

### Transcript Details

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Asthma CSI: Behind the Cytokine Curtain, Part 2: Scene of the Crime

### Announcer

You're listening to *Asthma CSI: Behind the Cytokine Curtain*, sponsored by Amgen and AstraZeneca.

Part 2: Scene of the Crime

*[The sound of boots on wet pavement is heard as Doc makes her way down the street to the crime scene. She passes by a Paperboy shouting out the latest headline.]*

### Paperboy

*"Extra, Extra, read all about it! Trouble at the Airway Epithelium! Inflammation strikes again at the Pillar of the Pulmonary Community! Extra!"*

### Doc (inner monologue)

*Word travels fast. I've got to get the scoop on this case of severe asthma before it gets away from me and the team. I'm just a couple of blocks away from the Airway Epithelium, the scene of the crime. My mind whirs with images of what I might find there and what my team had to say about the case before I left—*

### Professor [in flashback]

*...You need to keep in mind that asthma patients can have overlapping inflammatory phenotypes, and their dominant phenotype can change over time<sup>1-3</sup>...*

### Cipher [in flashback]

*...There are a lot of players involved in the asthma inflammatory cascade, from cells to cytokines to alarmins to everything in between. There even seem to be multiple types of inflammation<sup>4-6</sup>...*

### Doc (inner monologue; in the present)

*Professor and Cipher are right on the ball, as usual. Everything they're saying points to asthma as complex, heterogenous, and dynamic. But all complexities aside, I'll get to the bottom of this case. I have to. People are counting on me.*

*[Doc stops. She's arrived: The Airway Epithelium stands across the street from her with a crowd of Insults loitering out front.]*

### Doc (inner monologue)

*Ah, the Airway Epithelium: Protective barrier<sup>7,8</sup>. Mediator of immunity<sup>8</sup>. "Pillar of the pulmonary community," to quote the papers. And yet, on the outside at least, I've never seen so many shady characters in one place. Viruses, allergens, pollutants, and bacteria<sup>4-6</sup> are gathered around like a flock of birds, chattering amongst themselves. They size me up as I cross the street and approach the airway.*

*[Doc approaches the crowd. The Insults' conversations focus on her as she nears.]*

### Virus

Ay, you goin' in there, Doc? Mind if I take a peek?

### Allergen

Yeah, how 'bout I tag along with ya?

### Bacterium (winking)

You look like you could use a friend on the inside, am I right? Or am I right?

*[Doc pushes through the crowd]*

**Doc**

I'm good, thanks.

**Bacterium (annoyed)**

Well you can just keep movin', then! Or take a picture! It'll last longer.

*[Doc pauses, but then continues through the crowd]*

**Doc (throwaway)**

I would, but it wouldn't be a pretty picture to look at, would it?

**Several Insults (simultaneous)**

Oooooooh!

*[The Insults' chatter resumes as Doc continues to the door. When she tries it, she realizes it's locked. The Insults sneer and mumble various taunts]*

**Doc (inner monologue)**

*Locked. Rats! The Airway Epithelium must be on high alert. Getting eyes on the scene inside may not be as easy as just walking through the front door. Guess it's time to put Cipher's earpiece to use.*

*[Doc pages Cipher with the earpiece. Cipher picks up]*

**Cipher (all business)**

Go for Ciph.

**Doc**

Hey Ciph, it's Doc. I'm— What are you doing?

**Cipher**

Sorry, Doc. Lots going on around here. What's up?

**Doc**

I need to get into the Airway Epithelium. I'm outside and the door is locked.

**Cipher**

Hmm, did ya try jiggling the handle?

**Doc**

Cipher...

**Cipher**

You never know!

**Doc (sighing)**

Aren't you the one always saying that the Airway Epithelium is a key factor in asthma pathology and the first point of contact for external triggers<sup>4-7</sup>? *[lowers voice]* I'm surrounded by some of those external stimuli. They're not very nice, and I'm pretty sure they tried jiggling the door handle a few times.

*[a beat. Cipher waits.]*

Okay, fine!

*[Doc jiggles the handle. The door doesn't budge.]*

See?

**Cipher**

Alrighty! Well I always like to try the old-fashioned way before bringing in the super-tech.

*[Cipher types lightning-fast keycodes into her computer, gaining access to the lock.]*

*[The door lock releases and the heavy door swings open with a gush of released air.]*

**Doc**

Thanks, Ciph.

**Cipher**

No problem, Doc. Hey, be careful in there.

**Doc**

I will.

*Doc (inner monologue)*

*Cipher might seem pretty intense, but she's a big softie on the inside. Sometimes I think she sends an earpiece with me on every case for her own sake.*

*[With Cipher still on the line, Doc passes through the doorway into the Airway Epithelium. Doc clocks the details of the scene and describes them to Cipher]*

**Doc**

Sheesh, looks like a tornado decided to walk in and get cozy for a while. These walls are thickened and inflamed<sup>7</sup>. I see increased mucus production along the tissue lining, and some branching airways are almost completely blocked off<sup>7,9</sup>. There's even evidence of sub-epithelial inflammation and fibrosis going on, which can lead to fixed airway obstruction<sup>10</sup>. It's a real mess in here, alright.

**Cipher (serious)**

Okay. There are few things you should know before you go any further, Doc.

What you're seeing – the structural changes in the airway wall, the thickening of the airway smooth muscle – those are the features of airway remodeling, which in addition to airway inflammation, likely contributes to abnormal lung mechanics<sup>11</sup>.

**Doc**

Roger that.

**Cipher**

Good. But there's more you'll need to know if you want to understand what's really going on in there. I mentioned airway remodeling, but there are actually several structural changes that can be consistent with remodeling, including smooth muscle hypertrophy, basement membrane thickening, and goblet cell hyperplasia<sup>7,9-11</sup>. And don't forget about the problem of airway hyperresponsiveness, which is an exaggerated broncho-constrictive response to various stimuli resulting in narrowing of the airway<sup>11</sup>.

**Doc**

Got it. Airway inflammation and remodeling, abnormal lung mechanics, and airway hyperresponsiveness. Anything else?

**Cipher**

There's *always* something else! But those are key processes in the pathophysiology of severe asthma<sup>7,9-11</sup>, so keep them in mind, keep your eyes peeled, and keep me posted.

**Doc**

Thanks, Cipher.

*[Doc ends the call.]*

*[Doc makes her way around the crime scene when she hears heavy footsteps approaching her. The PI rounds the corner and marches over.]*

*Doc (inner monologue)*

*I know who's making those heavy footsteps without needing to turn around. That's the PI, short for Pulmonary Investigator. The first guy on the scene. The last guy to leave. If anyone's got an inside scoop on this crime, it's going to be him. He lives and breathes this stuff.*

**Doc (familiar)**

Well look who the cat dragged in. Been a while. What've you got so far?

**PI**

Hey Doc. Welcome to the case. It may look like a downright mess, but at the end of the day, you won't need to look much further than all

those IgE antibodies and other telltale proteins left behind. They're all over the place, really.

**Doc (inner monologue)**

*Interesting. Protein calling cards left at the scene. I make a mental note to bring this up to the Professor later.*

**Doc**

I think I'll take a look around. Get the lay of *the lung*, so to speak.

**PI**

It's all yours, Doc. Gimme a holler if you need anything.

*[With that, the PI trods heavily away]*

**Doc (inner monologue)**

*The PI isn't wrong. This place is littered with IgE antibodies and other proteins, which points a few fingers at whoever left them behind. But Cipher's warnings on airway remodeling and hyperresponsiveness make me think this could go beyond some protein-trailing or IgE-producing cells. The PI didn't mention any of that—*

*[Suddenly, bands of smooth muscle get agitated]*

*The floor just moved under me and one of the smaller airways to my left tightened into a small opening at best. It looks like this Airway Epithelium still has more hyperresponsiveness in store for us. That puts me in the middle of an active crime scene, which is not a good place to be for long.*

*[Doc dials but there's no signal]*

*I can't get through to the Professor. This remodeling and hyperresponsiveness must be messing with both the airway and my earpiece's airwaves by extension. Not sure the Professor would have answered my call anyway. But something's not adding up. I better check back in on the PI.*

*[Doc walks up to the PI]*

**Doc**

Hey, I noticed things are still pretty active around here. Is there anything else you can tell me?

**PI (confident)**

Well, with these trails of evidence and signs of airway narrowing, three main suspects come to mind: the Eosinophil, the IgE-Producing B cell, and the Airway Smooth Muscle Cell. Pretty open and shut case to me, whether it's one of 'em acting solo or all of 'em working in cahoots. Tell ya what: why don't I bring 'em by Asthma HQ so you can wrap things up before lunch? Sound good to you?

**Doc (inner monologue)**

*This PI has picked out an interesting cast of characters, and he's right to look their way first given everything we're seeing in here. But I think he may be quick on the draw. Who's to say which of these suspects, if any, are calling the shots on this exacerbation?*

**Doc**

Happy to speak with each of them back at HQ, but let's keep the line open and an open mind alongside it just in case there's more to what we're seeing. Speaking of which, would you mind setting up some surveillance in here so we can keep eyes on the crime scene? I've got a feeling there's still more to see and hear from this side of the Airway Epithelium.

**PI**

Done and done, Doc. Let's stay in touch if anything comes up.

**Doc**

I like the sound of that. So long!

*[Doc exits back through the door and starts heading to Asthma HQ. She walks past the Insults as they continue to taunt her]*

**Virus**

Hey, look who's back! Where you goin'? Leaving so soon?

**Allergen**

You want us to keep an eye on the place while you're gone? We can do that!

**Bacterium**

Yeah, we'll be your eyes on the inside! Give you all the *hot* goss with our solid intel!

**Doc**

Intel requires intelligence. I'll pass.

**Several Insults (simultaneous)**

Ooooohhh!

*[Insults continue chattering away as Doc heads back to Asthma HQ]*

**Doc (inner monologue)**

*They're nothing if not persistent. But I hurry out of there and I move back toward Asthma HQ. I've got to get this information to the team while it's still fresh in my mind. Suspects like the Eosinophil, IgE- Producing B cell, and Airway Smooth Muscle Cell need some thinking through... definitely more to investigate here.*

*[Doc continues walking. Suddenly a second pair of footsteps falls into rhythm with hers.]*

**Doc (inner monologue)**

*I've been so wrapped up in my own thoughts, I almost miss the sound of someone following behind me, staying out of sight.*

*[Doc stops, and the footsteps stop as well. She continues on and the second footsteps continue again.]*

*The footsteps are moving in sync with mine, like the stepper doesn't want to draw my attention. But in this job, everything draws my attention...*

*And just like that, the plot thickens, again. I believe I've just picked up a Tail.*

**Announcer**

You've been listening to *Asthma CSI: Behind the Cytokine Curtain*, sponsored by Amgen and AstraZeneca.

Join us next time for Part 3: The Tail.

For access to additional episodes and information about severe asthma, visit [ReachMD.com/AsthmaCSI](https://ReachMD.com/AsthmaCSI)

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