# ALOPECIA AREATA MECHANISM OF DISEASE

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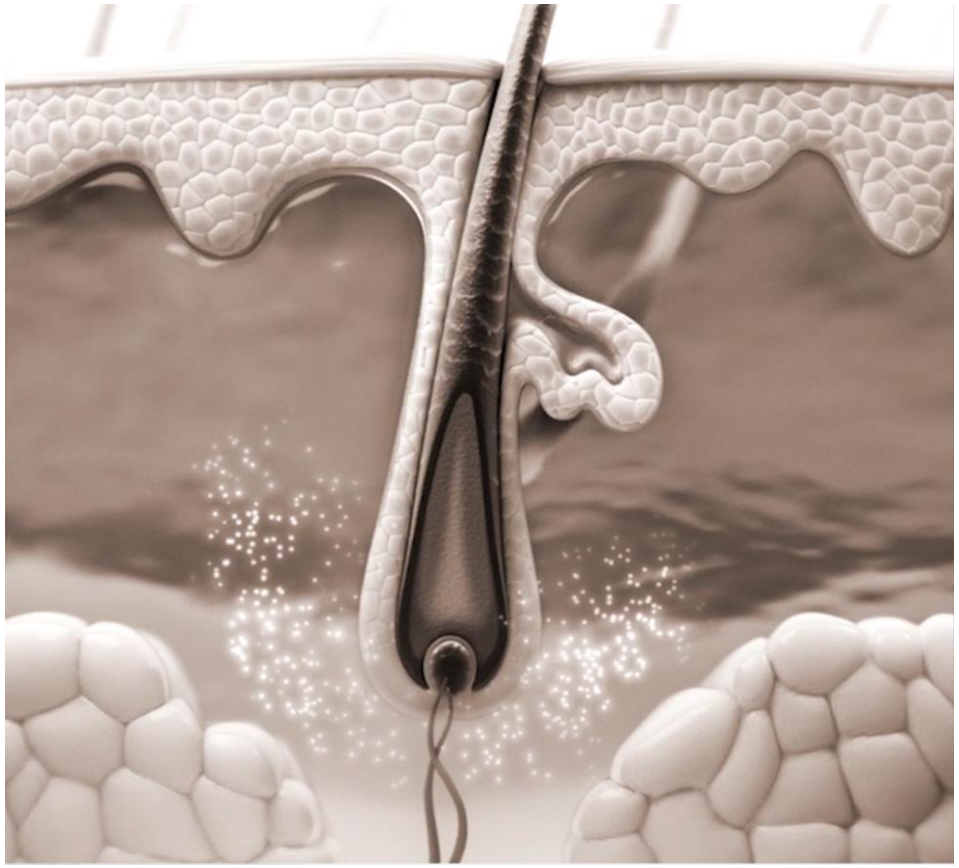
HCP=Healthcare Provider.

# Chapter 1

Unmet Needs in Alopecia Areata

# Introduction and Unmet Needs in Alopecia Areata



# Defining AA



- **Alopecia areata**, or AA, is an autoimmune hair loss disorder[1,2]
- AA causes well-defined, coin-shaped patches of non-scarring hair loss[1,2]

AA=Alopecia Areata.

1. Pratt CH, et al. *Nat Rev Dis Primers.* 2017;3:17011. 2. King BA, et al. *Dermatol Ther (Heidelb).* 2022;12(4):825-834.

# Presentation and Prevalence


**Hair loss in AA is varied and can include[1]:**

- Single well-defined patches
- Multiple discrete or overlapping patches
- Loss of hair in all hair-bearing sites, known as alopecia universalis

**AA affects nearly 2% of the population[2]**

AA=Alopecia Areata.

1. Pratt CH, et al. *Nat Rev Dis Primers.* 2017;3:17011. 2. Strazzula LC, et al. *J Am Acad Dermatol.* 2018;78(1):1-12.

# Comorbidities

Common comorbid disorders associated with AA include:

**Atopic dermatitis**

**Thyroid disease**

**Allergic rhinitis**

**Vitiligo**

AA=Alopecia Areata.

Wang EHC, et al. *Journal of Investigative Dermatology.* 2018;138(9):1911-1916.

# Psychiatric Comorbidities

- AA is also associated with psychiatric comorbidities such as **anxiety** and **depression**, affecting patients' quality of life

AA=Alopecia Areata.

Lee S, et al. *J Am Acad Dermatol*. 2019;80(2):466-477.

# Complex Etiology

- AA has a complex etiology with an unpredictable disease course, making management difficult

AA=Alopecia Areata.

Pratt CH, et al. *Nat Rev Dis Primers.* 2017;3:17011.

# FDA-Approved Therapies

Currently there are FDA-approved therapies, and the responses to current treatment options are variable

**FDA-approved therapies**

**Variable treatment responses**

FDA=Food and Drug Administration.

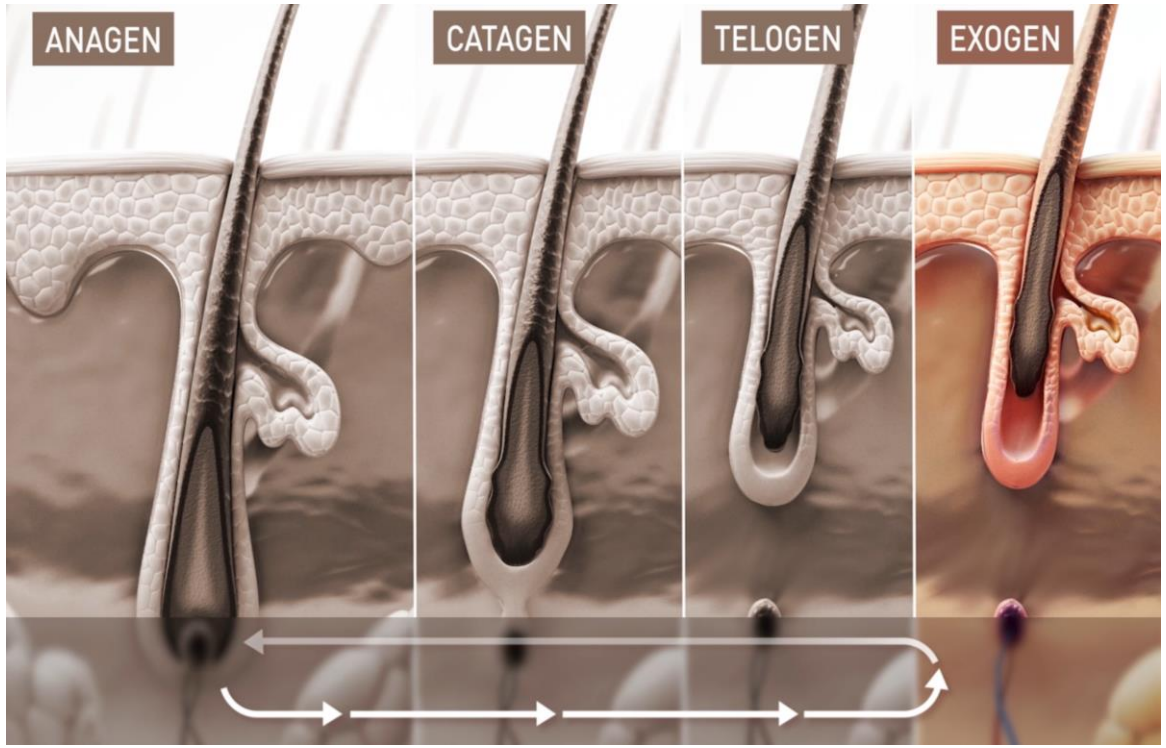
https://www.naaf.org/navigation-toolkit/fda-approved-jak-inhibitors/ (Accessed July 02, 2025).

# Chapter 2

Mechanism of Disease of Alopecia Areata

# Mechanism of Disease of Alopecia Areata

# The Human Hair Cycle

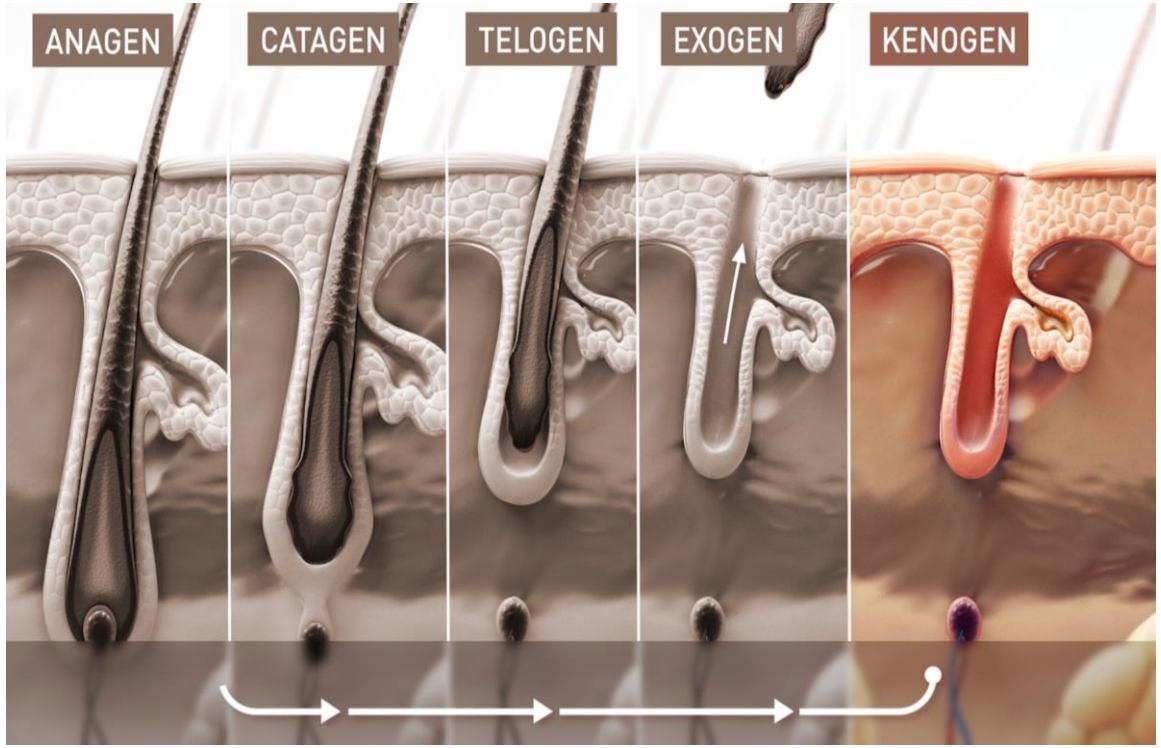



**The human hair cycle has 4 distinct phases:**

- **Anagen** is the growth phase
- **Catagen** is the transitional phase
- **Telogen** is the resting phase, where hair is shed towards the end
- **Exogen** is the phase where the follicle remains empty until the onset of the next anagen phase

Cotsarelis G, Botchkarev V. In: Kang S, Amagai M, Bruckner AL, Enk AH, Margolis DJ, McMichael AJ, Orringer JS, eds. *Fitzpatrick's Dermatology*; 9th edition. 2019:89-105.

# AA Disrupts the Hair Cycle

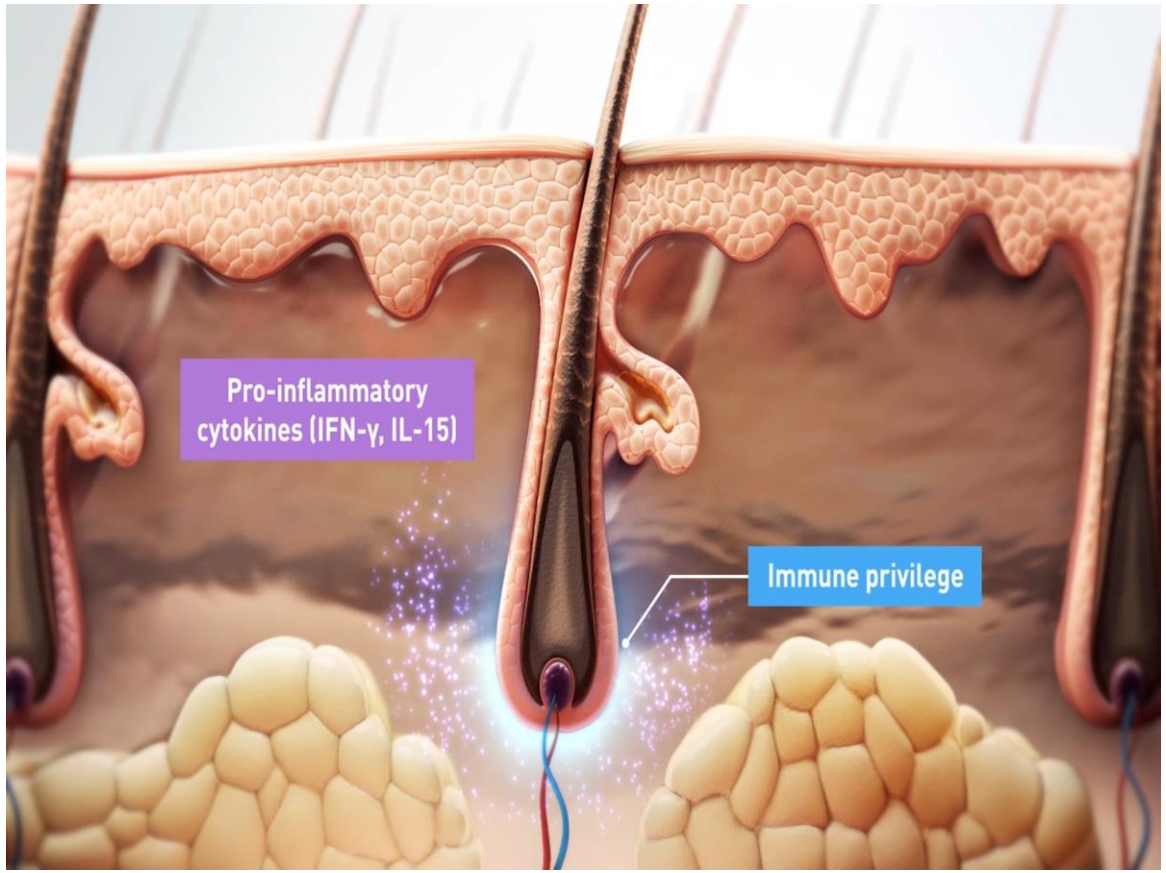



- In AA, the cyclical nature of hair growth is disrupted[1,2]
- Hair prematurely leaves the anagen phase and transitions through the catagen, telogen, and exogen phases[1,2]
- It then enters the **kenogen phase**, where the hair follicle remains empty and does not re-enter the growth phase[1,2]

AA=Alopecia Areata.

1. Bhat YJ, et al. *Hair Ther Transplant.* 2014;4:2. 2. Rebora A, Guarrera M. *Dermatology.* 2002;205(2):108-110.

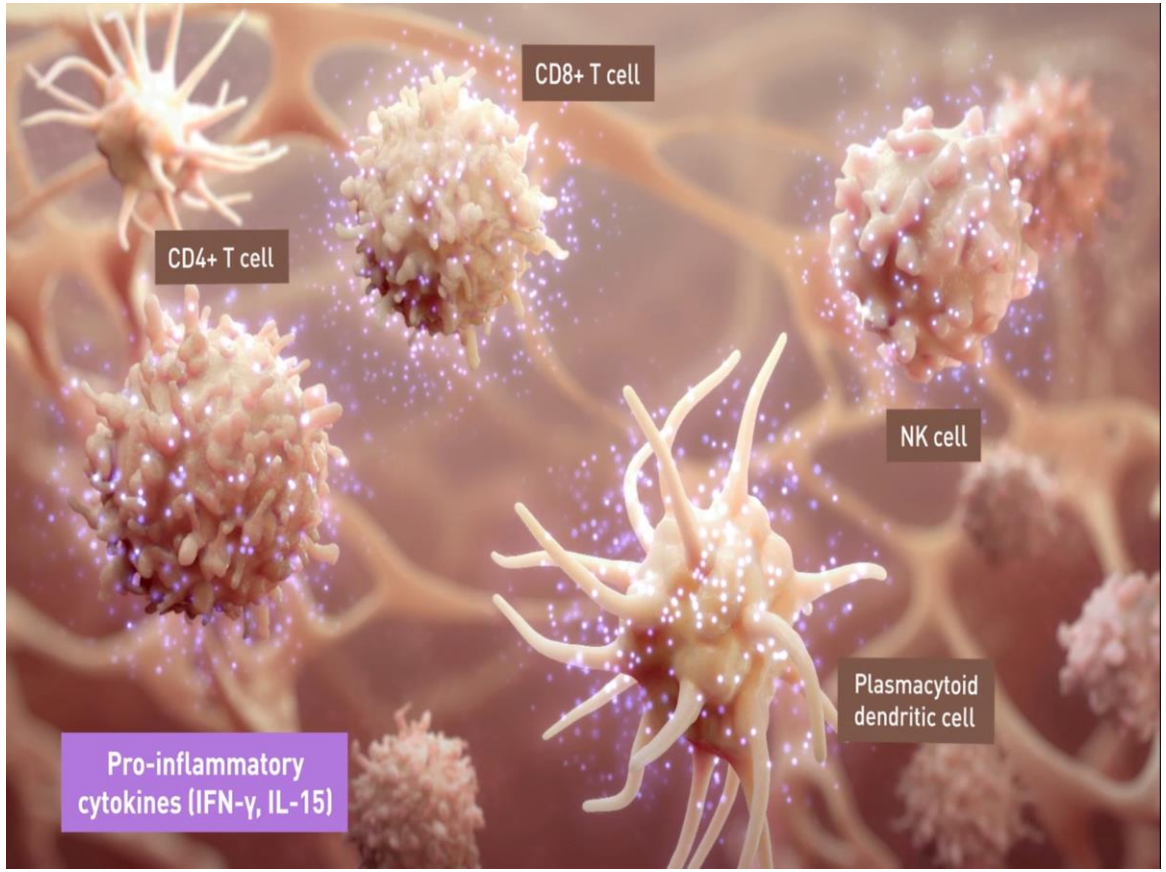
# Loss of Hair Follicle Immune Privilege




- The pathogenesis of AA and the interference of the hair growth cycle are believed to be phenomena resulting from loss of hair follicle immune privilege

AA=Alopecia Areata; IFN-γ=Interferon Gamma; IL-15=Interleukin-15.
Ito T. *Clin Dev Immunol.* 2013;2013:348546.

# Immune Privilege

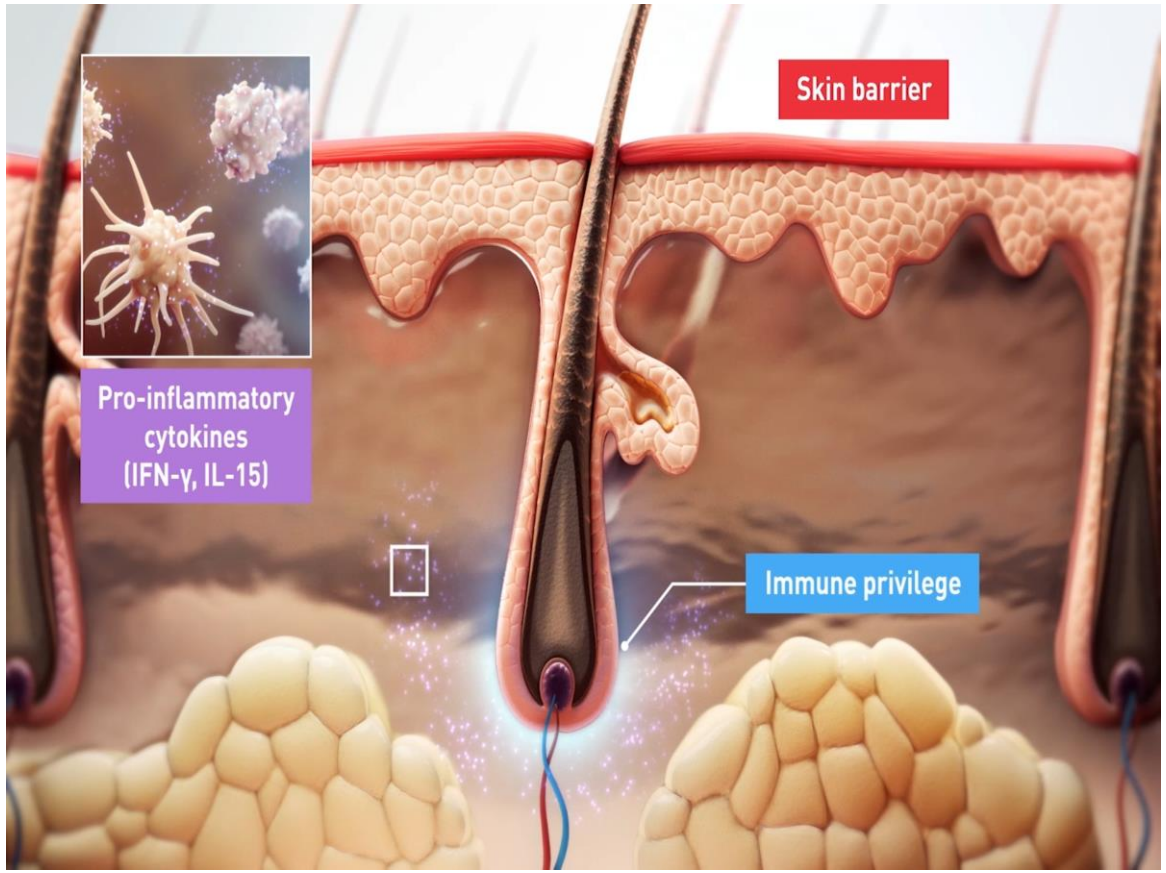



- Immune privilege is a complex mechanism that suppresses inflammation and promotes immune tolerance in the hair follicle[1-3]

CD4+ T cell=Cluster of Differentiation 4 T Helper Cell; CD8+ T cell=Cluster of Differentiation 8 T Helper Cell; IFN-γ=Interferon Gamma; IL-15=Interleukin-15; NK cell=Natural Killer Cell.

1. Ito T. *Clin Dev Immunol.* 2013;2013:348546. 2. Paus R, et al. *J Investig Dermatol Symp Proc.* 2018;19(1):S12-S17. 3. Azzawi S, et al. *Skin Appendage Disord.* 2018;4(4):236-244.

# Immune Privilege

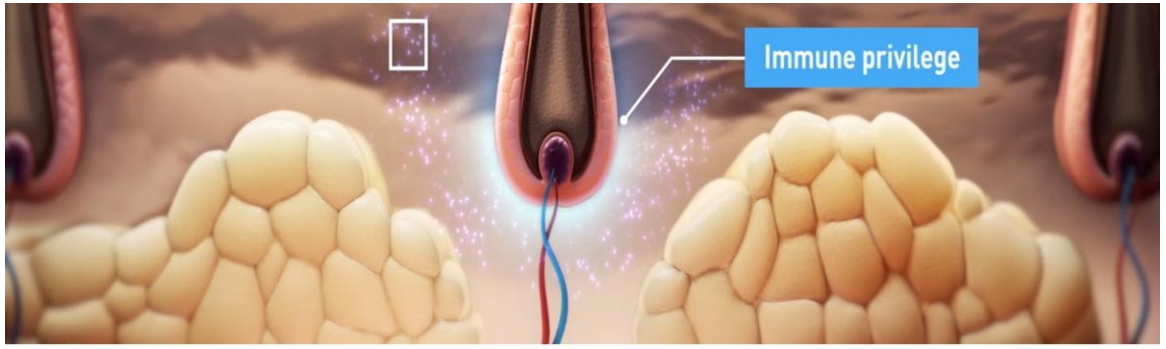



- Immune privilege protects the follicle from autoimmune attack[1,2]
- This process may be triggered by immunogenic autoantigen generated during anagen and exposed as a result of the apoptosis associated with cyclical hair growth[1,2]

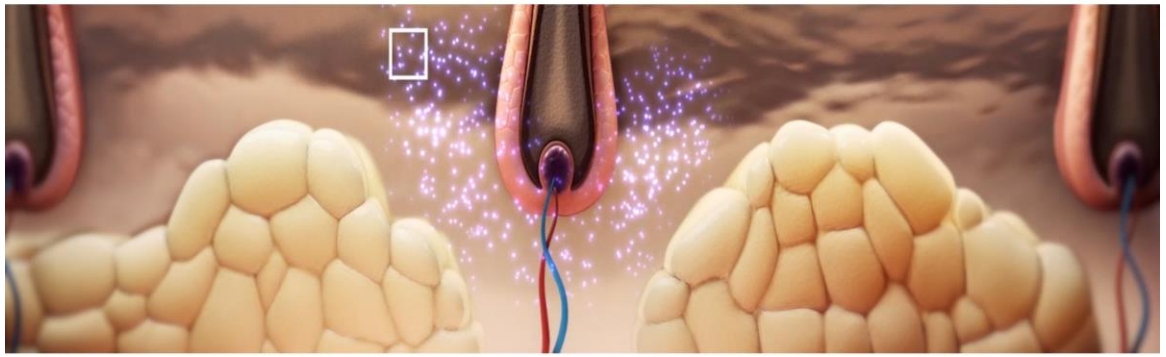
IFN-γ=Interferon Gamma; IL-15=Interleukin-15.

1. Pratt CH, et al. *Nat Rev Dis Primers.* 2017;3:17011. 2. Azzawi S, et al. *Skin Appendage Disord.* 2018;4(4):236-244.

# Immune Cell Infiltration




**Hair bulb with immune privilege**



**Hair bulb with loss of immune privilege and inflammatory cytokine swarm**

- Loss of immune privilege allows immune cells to infiltrate the hair follicle, leading to an inflammatory swarm around the anagen hair bulb

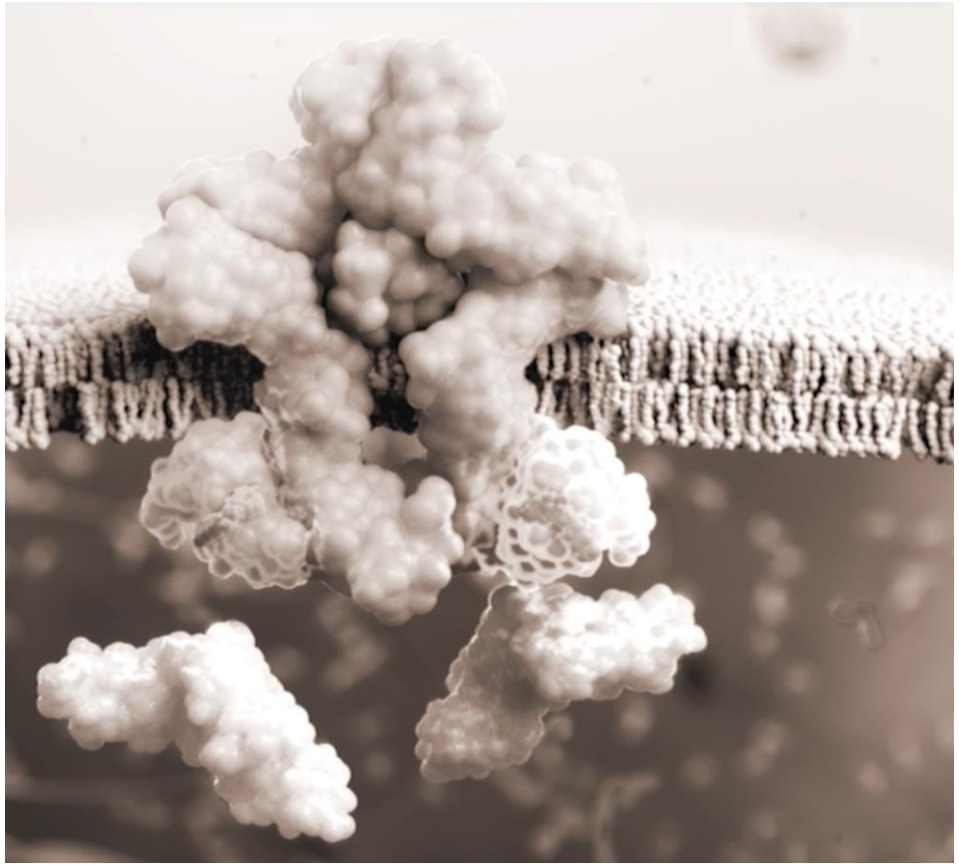
Ito T. *Clin Dev Immunol.* 2013;2013:348546

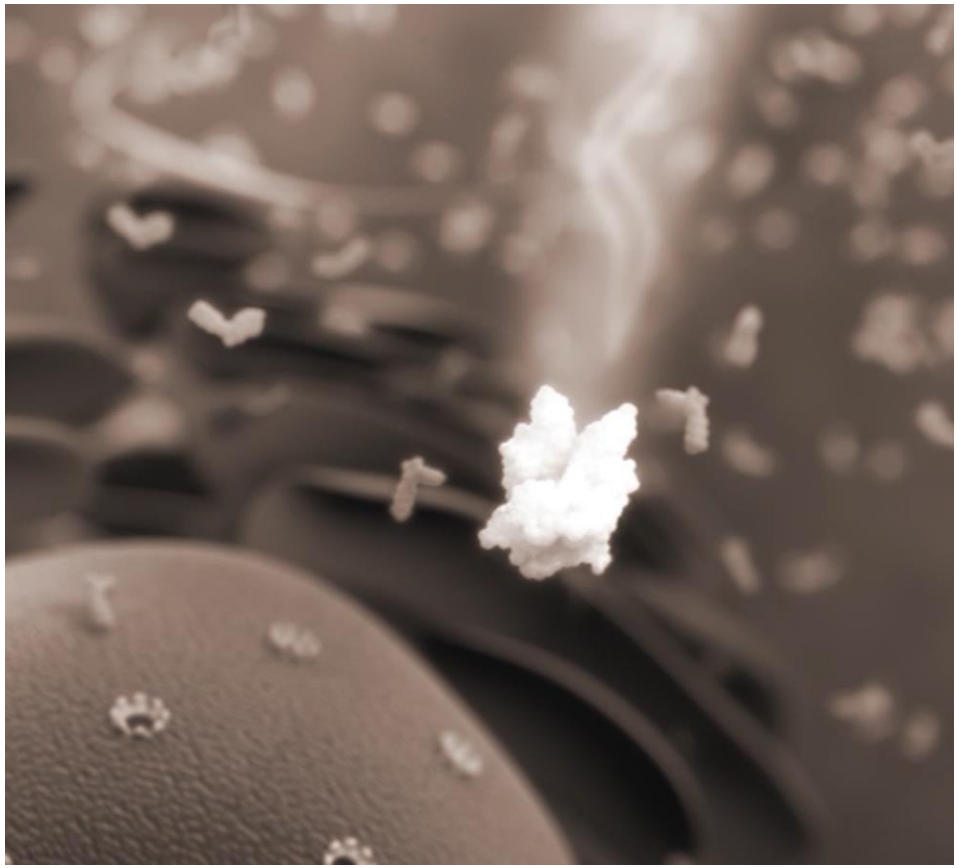
# Chapter 3

## The JAK-STAT Pathway in Alopecia Areata

JAK=Janus Kinase; STAT=Signal Transducer and Activator of Transcription.

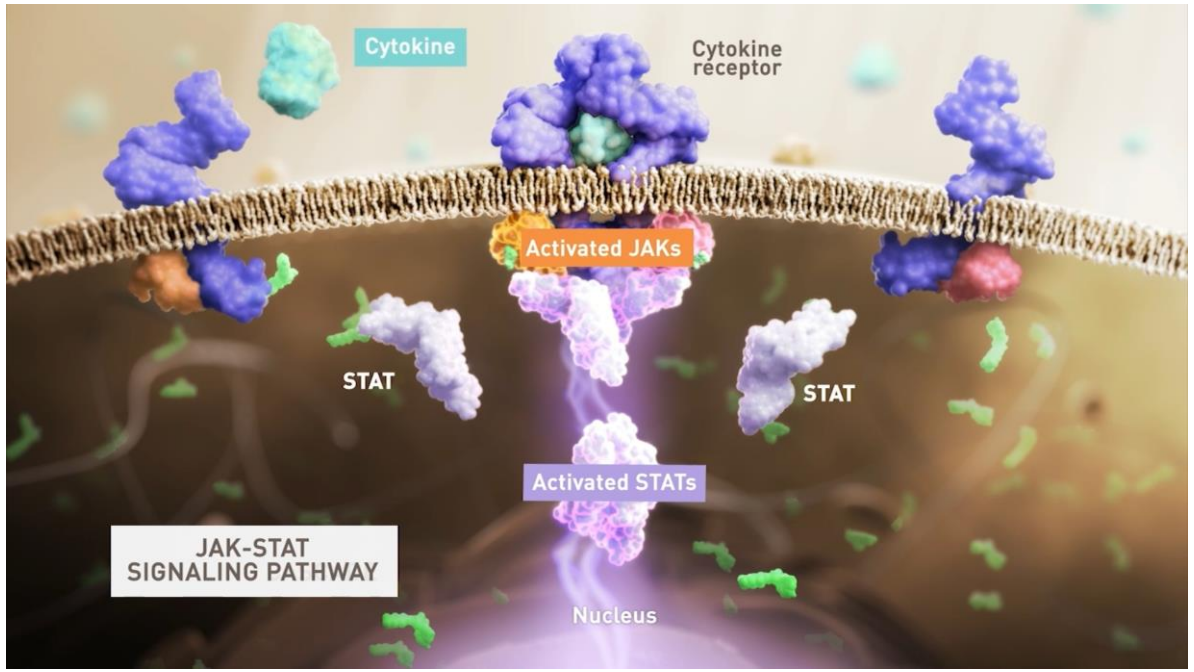
# The JAK-STAT Pathway in Alopecia Areata





JAK=Janus Kinase; STAT=Signal Transducer and Activator of Transcription.

# The JAK-STAT Pathway

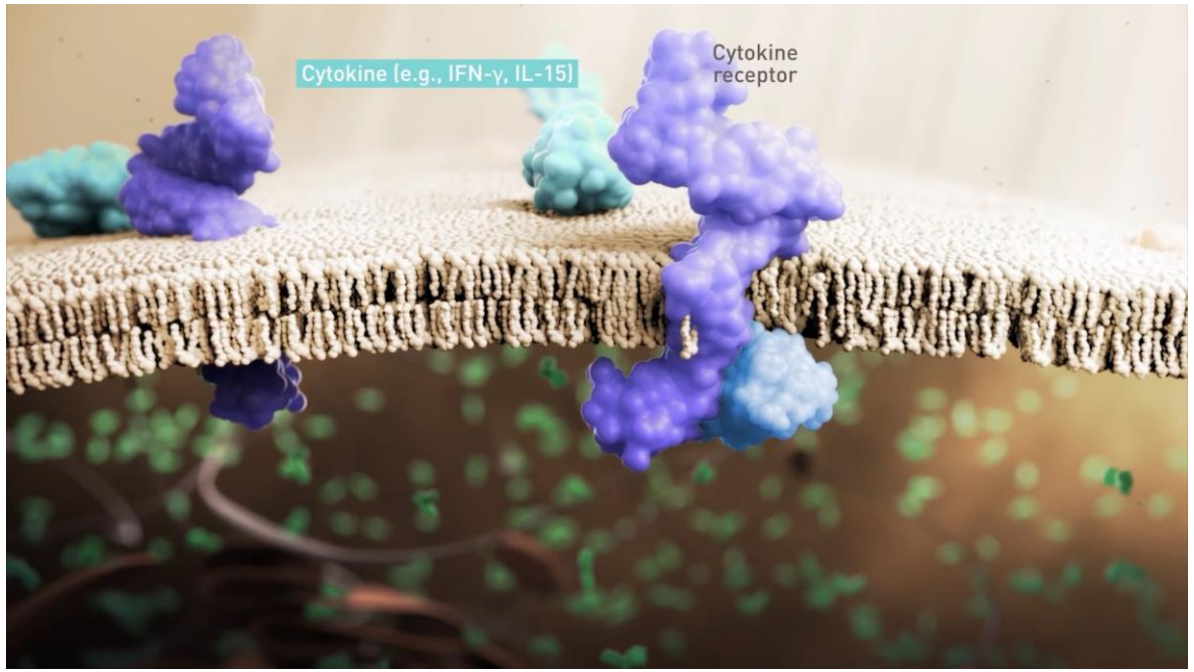



- The JAK-STAT pathway is a proinflammatory signaling pathway utilized by cytokines in AA[1,2]

AA=Alopecia Areata; JAK=Janus Kinase; STAT=Signal Transducer and Activator of Transcription.

1. Wang EHC, et al. *J Invest Dermatol*. 2018;138(9):1911-1916. 2. O'Shea JJ, et al. *Annu Rev Med*. 2015;66:311-328.

# The JAK-STAT Pathway




- Cytokines such as IFN-$\gamma$ and IL-15 are mediated by JAK kinases of the JAK-STAT pathway[1,2]

IFN-$\gamma$=Interferon Gamma; IL-15=Interleukin-15; JAK=Janus Kinase; STAT=Signal Transducer and Activator of Transcription.

1. Wang EHC, et al. *J Invest Dermatol*. 2018;138(9):1911-1916. 2. O'Shea JJ, et al. *Annu Rev Med*. 2015;66:311-328.

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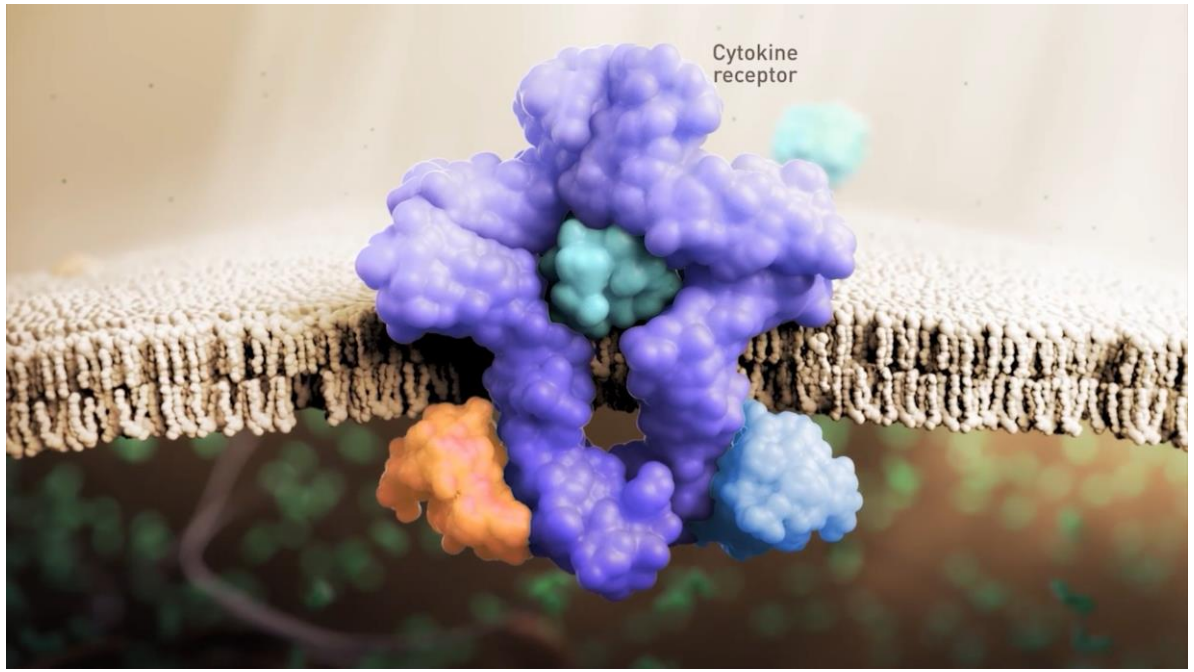


- The pathway is activated when ligand binding induces the dimerization of receptor subunits[1,2]

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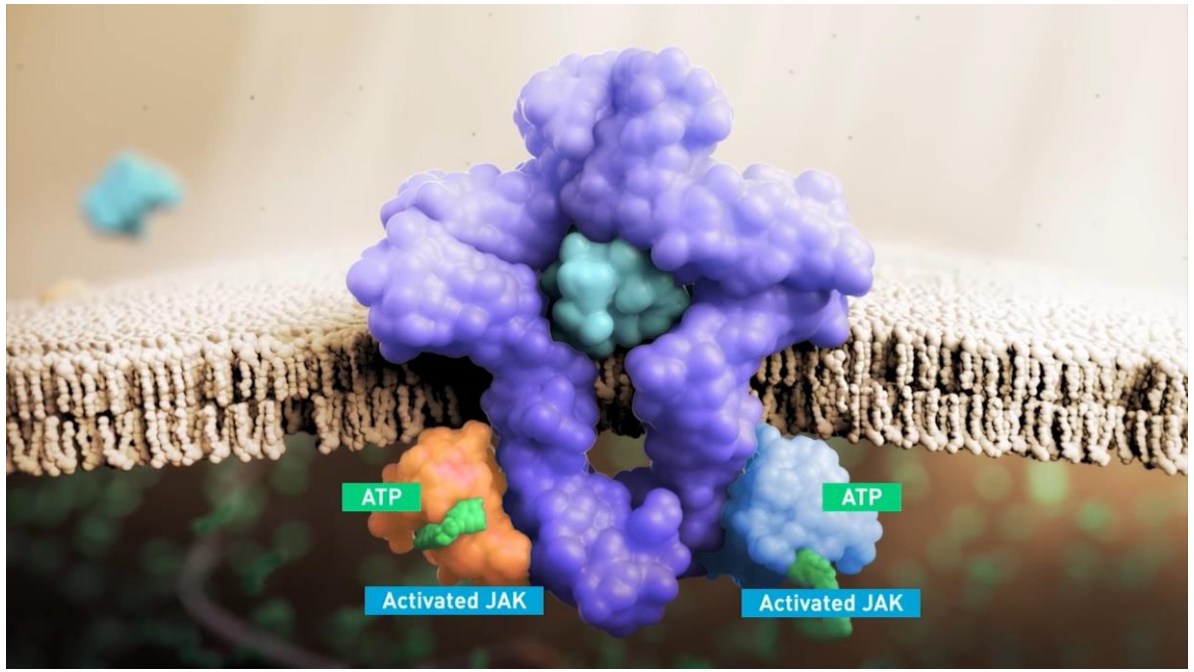
# The JAK-STAT Pathway




- Receptor-associated JAKs then bind ATP and become active[1,2]

ATP=Adenosine Triphosphate; JAK=Janus Kinase; STAT=Signal Transducer and Activator of Transcription.

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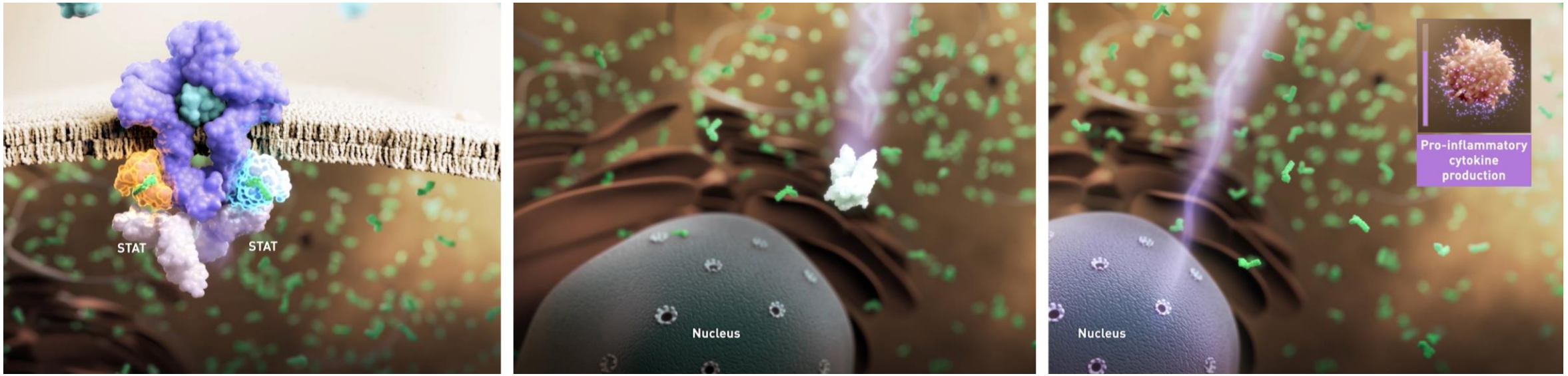
# The JAK-STAT Pathway




- Subsequent activation of STAT transcription factors, which translocate to the nucleus, regulate the transcription of genes involved in the production of proinflammatory cytokines responsible for disease maintenance in AA[1,2]

AA=Alopecia Areata; JAK=Janus Kinase; STAT=Signal Transducer and Activator of Transcription.

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