outer dynein arm defect with defined genetic defect: *DNAH5, DNAI1, DNAI2, CCDC114, ARMC4, LRRC6, HEATR2, SPAG1, DNAAF1, DNAAF2*

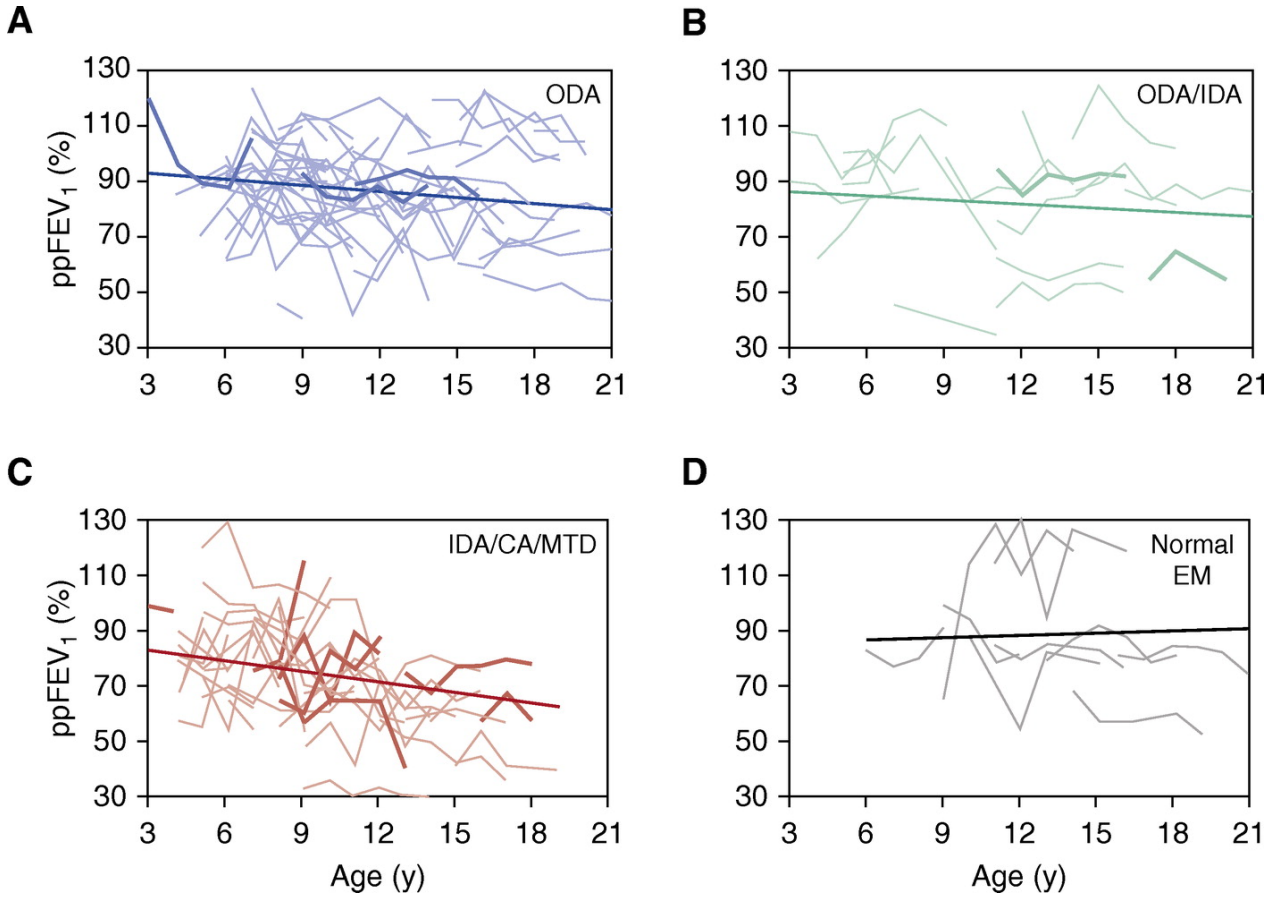
Microtubular disorganization

Microtubular disorganization with defined genetic defect: *CCDC39, CCDC40*

Davis SD: Am J Respir Crit Care Med 191:316-24, 2015

PCD in Childhood: Lung Function vs Age

Longitudinal Analysis by Ultrastructural Phenotype



Mean annual change in ppFEV1 for whole cohort is -0.57% (SE 0.25; p=0.03)

Davis SD et al. Am J Respir Crit Care Med 199:190-198, 2019

PCD Genotype - Lung Disease Severity

ODA alone defects
ODA structural proteins
DNAH5**
DNAI1*
DNAI2
DNAL1
NME8 (TXNDC3)
ODA Docking protein
CCDC114
CCDC151
ARMC4
TTC25
ODA Attachment Factor
CCDC103

ODA+IDA defects
Cytoplasmic pre-assembly factors
DNAAF1 (LRRC50)
DNAAF2 (KTU)
DNAAF3
DNAAF4 (DYX1C1)
DNAAF5 (HEATR2)
CFAP298 (C21orf59)
CFAP300 (C11orf70)
LRRC6
ZMYND10
SPAG1
PIH1D3 **(x-linked)**

IDA defect + MTD
N-DRC
CCDC39* ← Worse lung disease
CCDC40* ←

Oligocilia
Ciliary biogenesis
CCNO
MCIDAS

EM not done
DNAH1
DNAH8

IDA alone defect
No gene identified

Most prevalent genes
* in 4-10% of PCD patients
** in >15% of PCD patients

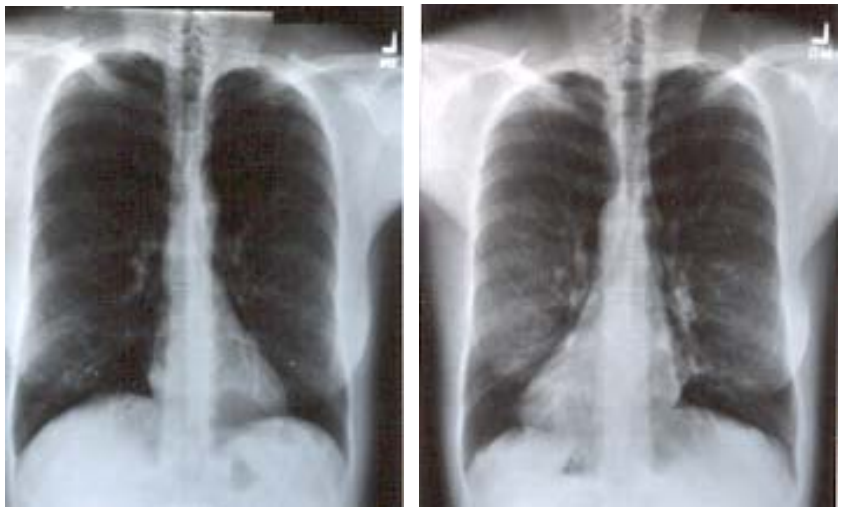
Normal/Near normal EM
ODA structural protein
DNAH11*
DNAH9
Central pair protein
HYDIN
STK36
Nexin-link proteins
CCDC164 (DRC1)
CCDC65 (DRC2)
GAS8 (DRC4)
Radial spoke proteins
RSPH1 ← Milder lung dz
RSPH3
RSPH4A
RSPH9
DNAJB13
Cilia orientation
GAS2L2
IFT protein
LRRC56

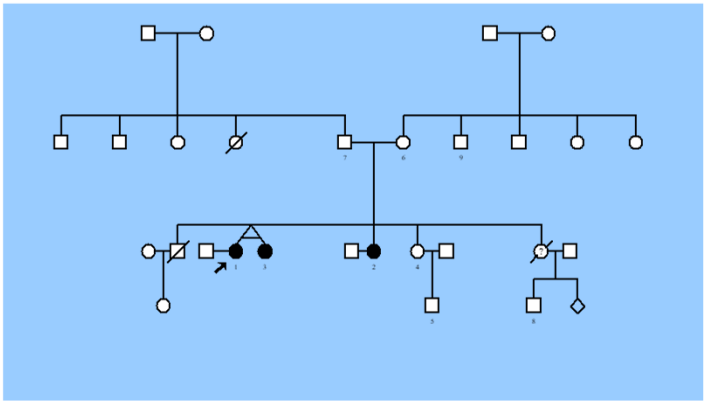
PCD + other syndrome
Retinitis pigmentosa +PCD
RPGR **(x-linked)**
Oro-facial-digital Syn +PCD
OFD1 **(x-linked)**

Role of Cilia in Directing Orientation of Organs:
More than Situs Inversus

Situs Inversus Totalis is Random in PCD: Identical twins with PCD

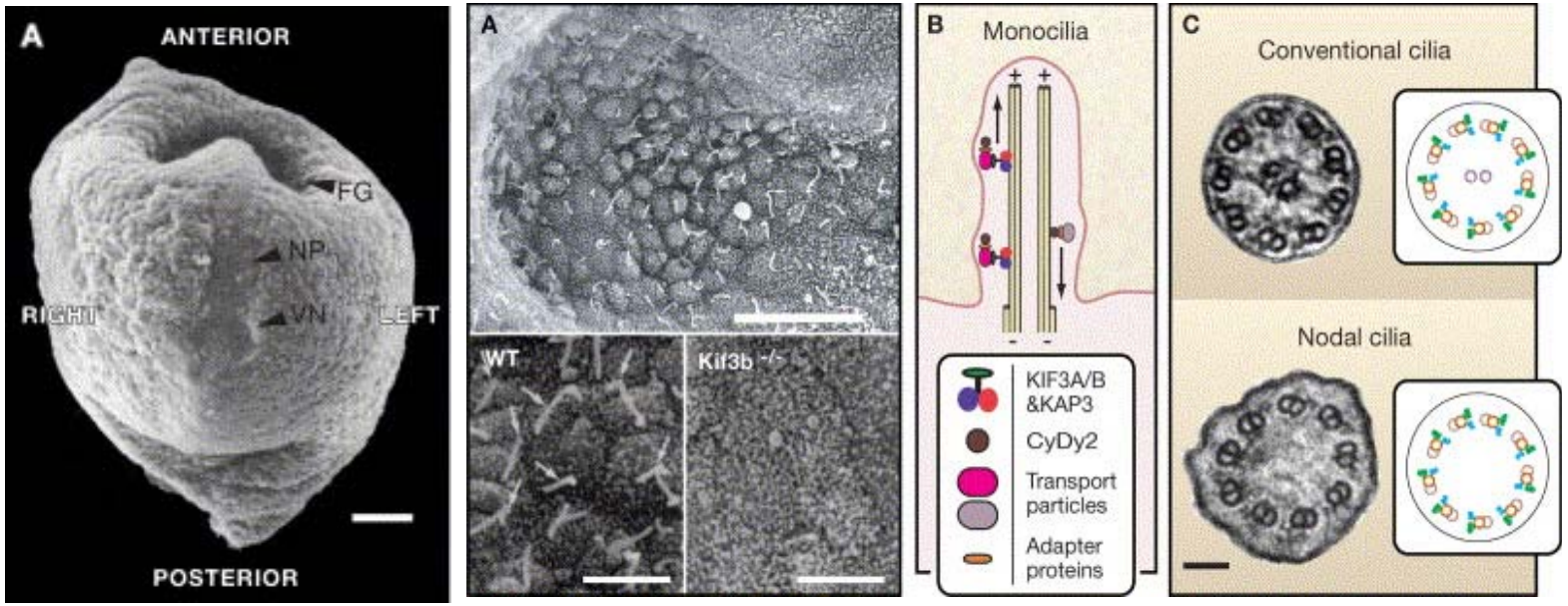
- Identical (monozygotic) twins with discordant organ sidedness:
  - situs solitus
  - situs inversus totalis
- Supports hypothesis that situs inversus is a random event in PCD





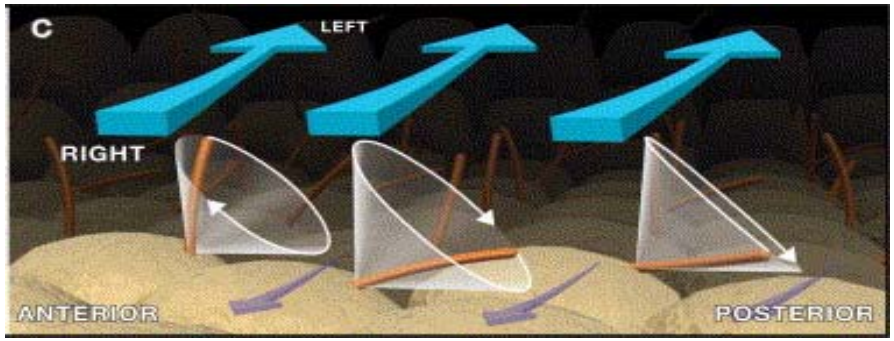
Noone PG et al. Am J Med Genet 82:155, 1999

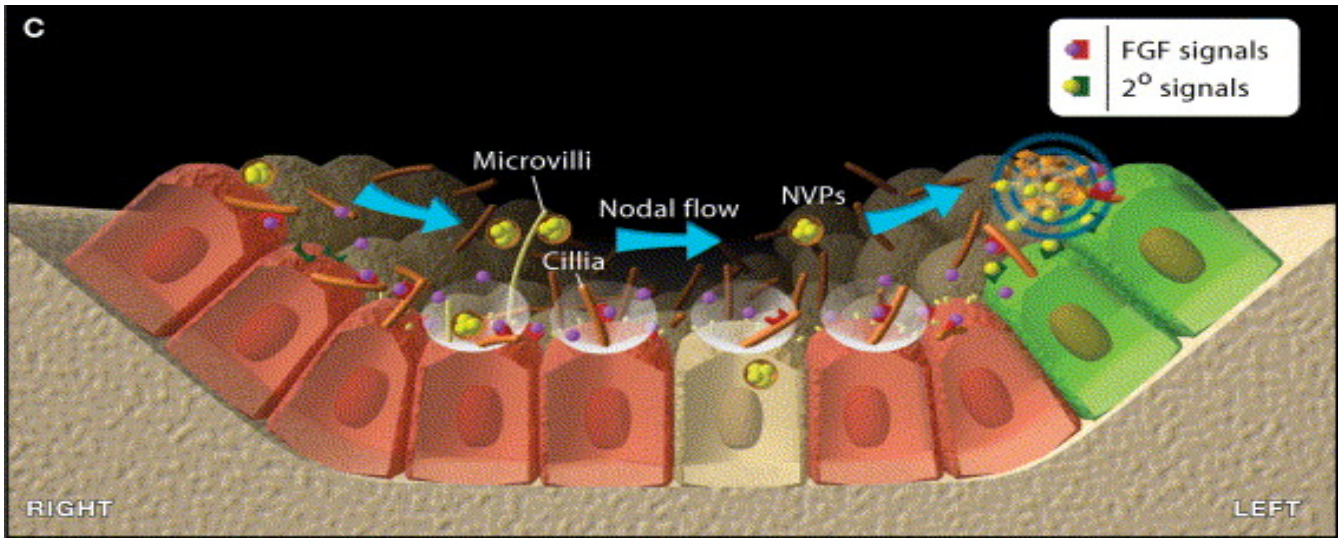
Nodal Cilia and Left-right Asymmetry



Hirokawa N, Tanaka Y, Okada Y, Takeda S, Nodal Flow and the Generation of Left-Right Asymmetry. Cell *125:33-45*, 2006

Nodal Cilia and Left-right Asymmetry





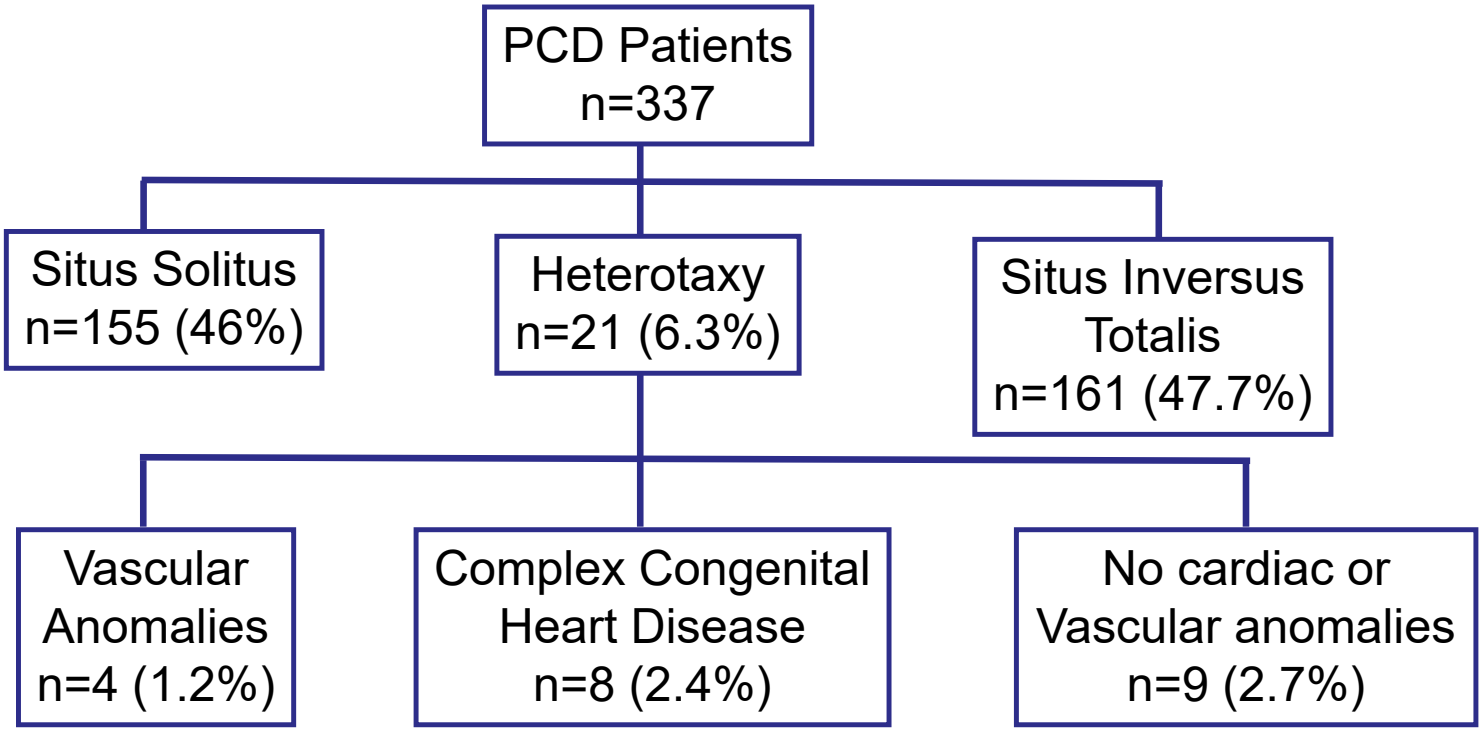
Hirokawa N, Tanaka Y, Okada Y, Takeda S, Nodal Flow and the Generation of Left-Right Asymmetry. Cell *125:33-45*, 2006

Congenital Heart Disease and Heterotaxy in PCD

- Background
  - 1982-2005: 3 case reports of PCD with heterotaxy [1-3]
- 2007: International retrospective study of prevalence of heterotaxic defects in PCD[4]
  - 337 PCD patients from 4 countries on 3 continents
    - USA (n=147)
    - Germany (n=128)
    - Canada (n=36)
    - Australia (n=26)

1. Schidlow DV et al. J Pediatr 100: 401-403, 1982
2. Engesath VG et al. Pediat Pulmon 16: 9-12, 1993
3. Schmura K et al. Respiration 72: 427-430, 2005
4. Kennedy MP, Omran H, Leigh MW, Dell S, Morgan L, Molina PL, Robinson BV, Minnix SL, Olbrich H, Severin T, Ahrens P, Lange L, Morillas HN, Noone PG, Zariwala M, Knowles MR. Congenital Heart Disease and other Heterotaxic Defects in a Large Cohort of Patients with Primary Ciliary Dyskinesia, Circulation, 115:2814-2821, 2007

Congenital Heart Disease and Heterotaxy in PCD



- Retrospective review of clinical data and imaging
- Combined data from Chapel Hill, NC (147), Toronto, Canada (36), New South Wales, Australia (26), Freiburg, Darmstadt & Cologne, Germany (128)

Kennedy MP et al, Circulation 115:2814-2821, 2007

Features Associated with Heterotaxy

Cardiovascular

- Atrioventricular discordance
- Transposition of great arter.
- Left atrial isomerism
- Right atrial isomerism
- Double outlet right ventricle
- Pulmonary stenosis/atresia
- Single ventricle
- L. vent. outflow obstruction
- Septal defects
- Total/partial anomalous pulmonary venous return
- Interrupted IVC
- Bilateral SVC
- Conduction system defects

Non-cardiovascular

- Asplenia
- Polysplenia
- Two bi-lobed (left) lungs
- Two tri-lobed (right) lungs
- Biliary atresia
- Abdominal situs inversus
- Thoracic situs inversus
- Intestinal malrotation

PCD Genotype–Laterality Defect

ODA alone defects
ODA structural proteins
*DNAH5***
*DNAI1**
DNAI2
DNAL1
NME8 (TXNDC3)
ODA Docking protein
CCDC114
CCDC151
ARMC4
TTC25
ODA Attachment Factor
CCDC103

ODA+IDA defects
Cytoplasmic pre-assembly factors
DNAAF1 (LRRC50)
DNAAF2 (KTU)
DNAAF3
DNAAF4 (DYX1C1)
DNAAF5 (HEATR2)
CFAP298 (C21orf59)
CFAP300 (C11orf70)
LRRC6
ZMYND10
SPAG1
PIH1D3 (x-linked)

IDA defect + MTD
N-DRC
*CCDC39**
*CCDC40**

Oligocilia
Ciliary biogenesis
CCNO
MCIDAS

EM not done
DNAH1
DNAH8

IDA alone defect
No gene identified

Most prevalent genes
* in 4-10% of PCD patients
** in >15% of PCD patients

Normal/Near normal EM
ODA structural protein
*DNAH11**
DNAH9
Central pair protein
HYDIN
STK36
Nexin-link proteins
CCDC164 (DRC1)
CCDC65 (DRC2)
GAS8 (DRC4)
Radial spoke proteins
RSPH1
RSPH3
RSPH4A
RSPH9
DNAJB13
Cilia orientation
GAS2L2
IFT protein
LRRC56

PCD + other syndrome
Retinitis pigmentosa +PCD
RPGR (x-linked)
Oro-facial-digital Syn +PCD
OFD1 (x-linked)

Management of PCD Lung Disease

- No published clinical trials to direct evidence-based therapy
- Management based on the “experience” of specialist with chronic lung disease
  - Few centers follow more than handful of patients with PCD

Management of PCD Lung Disease: General principles

- Enhance airway clearance
- Prevent respiratory infections
- Monitor respiratory cultures and respiratory function
- Treat respiratory infections appropriately
- Avoid exposure to airway irritants
- Maintain healthy lifestyle

Shapiro AJ, et al. Diagnosis, Monitoring, and Treatment of Primary Ciliary Dyskinesia: PCD Foundation Consensus Recommendations Based on State of the Art Review. Pediatr Pulmonol 51:115-32, 2016.

Audience Response Question 3

You are caring for a 7 year old with Primary Ciliary Dyskinesia (PCD). This child's parents inquire about specific therapies for PCD. Which of the following therapies has been tested in randomized, placebo-controlled trials in PCD patients and demonstrated to have clinical benefit?

A. Recombinant DNase

B. Hypertonic saline

C. Suppressive antibiotic therapy with azithromycin

D. None of the above

Audience Response Question 3

You are caring for a 7 year old with Primary Ciliary Dyskinesia (PCD). This child's parents inquire about specific therapies for PCD. Which of the following therapies has been tested in randomized, placebo-controlled trials in PCD patients and demonstrated to have clinical benefit?

A. Recombinant DNase

B. Hypertonic saline

C. Suppressive antibiotic therapy with azithromycin

→ D. None of the above

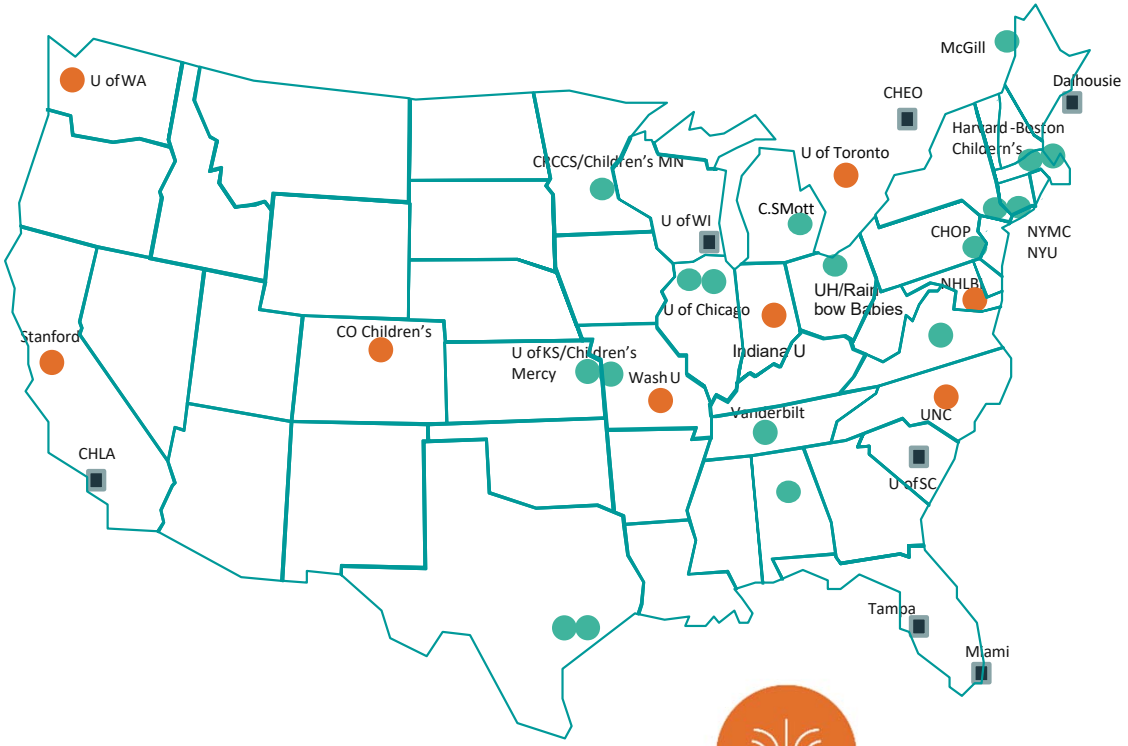
Priorities for PCD Clinical Care and Clinical Research Centers

- Create network of PCD Centers of Excellence and Clinical Practice Guidelines
- Make accurate and early diagnosis of PCD
  - Clinical clues / access to diagnostic testing
- Create centralized patient registry
  - Define true prevalence / incidence of PCD
  - Track longitudinal data on large # of PCD patients
  - Identify clinical features linked with prognosis / progression
- Assess outcome measures for clinical trials
  - Lung function/chest CT/ microbiology
  - Health-related Quality of Life Tool for PCD
- Perform clinical trials

PCD Clinical and Research Centers Network Map
GDMCC, Full & Affiliate Centers

GDMCC RESEARCH CENTERS	
University of North Carolina	Chapel Hill, NC
NHLBI	Bethesda, MD
Washington University	St. Louis, MO
Colorado Children's Hospital	Aurora, CO
University of Toronto	Toronto, Ontario, CA
Stanford University	Palo Alto, CA
University of Washington	Seattle, WA
Indiana University	Indianapolis, IN
PCDF FULL CENTERS	
Baylor/Texas Children's	Houston, TX
Boston Children's Hospital	Boston, MA
Brigham & Women's Hospital	Boston, MA
C.S. Mott Children's Hospital	Ann Arbor, MI
Children's Mercy Hospital	Kansas City, MO
Children's Hospital of Phil	Philadelphia, PA
CRCCS/MN Children's Hospital	Minneapolis, MN
Lurie Chidlren's Hospital	Chicago, IL
McGill University	Montreal, Quebec
Northwestern University	Chicago, IL
NYMC	Valhalla, NY
NYU/Langone Children's Hosp	New York, NY
UH/Rainbow Babies Hospital	Cleveland, OH
University of Alabama	Birmingham, AL
University of Kansas	Kansas City, KS
University of Chicago	Chicago, IL
University of Virginia	Charlottesville, VA
UT Health	Houston, TX
Vanderbilt	Nashville, TN
AFFILIATE CENTERS	
University of Florida	Miami, FL
Children's Hospital of LA	Los Angeles, Ca
University of South Florida	Tampa, FL
University of Wisconsin	Milwaukee, WI
University of South Carolina	Columbia, SC
CHEO	Ottawa, Ontario, CA
Dalhousie University	Halifax, Nova Scotia, CA

Last Update 4/17/2018



PCD FOUNDATION
PRIMARY CILIARY DYSKINESIA

PCD Research Teams

PCD Group: UNC-CH

Michael Knowles, MD
Maimoona Zariwala, PhD
Stephanie Davis, MD
Milan Hazucha, PhD
Kunal Chawla, BS
Peadar Noone, MD
Leigh Anne Daniels, MD
Marcus Kennedy, MD
David E Brown III, MD
Adam Shapiro, MD
Jessica Pittman, MD
Catherine Donnellan Sanders, MD
Susan Minnix, RN
Kelli Sullivan, MPH
Johnny Carson, PhD
Kim Burns, BS
Larry Ostrowski, PhD

GDMCC Consortium

Thomas Ferkol, MD - St. Louis, MO
Scott Sagel, MD – Denver, CO
Margaret Rosenfeld, MD – Seattle, WA
Sharon Dell, MD – Toronto
Ken Olivier, MD – NIH
Carlos Milla, MD – Palo Alto, CA
Adam Shapiro, MD - Montreal
Jeff Krischer, PhD – Tampa, FL

Support:

NIH ORD/NCATS/NHLBI
PCD patients and families