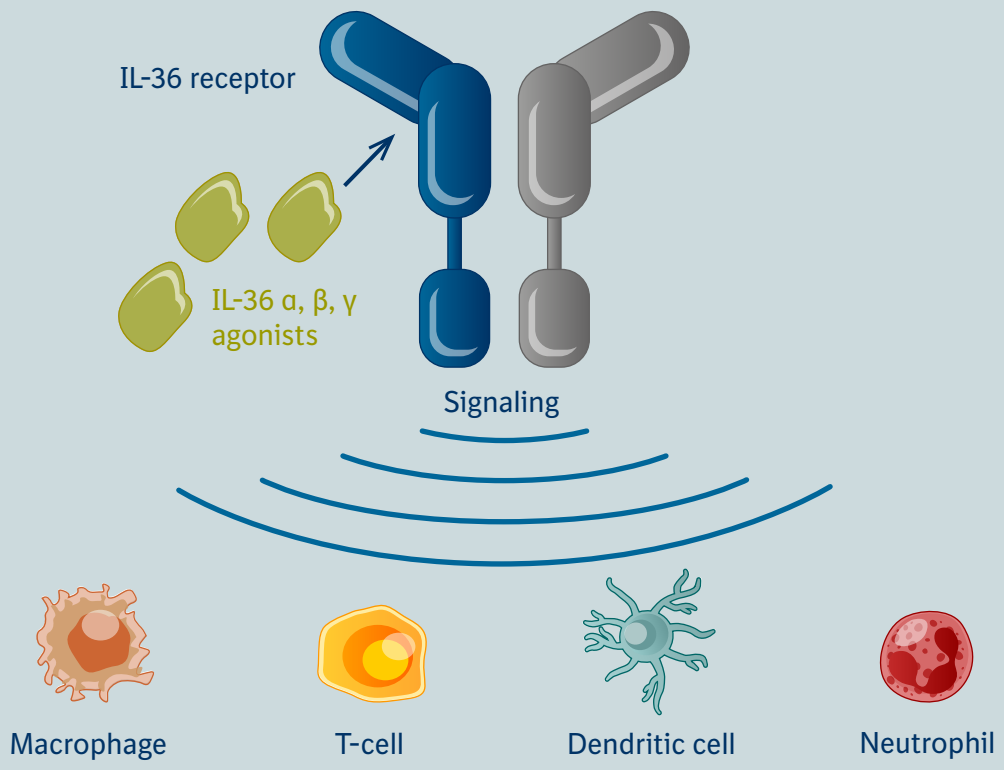
The IL-36 pathway and generalized pustular psoriasis

The **interleukin-36 (IL-36) pathway** plays an important role in **inflammation.**[1]

IL-36 cytokines are expressed by, and act upon, various types of cells – such as keratinocytes, epithelial cells and immune cells – and work together in balance to **regulate the inflammatory response.**[2–5]

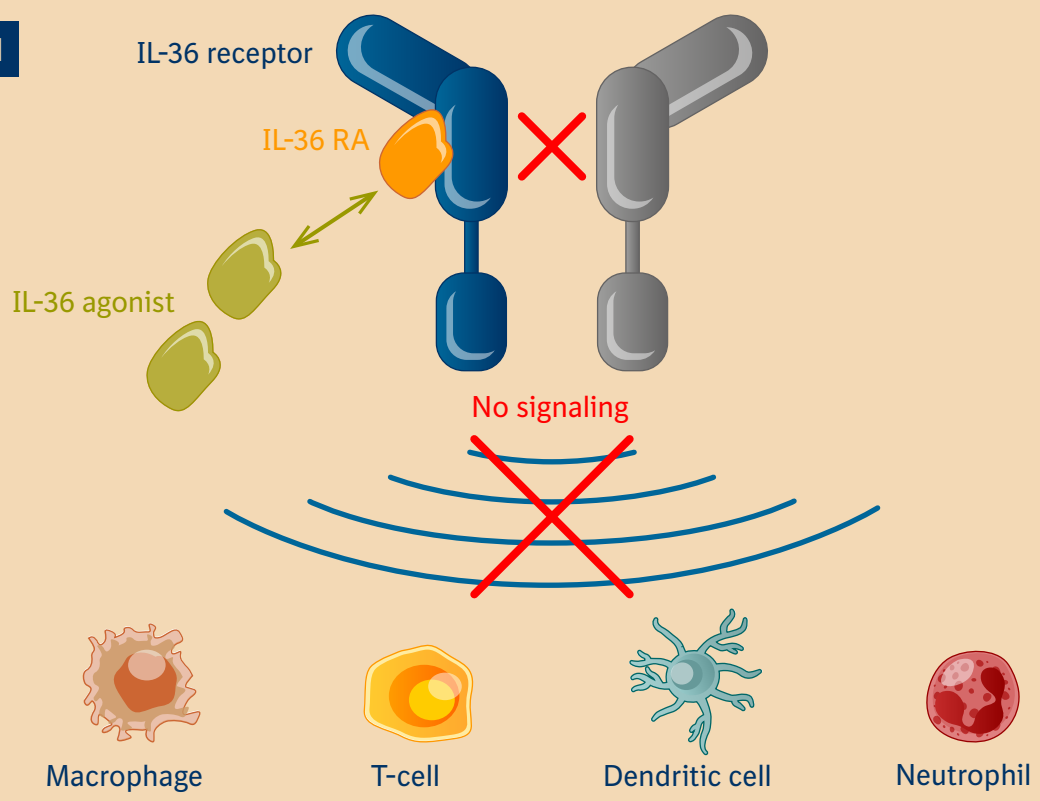
IL-36 PATHWAY ACTIVATION

IL-36 agonists bind to the **IL-36 receptor** to activate the pathway and stimulate the **inflammatory response**, including the **recruitment** and **activation** of **immune cells.**[4, 6]



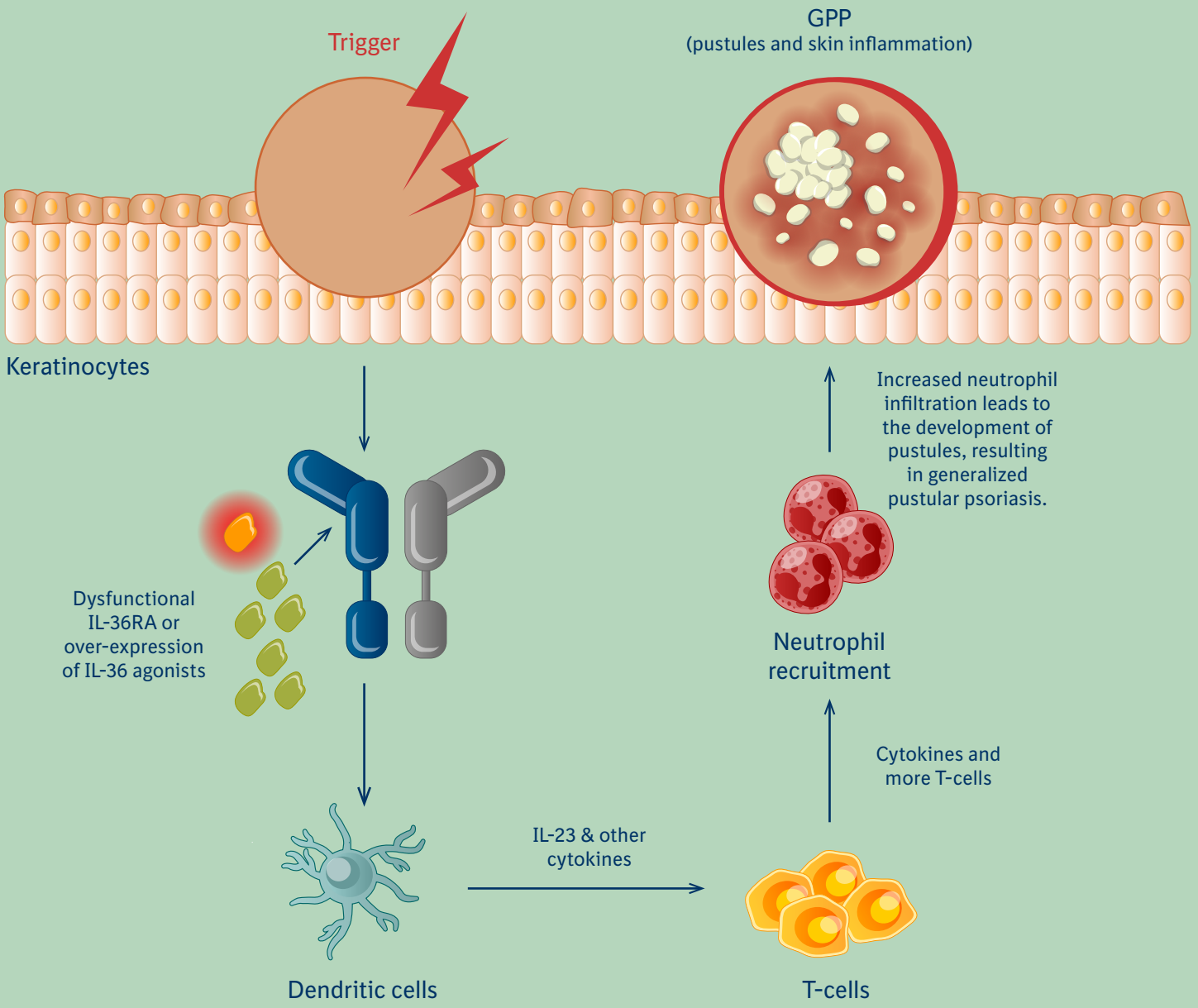
IL-36 PATHWAY INHIBITION

The IL-36 receptor antagonist (IL-36RA) binds to the IL-36 receptor to **block signaling** and **suppress** the inflammatory response.[3,4]



DYSFUNCTION OF THE IL-36 PATHWAY: *a key driver of generalized pustular psoriasis*

Uncontrolled inflammatory signaling, resulting from IL-36 receptor antagonist (IL-36RA) dysfunction or over-expression of IL-36 agonists can lead to **autoinflammatory skin diseases,** such as **generalized pustular psoriasis (GPP).**[2,5,7–9]



While **GPP** and **plaque psoriasis** are phenotypically, genetically and immunologically distinct conditions, driven by separate underlying pathways, crosstalk between these pathways can sometimes lead to a vicious **cycle of inflammation** and **mutually-reinforced disease.**[8–13]

Boehringer Ingelheim's randomized, placebo-controlled clinical trial program targeting the IL-36 pathway has advanced scientific knowledge in GPP.[14,15]

The Effisayil™ clinical trial program involves the largest and broadest patient population ever studied globally in GPP,[14,15] leading to the first specific treatment approved for GPP flares across multiple countries and regions.[16,17]

Definitions:
Agonists: molecules that bind to a receptor to activate a biological response
Antagonists: molecules that bind to a receptor or a cytokine to block or inhibit a biological response
Cytokines: molecules involved in cell signaling and the immune response

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