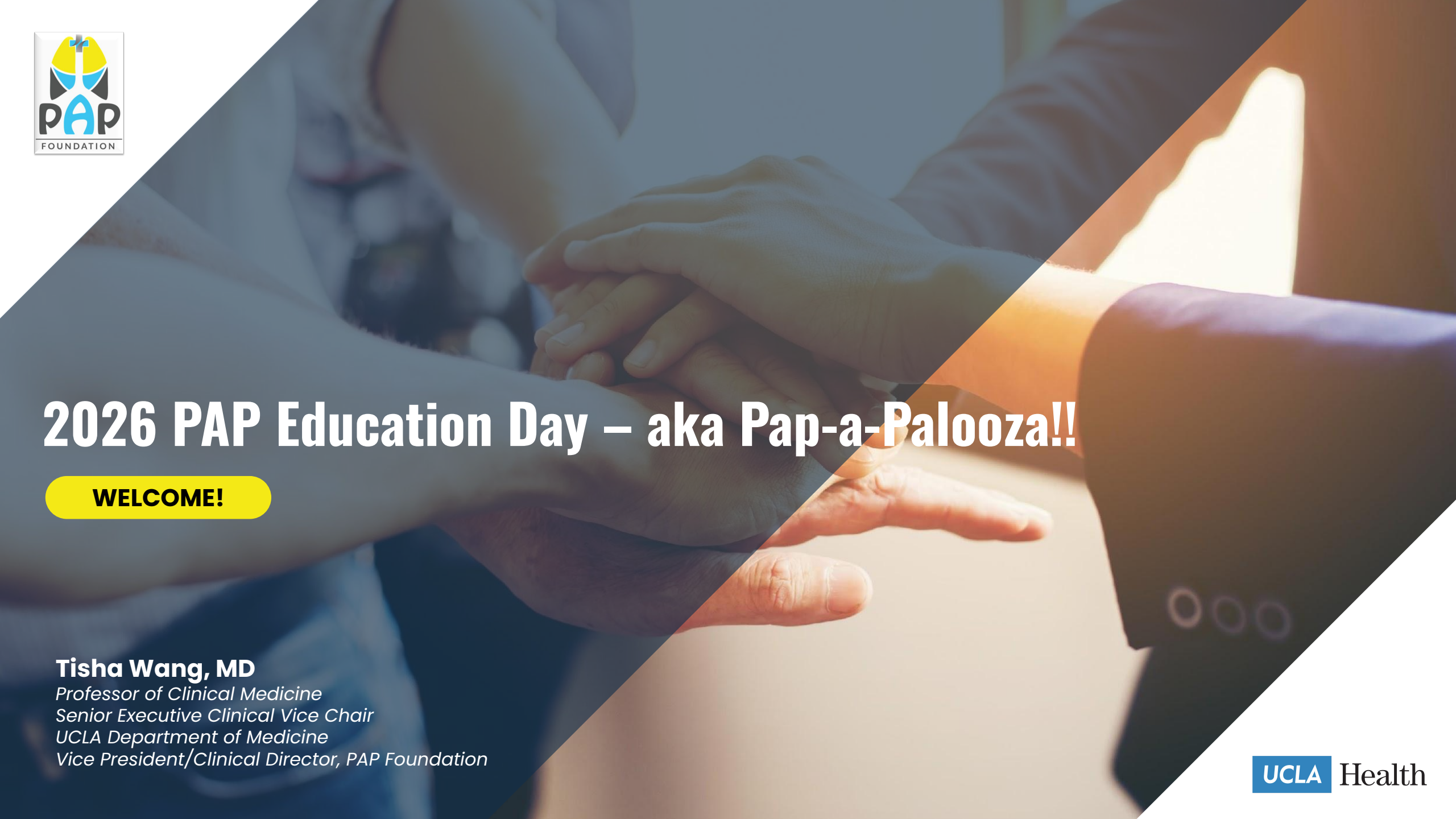

2026 PAP Education Day – aka Pap-a-Palooza!!

WELCOME!

Tisha Wang, MD
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UCLA Department of Medicine
Vice President/Clinical Director, PAP Foundation

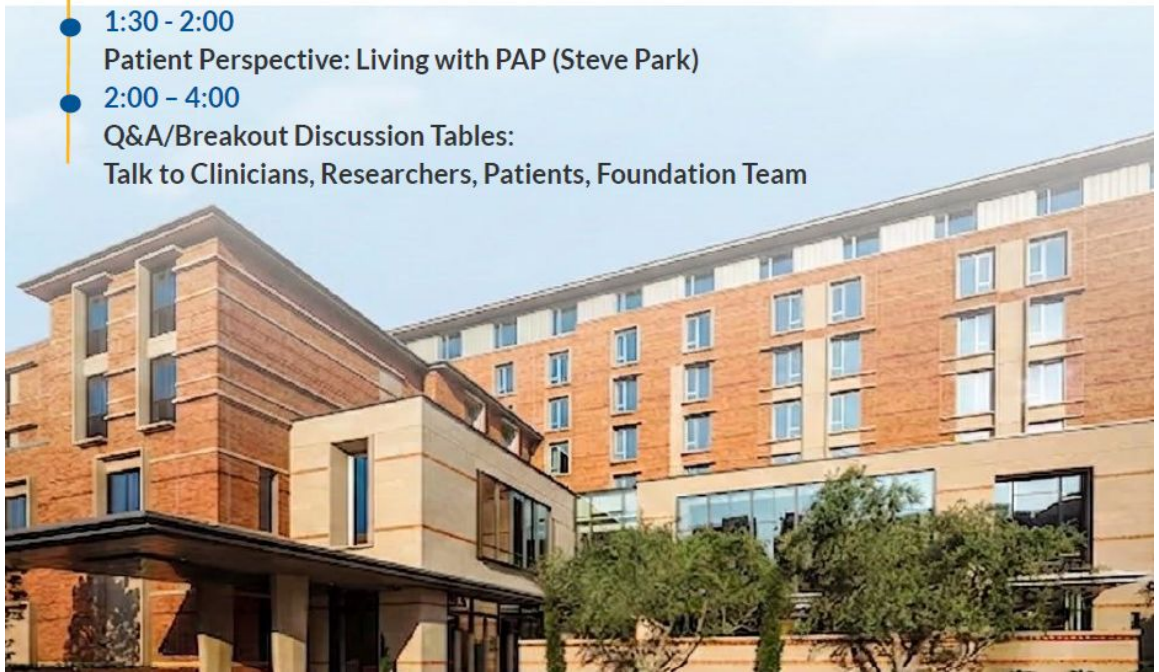
Agenda

2026 PAP Education Day

May 2, 2026

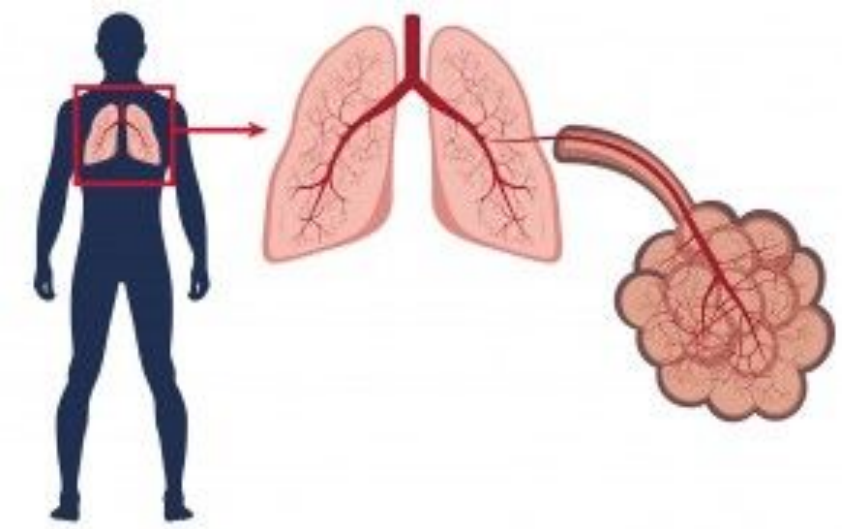
University of California, Luskin Conference Center,
425 Westwood Plaza, Los Angeles, CA 90095

- 9:00 – 9:30
  Registration/Coffee (All)
- 9:30 - 10:30
  Welcome/Introductions (Tisha Wang, MD)
- 10:30 - 11:00
  PAP 101 – Definition and Therapies (Tisha Wang, MD)
- 11:00 - 11:30
  Clinical Trials and National Registry (Brenna Carey, PhD)
- 11:30 – 12:30
  Lunch
- 1:00 – 1:30
  PAP Foundation: Community, Resources (Chris Hameetman)
- 1:30 - 2:00
  Patient Perspective: Living with PAP (Steve Park)
- 2:00 – 4:00
  Q&A/Breakout Discussion Tables:
  Talk to Clinicians, Researchers, Patients, Foundation Team

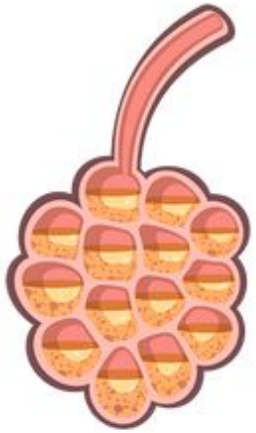


Pulmonary Alveolar Proteinosis (PAP)

- Normally our body makes a substance called **surfactant** to coat the alveoli (air sacs) of the lungs
- **Surfactant** is made up of lipids, proteins, and cholesterol and helps prevent the air sacs from collapsing
- PAP is a condition where **surfactant** builds-up in the alveoli (air sacs) of the lungs



Healthy alveoli



PAP affected alveoli

Pulmonary Alveolar Proteinosis (PAP)

- Immune cells called "**alveolar macrophages**" normally keep the air sacs clean by removing any extra surfactant from the lung
- In PAP, these cells do not mature since they are denied a normally occurring protein called Granulocyte Macrophage Colony-Stimulating Factor (**GM-CSF**)
- This leads to a build-up of surfactant in the lungs which results in symptoms of PAP

PAP Demographics

- Rare lung disease: 7-10 patients per 1,000,000 population
  - ✔ Roughly 3,000 patients in the US
  - ✔ More than 75,000 patients in the world
- More frequently seen in smokers
- Typically occurs in the prime of life (age 30-50) but affects men, women, and children of all ages
- Affects people of all ethnicities and geographic locations

PAP Causes

Primary PAP (~90% of cases)

An autoimmune disease where antibodies in the blood and lungs block the naturally occurring GM-CSF, preventing the alveolar macrophages from maturing. Primary PAP is also called “idiopathic”(from unknown cause).

Secondary PAP (~10% of cases)

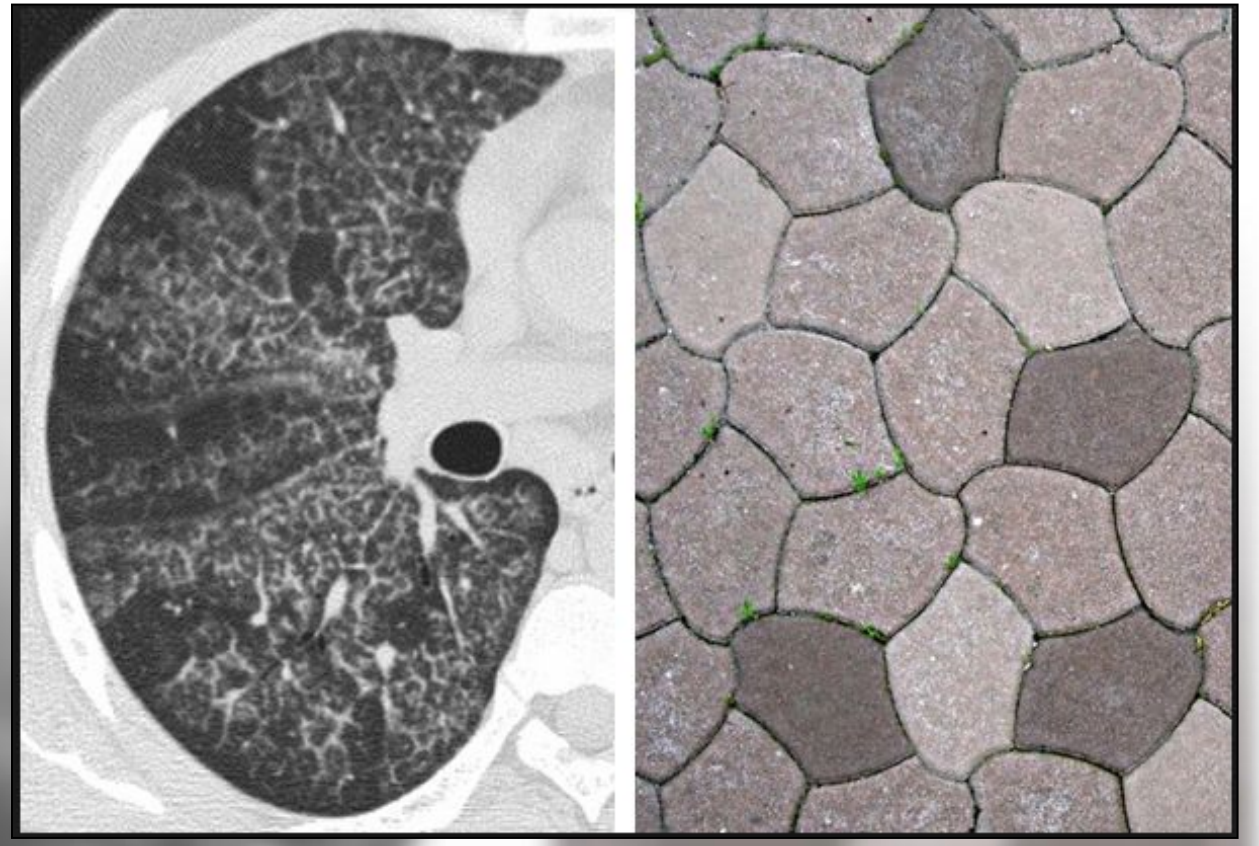
Occurs as a result of blood disorders, medications, infections, or large inhalation exposures.

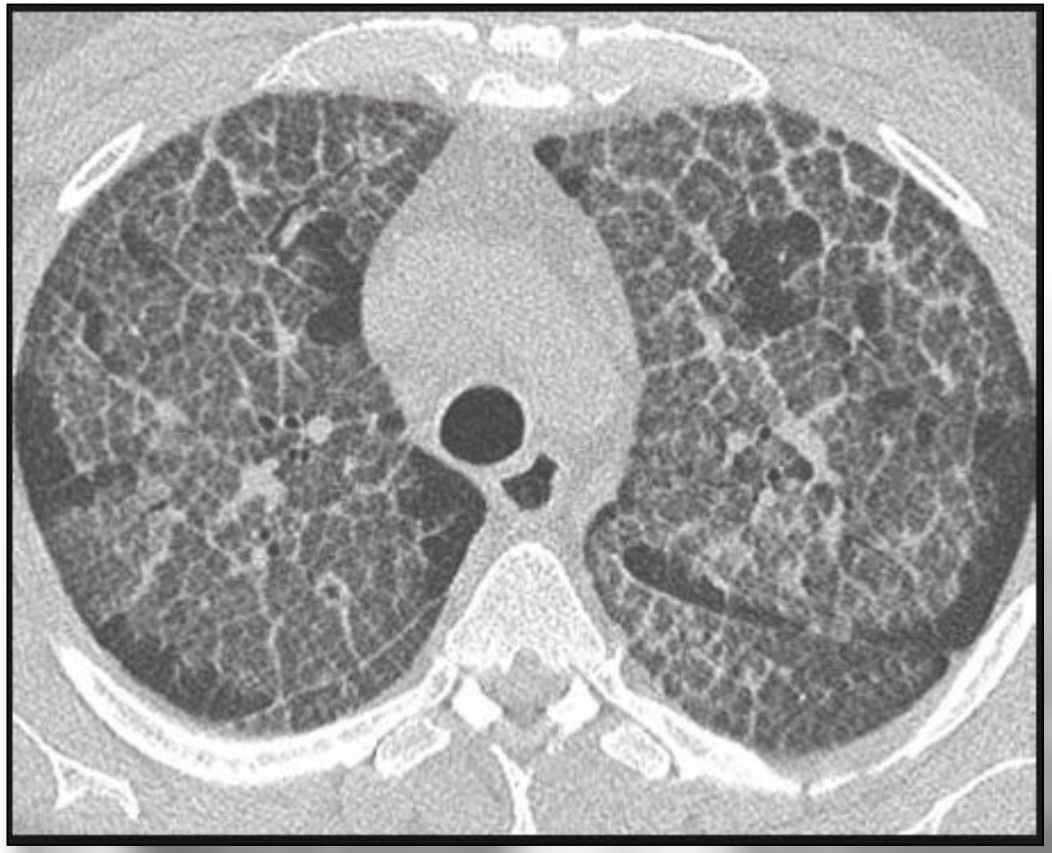
PAP Symptoms

- Shortness of breath
- Cough
- Chest pain
- Fatigue
- Low oxygen
- Respiratory failure (in severe cases)

PAP Diagnosis

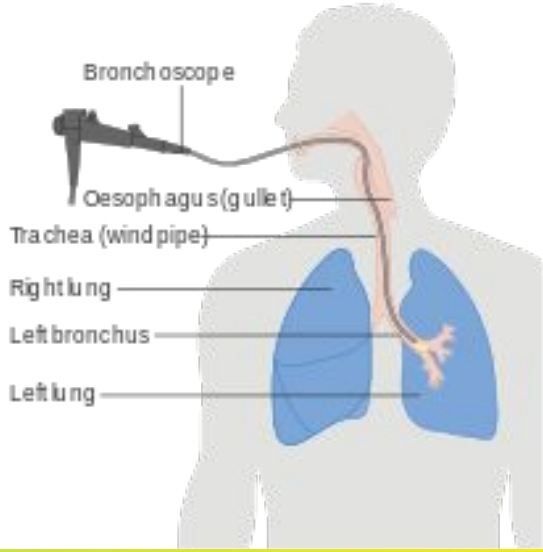
Chest CAT scan (CT) typically shows a pattern called “crazy paving”





PAP Diagnosis

- Diagnosis can be made with a bronchoscopy
- For “Primary PAP” (autoimmune; most common type), a blood test showing elevated levels of the GM-CSF antibody is nearly 100% accurate for diagnosis
- There is no need for lung biopsies but given the rarity and lack of experience with PAP, many patients still get biopsies – these can help with diagnosis but do not identify the cause (i.e., primary or secondary)



PAP Complications

- Low oxygen requiring home oxygen
- Respiratory failure requiring ventilator support or lung transplant
- Infections involving the lung and other parts of the body, including “opportunistic” infections, commonly involving a bacteria called Nocardia which can also cause abscesses in the brain
- Pulmonary fibrosis (permanent scarring of the lungs)
  - ✔ Appears to occur in 10-20% of PAP patients
  - ✔ Active area of research

The Good News

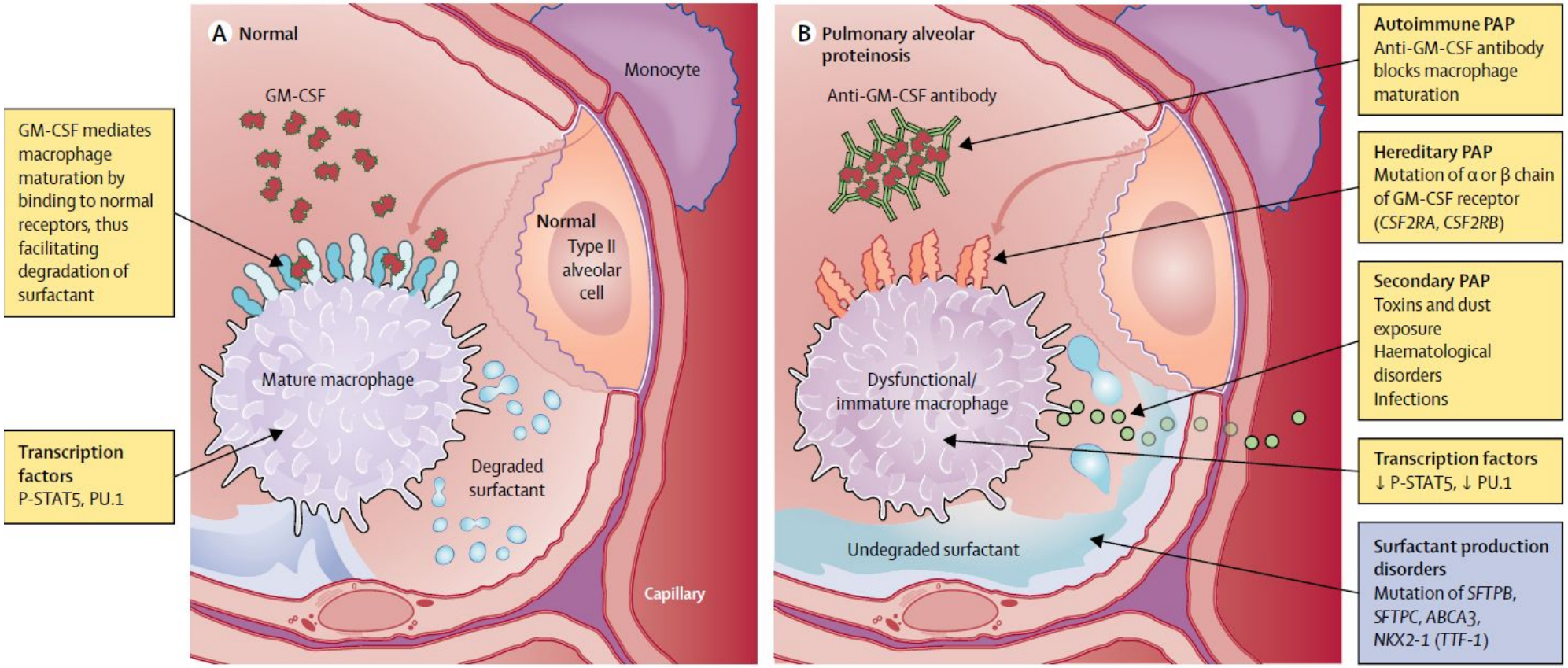
- Most PAP patients will have a relatively normal lifespan with proper identification, management, and therapies
- There is lots of hope as there are multiple therapies currently being researched by dedicated and caring doctors who are united with the PAP community through the PAP Foundation and Rare Lung Disease Consortium

PAP Therapies

- **Whole lung lavage** – performed in operating room under general anesthesia (you are asleep) with typical 0-2 day hospital stay
- Patients can require 30+ liters of the salt water "lavage" to thoroughly wash out each lung (~16 gallons for both lungs!)
- Generally effective but a bit invasive (risky) and the benefit is only temporary (until surfactant fills the lungs again)

PAP Therapies

1. **Give GM-CSF back to the alveolar macrophages (immune cells) to allow them to mature and work properly again**



GM-CSF Clinical Trials

- IMPALA-1 trial showed improvement in quality of life and improvement of one pulmonary function test called the “DLCO”
- PAGE trial showed improved A-a gradient (another way of measuring oxygen levels in blood) and an improved amount of protein on CT scans
- Both used inhaled forms of GM-CSF and side effects were minor/minimal but overall results not good enough for FDA approval
- IMPALA-2 trial recently published and showed improvement in quality of life, DLCO, and exercise capacity – fingers crossed for an FDA approval late this year!!
- Two ways to get inhaled GM-CSF therapy currently
  - Off-label leukine through your insurance company (Partners has patient assistance program available)
  - Expanded access program for molgramostim through a participating site

PAP Therapies

2. Get rid of the antibodies that are inactivating the GM-CSF

- **Option 1: Rituxan**
  - ✔ A chemotherapy type agent
  - ✔ Knocks out all of the body's B cells (cells in your body that make antibodies)

- **Option 2: Plasmapharesis**
  - ✔ A machine that filters your blood to get rid of antibodies quickly
  - ✔ Requires large IV in leg or neck

Therapies of Interest

3. Decrease cholesterol to <u>reduce the severity</u> of the disease

- **Pioglitazone (medication for diabetes)**
  - ✔ Helps alveolar macrophages (immune cells) clear out cholesterol and surfactant
  - ✔ Found to significantly improve PAP lung disease in mice
  - ✔ Clinical trial completed at Cincinnati Children's

- **Statins (medications for high cholesterol)**
  - ✔ Improves PAP lung disease in mice by reducing cholesterol levels
  - ✔ We have seen cases of patients improving on statins

nature COMMUNICATIONS

ARTICLE

DOI: 10.1038/s41467-018-05491-z OPEN

Statin as a novel pharmacotherapy of pulmonary alveolar proteinosis

Cormac McCarthy[1,2,3,4], Elinor Lee[5,6], James P. Bridges[2], Anthony Sallese[1,2], Takuji Suzuki[1,2], Jason C. Woods[3], Brian J. Bartholmai[7], Tisha Wang[5,6], Claudia Chalk[1,2], Brenna C. Carey[1,2], Paritha Arumugam[1,2], Kenjiro Shima[1,2], Elizabeth J. Tarling[6,8] & Bruce C. Trapnell[1,2,3,4]

Other Therapies

- Oxygen
- Pulmonary rehabilitation (structured exercise program for people with lung disease)
- Prevention of infections
  - ✔ Hand washing
  - ✔ Antibiotics – I routinely prescribe antibiotics 2-3 times per week in an attempt to prevent Nocardia and other infections seen in PAP
  - ✔ Routine vaccines
- Lung transplant
  - ✔ Last resort but the only therapy for severe permanent lung scarring
  - ✔ Unfortunately PAP has been reported to recur after lung transplant

Thank you so much for attending today!

This is **our time** - let's make a difference together.

Thank you to UCLA and all of the wonderful patients and families! We did some amazing research here that would not have been possible without you!