A GUIDE TO UNDERSTANDING INFLAMMATORY PATHWAYS IN PRIMARY CILIARY DYSKINESIA

A two-level explanation of the multi-omics study by Mosquera and colleagues (2026)

PCD and Friends · Research explained to help us understand PCD

For patients, families, healthcare professionals and students.
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Before we begin

Two reading levels in one guide

If you want the simple idea: start with the yellow boxes containing the plain-language parallels.

If you want to go deeper: continue with the molecular and clinical explanation beside them. You do not need to memorise abbreviations. What matters is understanding how the pathways connect.

This guide explains the inflammatory pathways reported in Multi-Omics Analysis Defines Endotypes and Systemic Inflammation in Primary Ciliary Dyskinesia. The study examined genes, proteins and the microbiome together to identify patterns of inflammation in people with PCD.

This is neither a translation of the paper nor a treatment guideline. It is an independent plain-language interpretation based on the published scientific abstract and general immunological knowledge. It aims to help readers explore the study without confusing findings, interpretation and possible future applications.

What to take away

• An inflammatory pathway is a chain of signals, not a single molecule.

• Pathways form a connected network: some detect, amplify, attack, restrain or repair.

• PCD may share a neutrophilic foundation, but not everyone shows exactly the same pattern.

• The study identifies molecular signatures; it does not yet assign a treatment to each patient.

Core idea

Ciliary dysfunction not only allows mucus and microorganisms to remain in the airways for longer. It may also keep a defensive network active which, if persistent, can contribute to tissue damage.

1. What question did the study try to answer?

PCD is associated with chronic airway inflammation and progressive lung damage. However, the dominant inflammatory mechanisms, the extent of systemic signalling and the ability of a simple saliva sample to reflect this activity had not been well characterised.

How it was conducted

Design	Participants	Samples and analyses
Multicentre, cross-sectional study. Data were collected in the absence of acute infection.	76 people: 51 with PCD and 25 healthy controls from Houston, Puerto Rico and Mexico.	Oral swabs for 590-gene transcriptomics and metagenomics; 250 proteins measured in saliva and plasma.

What does “multi-omics” mean?

	Looking at several biological layers at once
PLAIN-LANGUAGE PARALLEL It is like investigating a city by studying its plans, circulating messages, working machinery and resident communities at the same time.	Transcriptomics: which genes are being expressed. Proteomics: which proteins are present. Metagenomics: which microorganisms make up the microbiome. Integration can reveal patterns that a single layer might miss.

Main findings reported in the published abstract

• Higher expression of inflammatory genes and proteins in saliva and plasma, especially in people over 10 and those with microtubular defects.

• Activation of ten pathways: NF-κB, oxidative stress, T-cell receptor, TREG, Th17, TNF, Th1, Th2, TGF-β and TLR.

• Good molecular concordance between saliva and plasma.

• Microbiome changes associated with inflammatory pathways.

What “activated pathway” means here

The analysis found a coordinated gene or protein signature consistent with activity in that pathway. It does not mean every molecule was increased or that activity was equally strong in every person.

2. The overall map: from alarm to damage and repair

An inflammatory cascade can be understood as a series of decisions. A threat is detected and translated into instructions; defensive cells arrive and deploy chemical and enzymatic weapons; finally, the body tries to restrain the response and repair the tissue.

1	Retention Mucus, microbes and damage signals
2	Detection TLR recognises danger
3	Alarm NF-κB switches on inflammatory genes
4	Amplification TNF and other cytokines spread the signal
5	Response Th1, Th2, Th17 and neutrophils
6	Effectors Proteases and oxidants fight, but may injure
7	Control TREG restrains; TGF-β repairs and remodels

The self-perpetuating cycle

Impaired mucociliary clearance → persistent mucus and microorganisms → immune alarm → neutrophil recruitment → proteases and oxidative stress → epithelial damage → new danger signals.

Defence remains necessary. The problem begins when its intensity or duration exceeds what the tissue can tolerate.

This is a useful simplification, not a rigid sequence. In real biology, many signals occur together, feed back on one another and vary with microorganisms, age, genotype, epithelial condition and other factors.

3. The pathways that detect danger and sound the alarm

TLR	Innate danger sensors
PLAIN-LANGUAGE PARALLEL Smoke detectors. They recognise signs of microbes or damaged tissue and alert the cell.	Toll-like receptors are found on epithelial and immune cells. They recognise microbial patterns and damage signals and can initiate inflammatory programmes including NF-κB. With impaired mucociliary clearance, stimulation may recur.

	Central transcriptional switch
PLAIN-LANGUAGE PARALLEL The alarm control centre. It receives the sensor's warning and converts it into instructions that mobilise defence.	NF-κB is a family of transcription factors. Once activated, it promotes expression of cytokines, chemokines, adhesion molecules and other mediators. It is essential for defence; persistent activation can sustain inflammation.

TNF	Pro-inflammatory amplifying cytokine
PLAIN-LANGUAGE PARALLEL A siren that sets off other sirens. It spreads the warning, helps assistance arrive and can stimulate the control centre again.	Tumour necrosis factor activates immune cells, endothelium and other pathways. It may facilitate leukocyte entry into tissue and reinforce NF-κB, creating a feedback loop.

Quick connection

TLR detects → NF-κB translates the alarm into inflammatory genes → TNF amplifies.

Why this matters in PCD

These pathways show how repeated exposure to retained mucus, microorganisms and epithelial damage may become a sustained inflammatory signal. The study alone does not identify the initial trigger in each episode or show that blocking any one pathway would be safe or effective in PCD.

4. The T-cell receptor and specialised defence programmes

	T-cell receptor
PLAIN-LANGUAGE PARALLEL The ID scanner. It checks a specific fragment presented by another cell and helps determine which specialised response should be organised.	The T-cell receptor recognises antigens presented by major histocompatibility complex molecules. Alongside co-signals and local cytokines, it activates the lymphocyte and guides differentiation into Th1, Th2, Th17 or regulatory programmes.

T-cell receptor activation indicates that the observed inflammation is not limited to innate immunity - epithelium, sensors and neutrophils. Adaptive immunity, which recognises specific antigens and organises more specialised responses, is involved too.

Three helper programmes

Programme	Simplified role	If persistent or dysregulated
Th1	Supports cellular defence and macrophage activation, particularly against intracellular microorganisms.	May contribute to an intense tissue response.
Th2	Associated with eosinophils, IgE, IL-4, IL-5, IL-13, mucus and allergic-type responses.	May add an eosinophilic/type 2 component; it does not automatically mean asthma.
Th17	Supports barrier defence and neutrophil recruitment, partly through IL-17.	May sustain a neutrophil influx capable of damaging tissue.

A useful parallel

The TCR assembles the team and the local environment supplies the work plan. Th1, Th2 and Th17 are not three separate diseases: they are immune programmes that can coexist and carry different weight in each person.

5. Th17 and neutrophil recruitment

Th17	Neutrophil recruitment
PLAIN-LANGUAGE PARALLEL The call for reinforcements. It sends messages that bring neutrophils to the barrier where microorganisms need to be fought.	Th17 cells produce cytokines such as IL-17. These induce epithelial and other cells to make chemokines and factors that mobilise and recruit neutrophils. This helps control extracellular bacteria and fungi, but a sustained signal may contribute to chronic neutrophilic inflammation.

Simplified chain

Th17 → IL-17 → chemokines → neutrophil recruitment.

The study abstract identified a high-Th17 neutrophil recruitment endotype in 71% of people with PCD. The percentages are not mutually exclusive: one person could display more than one signature.

Neutrophils: essential defence, possible damage

Neutrophils engulf microorganisms, generate oxidants, release enzymes and may form extracellular traps. They are essential to immunity. However, persistent accumulation and activation may also damage airway epithelium and lung matrix.

DPP-1	Activation of neutrophil proteases
PLAIN-LANGUAGE PARALLEL The armourer preparing tools before battle. It activates certain enzymes so the neutrophil can use them later.	DPP-1, or cathepsin C, activates serine proteases during neutrophil maturation, including neutrophil elastase, proteinase 3 and cathepsin G. The study described a DPP-1-associated, protease-dominant neutrophilic endotype in 78%.

This mechanism is therapeutically relevant in bronchiectasis because DPP-1 inhibition aims to reduce several protease activities. However, a DPP-1 signature in this study does not itself prove that an individual with PCD will respond to a particular drug.

6. Proteases and oxidative stress: effector weapons

PROTEASES	Protein-cutting enzymes
PLAIN-LANGUAGE PARALLEL Molecular scissors. They help destroy microorganisms and clear damaged material, but can also cut healthy structures nearby.	Neutrophil elastase and other proteases support defence. In excess they may damage epithelium, degrade extracellular matrix, increase mucus secretion and disrupt repair, contributing to a harmful airway environment.

OXIDATIVE STRESS	Imbalance between oxidants and antioxidant defences
PLAIN-LANGUAGE PARALLEL A powerful disinfectant. At the right dose it helps eliminate microbes; continuously spilled, it also damages the surface it was meant to clean.	Neutrophils and other cells generate reactive oxygen species. When production exceeds antioxidant capacity, lipids, proteins and DNA may be altered. Cellular damage releases new danger signals and may reactivate pathways such as NF-κB.

Another feedback loop

Inflammation → oxidants and proteases → cell damage → new danger signals → more inflammation.

An important distinction

The ability of these weapons to cause damage does not mean they should be eliminated: they also protect against infection. Precision medicine aims to modulate the damaging mechanism without unnecessarily weakening defence.

The right therapeutic question

It is not simply “How do we switch off all inflammation?”, but “Which part of the response is excessive in this person, at this time, and how can we reduce harm while preserving protection?”

7. Th2: a different signature on a shared foundation

Th2	Type 2 immune response
PLAIN-LANGUAGE PARALLEL Another department of defence. It specialises in tasks different from those of neutrophils, but both can work at the same time.	The Th2 response is associated with IL-4, IL-5, IL-13, eosinophils, IgE production, mucus secretion and epithelial changes. It is well known in allergy and asthma, although a Th2 signature alone is not an asthma diagnosis.

The study identified a high-Th2 eosinophil-dominant signature in 51%, as well as combined Th2/Th17 profiles. This suggests that PCD's inflammatory landscape may be more heterogeneous than the classic idea of a single neutrophilic pattern.

What must NOT be concluded

This does not mean that 51% of people with PCD have asthma. Nor does it mean they should automatically receive corticosteroids or type 2 biologics. Clinical translation would require links with symptoms, eosinophils, lung function, exacerbations and treatment response.

Mixed profiles

The abstract reported five endotypes: DPP-1/proteases (78%), high Th17 (71%), high Th2 (51%), high Th2/Th17 (47%) and low Th2/Th17 (25%). Their overlap shows that the researchers were not placing every patient into one rigid box.

Plain-language parallel

A single building may have its smoke alarm, sprinkler system and repair crew active at the same time. Endotypes describe which systems appear to dominate; they are not immutable identities.

8. TREG and TGF-β: restraint, repair and remodelling

TREG	**Regulation of the immune response**
PLAIN-LANGUAGE PARALLEL The damage-control team. It tries to prevent defence from continuing after it is no longer needed or becoming disproportionate.	Regulatory T cells limit other cells' activation and help maintain immune tolerance and balance. An activated TREG signature may reflect an attempt to compensate; it does not prove the brake is sufficient or effective.

	Regulation, repair and remodelling
PLAIN-LANGUAGE PARALLEL The builder. It repairs a damaged wall; if told to rebuild without pause, it may eventually make the wall too thick and rigid.	TGF-β contributes to immune regulation, epithelial repair and extracellular matrix production. Persistent activation may promote fibrosis and remodelling. Its role depends on context, cell type and timing; it is not simply “good” or “bad”.

A dynamic balance

Inflammation cannot be divided neatly into accelerators and brakes. The same molecule may act differently depending on location and duration. TGF-β, for example, may contain inflammation and support repair, yet also contribute to structural change when stimulation persists.

Quick connection

TREG attempts to restrain the response. TGF-β helps regulate and repair. If injury recurs, repair may become remodelling.

9. How the ten pathways fit together

Pathway	Main role	Plain-language parallel
TLR	Detect microbial patterns and damage.	Smoke detector
NF-κB	Switch on inflammatory genes.	Alarm control centre
TNF	Amplify and coordinate the response.	Siren setting off other sirens
TCR	Recognise antigen and activate T cells.	ID scanner
Th1	Organise cellular defence and macrophages.	Cellular response team
Th2	Type 2 response, eosinophils and mucus.	Specialist department
Th17	Support neutrophil recruitment.	Call for reinforcements
Oxidative stress	Use oxidants against microbes; possible collateral damage.	Powerful disinfectant
TREG	Limit the response and maintain balance.	Damage control
TGF-β	Regulate, repair and, if persistent, remodel.	Builder

One network, several intervention points

These are not ten separate fires. They are connected parts of a network that detects, switches on, amplifies, specialises, attacks, restrains and repairs.

10. What this study really contributes

What it does contribute

• It expands the classic model: PCD inflammation does not appear uniform.

• It identifies heterogeneity: Th17, Th2 and other signatures may coexist on a frequently neutrophilic foundation.

• It connects biological layers: genes, proteins and microbiome are analysed together.

• It opens a monitoring route: saliva showed molecular concordance with plasma.

• It generates therapeutic hypotheses: endotypes might eventually help select or evaluate treatments.

What it does not yet demonstrate

• That these endotypes remain stable over time.

• That one sample can determine an individual's treatment.

• That saliva can already replace other clinical tests.

• That blocking one pathway improves the course of PCD.

• That the findings generalise to everyone with PCD worldwide.

Limitations that must accompany interpretation

This was a cross-sectional study involving 51 participants with PCD. It describes associations and molecular signatures at one point in time. Clinical usefulness requires larger cohorts, longitudinal follow-up, external validation and studies linking profiles with exacerbations, lung function, structural damage and treatment response.

The map metaphor

The study provides a more detailed map of inflammatory roads. It does not yet tell us which therapeutic route each patient should take or guarantee where every road leads.

11. What might this mean in clinical practice?

At present, these findings do not justify routine “endotype profiling” or independent treatment changes. Their current value is mainly scientific: they help frame better research questions.

Questions raised for follow-up

• Do inflammatory profiles change between stability and exacerbation?

• Do they persist over time or evolve with age and lung damage?

• Are they associated with genotype or ultrastructural defect?

• Can they predict exacerbations, lung-function decline or response to an anti-inflammatory treatment?

• Could repeated saliva sampling, especially in children, reduce blood draws?

• How should biomarkers be integrated with symptoms, cultures, spirometry and imaging?

A nursing perspective

Measurement alone is not enough: information must become care

If these biomarkers reach practice, we will need clear health education, reproducible collection procedures, understandable reporting, adherence follow-up and assessment of the burden of each test. A biomarker is useful only if it supports decisions that matter to the person.

Saliva is attractive because it is non-invasive, but “easy to collect” does not automatically mean “easy to interpret”. Collection timing, oral health, medication, recent infection and other factors may influence results and will need standardisation.

12. Essential glossary

Biomarker	A biological measure that provides information about a normal process, disease or response to an intervention.
Cytokine	A signalling protein used by cells to coordinate immune responses.
Endotype	A subtype defined by a biological mechanism, not only by visible symptoms.
Phenotype	The observable characteristics of a person or disease.
Molecular signature	A combined pattern of genes, proteins or other molecules associated with a biological state.
Metagenomics	Analysis of genetic material from microbial communities in a sample.
Multi-omics	Integration of several layers of biological information.
Protease	An enzyme that cuts proteins.
Proteomics	Large-scale study of proteins that are present or expressed.
Chemokine	A cytokine that guides immune-cell movement.
Transcriptomics	Study of RNA to identify which genes are being expressed.
Signalling pathway	A chain of molecular messages that converts a signal into a cellular response.

The final question

The future of precision medicine in PCD is not only about asking “How much inflammation does this person have?”, but also “Which mechanism is driving their inflammation, and how can we best modulate it without unnecessarily weakening their defences?”

Sources, authorship and disclaimer

Study explained

Mosquera RA, Magana-Ceballos IG, De Jesus Rojas W, et al. Multi-Omics Analysis Defines Endotypes and Systemic Inflammation in Primary Ciliary Dyskinesia: A Comparison with Healthy Controls. Annals of the American Thoracic Society. Published online 8 June 2026. https://doi.org/10.1093/annalsats/aaoag152

When this guide was prepared, the journal made the abstract publicly available and indicated that access was required for the full accepted manuscript. Numerical findings attributed to the study are taken from that published abstract.

About this guide

Editing and public engagement: PCD and Friends.
Editorial concept: explaining international PCD research with clear language, scientific rigour and practical value for patients, families and professionals.
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Disclaimer

Educational material

This document does not replace medical consultation, diagnosis or recommendations from the professionals responsible for a person's care. It must not be used to start, stop or modify treatment. The analogies support understanding but simplify complex biological processes.

PCD and Friends
Understanding the disease better is also a way of taking part in advancing research.