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### Perspectives on Psoriasis: A Look at Its Pathogenesis

#### Announcer

Welcome to ReachMD. This medical industry feature, titled "Perspectives on Psoriasis: A Look at Its Pathogenesis" is sponsored by Dermavant. Here's your host, Dr. Linda Stein Gold.

#### Dr Stein Gold

Hello, and welcome back. I am Dr Linda Stein Gold, Director of Dermatology Clinical Research at Henry Ford Health System in Detroit, Michigan. And for Episode 2, which is the aryl hydrocarbon receptor signaling in psoriasis, I am again thrilled to be joined by my friend and colleague, Dr Jonathan Weiss, who joins us from Georgia. He's the President and the comanaging partner for Georgia Dermatology Partners. Welcome back, Jon.

#### Dr Weiss

Thanks, Linda, it's great to be back.

#### Dr Stein Gold

So in this section, which is Episode 2 of a three-part pod series, I'd like to talk a little bit about the pathogenesis and our understanding of the pathophysiology of psoriasis. We know that this is something that continues to evolve,(Armstrong A. JAMA. 2020)and we've come to understand the role of the aryl hydrocarbon transcription factor in psoriasis. Now, for many of us, this is something we did not learn about in residency. It's kind of a new pathway. So, Jon, can you explain how this fits into the pathogenesis of inflammatory skin disease?

#### Dr Weiss

Oh absolutely, Linda. It's really quite fascinating. The aryl hydrocarbon receptor is a ligand-dependent transcription factor that's found in all skin cells, including keratinocytes and immune cells, such as T-cells.(Szelest M. Int J Mol Sci. 2021)(Furie M. Int J Mol Sci. 2019) And the aryl hydrocarbon receptor plays several roles in skin homeostasis. It has some immune regulatory functions in that it regulates the immune balance of Th17, and so it regulates the production of proinflammatory cytokines, such as IL-17A and -F. (Szelest M. Int J Mol Sci. 2021, Furie M. Int J Mol Sci. 2019, Blauvelt A.Clin Rev Allergy Immunol . 2018, Brembilla NC. Front Immunol. 2018) It also has a role in skin barrier function. The aryl hydrocarbon receptor plays a critical role in barrier protein production, and that includes loricrin and filaggrin in keratinocytes, and those are downregulated in psoriasis.(Berboer JGM. J Invest Dermatol. 2012, Furie M. Int J Mol Sci. 2019) Finally, it also has some antioxidant activity, and the aryl hydrocarbon receptor regulates the balance of reactive oxygen species and antioxidant activity in the skin.(Dietrich C. Stem Cells Int. 2016) And, again, one of the most fascinating things about this is that it is a ligand-dependent process.

#### Dr Stein Gold

So, Jon, thanks for that overview. I think that was a really nice summary. And, as you mentioned, this is a ligand-dependent process. (Szelest M. Int J Mol Sci. 2021)(Furie M. Int J Mol Sci. 2019) I think it's important to take a step back and realize, what does a ligand-dependent process actually mean?

And what it means is that there are different ligands that can bind to this particular receptor. To me, I think about it kind of like a relationship. You know, the same receptor or the same person can be in different relationships. You might be in a relationship where you have a wonderful relationship and you might be in a relationship where it has a toxic relationship, a bad relationship. Well, the same thing when we say something is ligand-dependent.

This pathway behaves differently depending on who's binding. So, it's the same way with the AhR, this receptor. It can behave

differently depending on the ligand or who's binding to it.

So that's kind of interesting because this particular pathway is involved in a number of different processes in the body. Now, can you give us a little bit more insight, Jon, as to where is this process actually occurring? Is this something that occurs inside the cell, or does it actually occur on the surface of the cell, or outside the cell?

Dr Weiss

Yes. The aryl hydrocarbon receptor is an intracellular protein. It is actually inside the cell, and it then binds to the ligand and that affects production of cytokines and other factors that can actually then go outside the cell and have effects outside the cell.

Dr Stein Gold

Okay. Well, that helps to keep it in perspective and help us to understand as the science is evolving, it can be a little bit more difficult to keep up. And I think that was a really nice overview of how, AhR plays into inflammatory skin diseases like psoriasis.

So, Jon, I'd like to thank you for joining me for this podcast, which was AhR signaling and psoriasis. Again, this was the second part of a three-part series. The first was the burden of psoriasis. And please join us for Episode 3, where we'll talk about patient perspectives and the impact on psoriasis. So, Jon, thank you so much and thanks to everybody for joining us.

Dr Weiss

Thank you, Linda.

Announcer

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