

Transcript Details

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Asthma CSI: Behind the Cytokine Curtain, Part 4: The Suspects

Announcer

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

Part 4: The Suspects

[Doc walks down the stairs, approaching the ground floor.]

Doc (inner monolog)

I'm on my way down to meet our inflammatory suspects in the case of severe airway exacerbation: Eosinophil, IgE-Producing B Cell, and Airway Smooth Muscle Cell. These three shift characters are somehow involved in the mess down at the Airway Epithelium, and it's my job to find out what they know.

Finally at the bottom of the stairs, I cross through the lobby and check in with Phil before descending into the conference rooms.

Doc

Hey, Phil.

Phil

If it isn't Doc! Guess what, the elevator's working!

Doc

What, really?!

Phil (laughing)

Nah, I'm just messing with ya. It's still out. But the PI is downstairs waiting for you in the conference area. He came in with a rag-tag bunch of suspicious-looking cells.

Doc

Thanks, as always. Bu- No more elevator jokes, though, please.

[Phil chuckles]

Doc (inner monolog)

Phil goes back to typing and I cross the lobby to the basement stairwell. With a deep breath, I pull open the door and descend yet another flight of stairs. I know I've got to go into questioning these cellular suspects with an open mind, but it's hard to keep what the Professor told me out of my head...

Professor [flashback]

the Eosinophil is inflammatory in nature and gets a little sloppy with its proteins everywhere it goes.^{1,2} Likewise, B cells usually don't produce allergen-specific IgE. It's only after they're exposed to IL-4 and IL-13 that they switch to produce allergen-specific IgE. And the cells producing that IL-4 and IL-13? Well, they in turn may be taking orders from somebody else higher up.^{1,3-5}

Doc (inner monolog)

He didn't mince words about our Airway Smooth Muscle Cell suspect, either...

Professor [flashback]

This cell has a penchant for hyperreactivity and an eagerness to constrict the airway at the slightest taunts.^{1,2,6-9}

Doc (inner monolog)

A rowdy bunch, these cells. I'll have to keep my wits about me, because I can't shake the feeling that we may be looking at this case of severe airway inflammation the wrong way. Especially after my encounter with The Tail, which keeps running through my mind...

Tail [flashback]

Those inflammatory cells? They may not be the ones you're looking for neither. This thing goes higher up. Straight to the top.^{1,2,6}

Doc (inner monolog)

Maybe our suspects know something about that, too. Like the Professor said, we can't assume anything at this point. And we need to know what these cells know. No time like the present...

[Doc enters the conference area. The PI is waiting for her.]

PI
I've always loved these conference rooms. Who knew that questioning suspects could be so stylish?

Doc
Asthma HQ sure has an eye for design. Any last bits of advice before I go in?

PI
Well, they're a stubborn bunch, I'll tell ya that. But once you get 'em talking, I will bet they'll sing like canaries.

Doc
Thanks, PI.

PI
Oh, please, call me "Pulmonary Investigator." Or, John. But it's all good.

Doc (inner monolog)
I take in the scene in front of me. Seated at the long conference table are three very different cells. To the left is a sight for sore eyes: Eosinophil, swaggering in a swivel chair. He's got his poker face on and almost looks bored. He could be a tough nut to crack. Next is IgE-Producing B Cell, who is practically shivering with nervous energy. She might be easier to get information from if I can just keep her calm. Finally, we have the brute squad, himself, Airway Smooth Muscle Cell. He looks angry and I haven't even said anything yet. If I can play my cards just right, his quick temper could work in my favor.

[Doc clears her throat and addresses the group.]

Doc
Hello, everyone.

Airway Smooth Muscle Cell (snarky)
Glad to see those Insults didn't get to you back at the Epithelium.

Doc
Well, that's very kind of you, Airway Smooth Muscle Cell.

IgE-Producing B Cell
Yeah, you sure you're not too shaken up, Doc? Must have been scary on both sides of that Airway Epithelium.

Doc
You don't have to worry about me, IgE-Producing B Cell. I've handled worse. But let's get to the point, shall we? I believe you all know why we're here today.

Doc (inner monolog)
Eosinophil gives me his best smug expression.

Eosinophil (sarcastic)
Beats me, Doc. We're all just passers-by here.

Doc
Okay, then, Eosinophil. Let's start with you.

Doc (inner monolog)

That gets his attention. The smile comes down as he straightens in his chair and averts his eyes, trying to stay cool.

Doc

It's clear you were at the Airway Epithelium earlier today, which as you know is the site of a severe asthma exacerbation under current investigation. Your levels in the sputum and blood were elevated, and your proteins were scattered all around the place.^{1,2,6} Would you care to tell me what you were doing there?

Eosinophil

Funny you should ask. No, I'd care not to.

[The other two cells snicker]

Doc (inner monolog)

Eosinophil crosses his arms and doesn't offer anything up. I try a different approach.

Doc (matter of fact)

You made a real mess down there.

Eosinophil (quick and defensive)

I'm always messy, all right? Sheesh, don't be so uptight. Can't a cell have any fun without worrying about every last protein?

[IgE-Producing B Cell and Airway Smooth Muscle cell hold back laughter.]

Doc (inner monolog)

Eosinophil's putting on a show, but he can't even look me in the eye. That means he's hiding something.

Doc

Fun is one thing, Eosinophil, but severe asthma is another story.

Eosinophil

Listen, Doc. I like to party. Proteins are just my thing. Don't you worry about it.

Doc (coldly)

Seems like maybe I *should* worry about it. And when I get worried, I get *really* curious about cells that throw parties for one.

Eosinophil

Parties for *one*? With *this* smile?

Doc (inner monolog)

Eosinophil flashes me his pearly granular whites.

Eosinophil

Look, maybe I *did* leave some proteins at the site of asthma inflammation, but it wasn't just me there. That's not how I roll. No one's gonna call me some kind of loner.

[IgE-Producing B Cell shushes Eosinophil]

IgE-Producing B Cell

Shhh, Eosinophil!

Eosinophil (defensive)

What?! I got an image to maintain!

IgE-Producing B Cell (hushed tones)

Maintain it without talking, then!

Doc

Something you want to add, IgE-Producing B Cell?

IgE-Producing B Cell (nervous)

Nope.

Doc

Then why don't I pick up where you left off. There were trails of IgE all over the scene, as well, leading us right to you. Can you tell us anything about that?

Doc (inner monolog)

IgE-Producing B Cell blanches. She's a real Nervous Nelly, all right. She looks to her left and her right for some support, but the two cells on either side of her shake their heads as if to say, "You're on your own." She bites her lip before launching into her defense.

IgE-Producing B Cell (nervous)

Okay, sure, there was IgE there. But it wasn't my fault! I usually don't even produce allergen-specific IgE!³⁻⁵ You can't pin this on me, Doc!

Doc

All right, all right, B Cell. I get that IgE isn't normally your style, but these aren't normal times. If this severe exacerbation isn't on you, who's responsible?

IgE-Producing B Cell (nervous and quick)

Well, *you're* the one calling out all those eosinophilic proteins. How about leaning back on my friend here?

Eosinophil

Wow, thanks a lot, B.

(Eosinophil starts to sound more defensive)

And about our other friend here? Airway Smooth Muscle Cell. Why don't you ask *him* why he got so riled up at the crime scene?

Airway Smooth Muscle Cell (shrugging it off)

Hey, sometimes it's worth getting riled up, know what I mean?

Doc

Hold that thought, Airway Smooth Muscle Cell. I'm not done talking with your B Cell compatriot.

[A pause]

So then, why were you there? At the Epithelium?

IgE-Producing B Cell (hesitating)

Well...You see...I...

Doc (inner monolog)

IgE-Producing B Cell looks to her neighbors. They shoot her stern looks in return. She's clearly torn between what she wants to tell me and what her two fellow suspects will think.

Doc (cautiously)

It's okay. I just need to know why.

IgE-Producing B Cell (hesitating)

I was there because... because...

[Airway Smooth Muscle Cell interrupts]

Airway Smooth Muscle Cell

Because she wanted to be there! So what?

Doc (inner monolog)

Seems like IgE-Producing B Cell is on the verge of sharing something important. But if I can't get it out of her, maybe Airway Smooth Muscle Cell will do the talking for her.

Doc

Airway Smooth Muscle Cell, nice of you to chime in. Would you like to share why *you* were at the scene of the crime?

Airway Smooth Muscle Cell (unbothered)

It's a fun place to hang out. You could say I got an "in" there.

Doc

I hear you were pretty hyperresponsive throughout the exacerbation, though. What happened?

Airway Smooth Muscle Cell (sarcastic)

I'm a hothead, what can I say?

Doc

Tell me, is constricting airflow a normal part of your day?

Airway Smooth Muscle Cell (getting agitated)

Look, you're talkin' to the wrong cell.

Doc

Is that so? Because I've got reasons to believe I'm not.

Airway Smooth Muscle Cell (more agitated)

I said you've got the wrong cell! I mean, it wouldn't have even started with me!

Doc

Well, who would it have started with?

Airway Smooth Muscle Cell (explosive)

Not me! Someone else! We get orders...from...from someone *else*, alright?!?

[Airway Smooth Muscle Cell starts grunting in a worked-up state]

Eosinophil (sighing, disappointed)

Nice going, muscle head.

IgE-Producing B Cell (smug)

And here you thought it'd be *me* spilling the beans, just because I spill antibodies. Hmph!

Doc

Everybody, calm down. We're past pointing fingers. It's the truth I'm looking for. So out with it, then. Who's giving the marching orders?

Eosinophil

Listen, Doc. No disrespect, but we've said as much as we're gonna say. Come on, guys. This room's getting cramped, and one of us has some loosening up to do while he can still fit through that door.

[Chairs slide back as the suspects get up and start to walk out]

Airway Smooth Muscle Cell (leaving)

I just get so worked up...

IgE-Producing B Cell (leaving)

We know. Come on.

Doc (inner monolog)

I stand aside as the three cells file out. Not necessarily a dead end, but not what I expected, either. The mystery's still unsolved, but we've got another player behind this asthma attack after all. I've got no choice but to chase this lead because someone out there is dishing orders. And if it isn't one or more of our suspects...

[Doc steps out of the conference room. The PI is standing there, waiting for her]

PI

Doc, great timing. I've got something to show you.

[PI flips through some papers he's holding]

Take a look at this.

Doc (inner monolog)

The PI pulls out a print of a grainy black and white photo and hands it to me. I see a shadowy figure lurking inside the Airway Epithelium.

Doc

Is this from the crime scene?

PI
Yep, taken a few minutes ago from our surveillance cameras while you were in there with the suspects.

Doc
So, there's someone else involved after all...

PI
'Fraid so. Any idea who that could be?

Doc (inner monolog)
I take a closer look. A familiar vibe coming from this lone figure, staying just out of the spotlight. He looks to be holding something... maybe an eosinophilic protein? Hang on...

Doc
I think I recognize this one. He tailed me on the way to Asthma HQ earlier. He must've gone back to the crime scene after he spoke with me.

PI
You had a Tail?

Doc
Yeah. Nothing I couldn't handle. But he said that we weren't looking at the right suspects. That there's someone higher up that may be calling the shots.^{1,2,6} And that's exactly what our suspects just indicated, too.

PI
What do you think we should do next, Doc?

Doc (confident)
Next? Well that's the easy part. We're gonna head straight over to Cipher's lab, grab a cuppa joe, and wait. These suspects are going back to the scene of the crime, I guarantee you. They sound ready to talk, just not to us. But we'll be ready to hear them anyway.

PI
Oh, you mean by listening in through my surveillance? We can check in with my investigation unit, sure.

Doc
No, I mean Cipher's lab. Knowing her, she's already patched into your surveillance feed. It's kind of what she does.

PI
Huh! Well I'll be...

Doc
Come on. The coffee around here's not particularly good, but it doesn't get any better cold. And this case is heating up already...

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

Join us next time for Part 5: A Mastermind Revealed

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References

1. Gauvreau GM, Sehmi R, Ambrose CS, Griffiths JM. *Expert Opin Ther Targets*. 2020;24(8):777- 792.
2. Lambrecht BN, Hammad H. *Nat Immunol*. 2015;16(1):45-56.
3. Rael EL, Lockey RF. *World Allergy Organ J*. 2011;4(3):54-64.
4. Galli SJ, Tsai M. *Nat Med*. 2012;18(5):693-704.
5. Corren J. *Curr Allergy Asthma Rep*. 2013;13(5):415-420.
6. Lambrecht BN, Hammad H, Fahy JV. *Immunity*. 2019;50(4):975-991.
7. Brusselle G, Bracke K. *Ann Am Thorac Soc*. 2014;11 Suppl 8:S322-328.
8. Kaur D, Doe C, Woodman L, et al. *Chest*. 2012;142(1):76-85.

9. Brusselle GG, Maes T, Bracke KR. *Nat Med*. 2013;19(8):977-979.

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