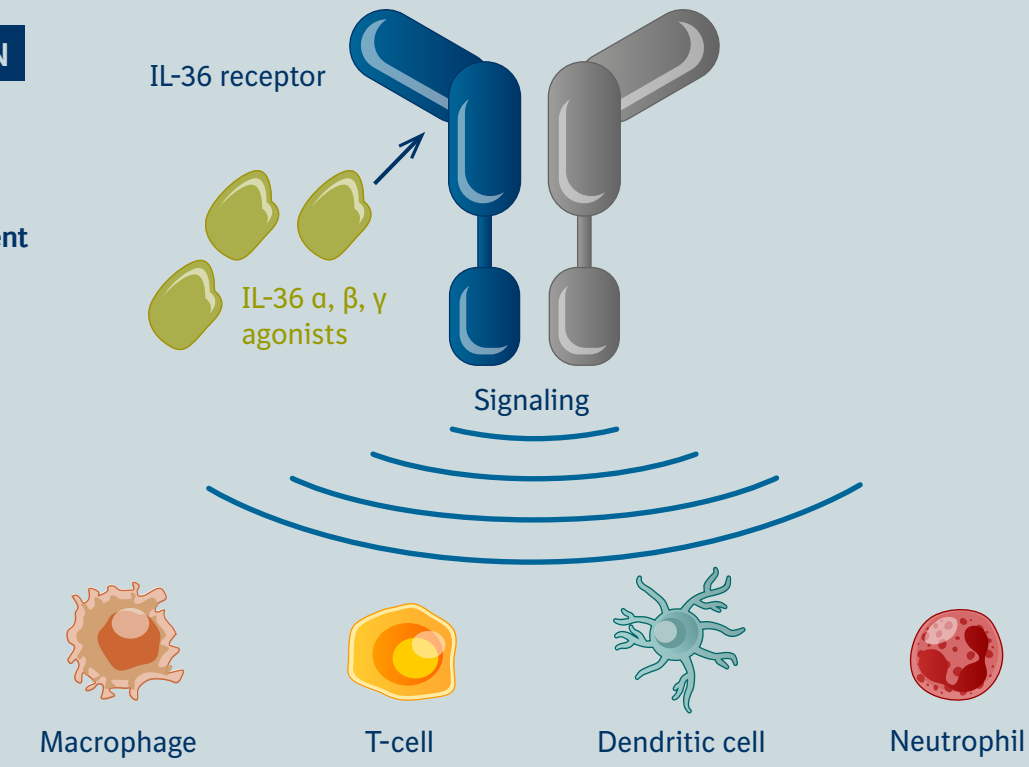
The IL-36 pathway and pustular psoriasis

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]

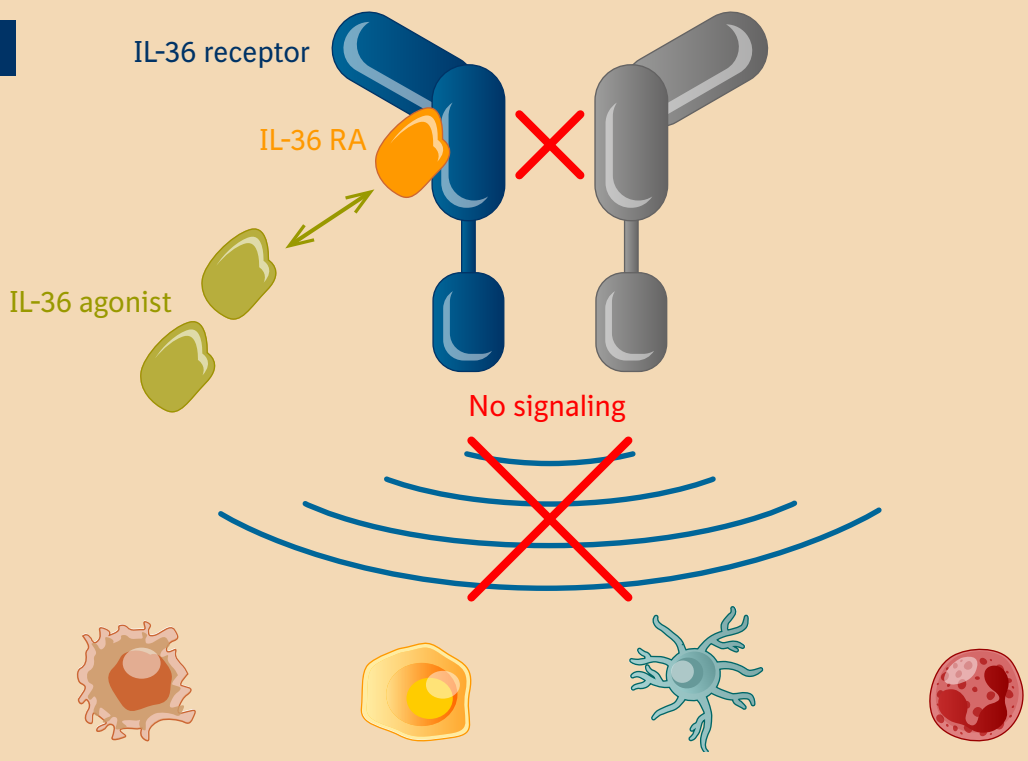
IL-36 PATHWAY ACTIVATION

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**.



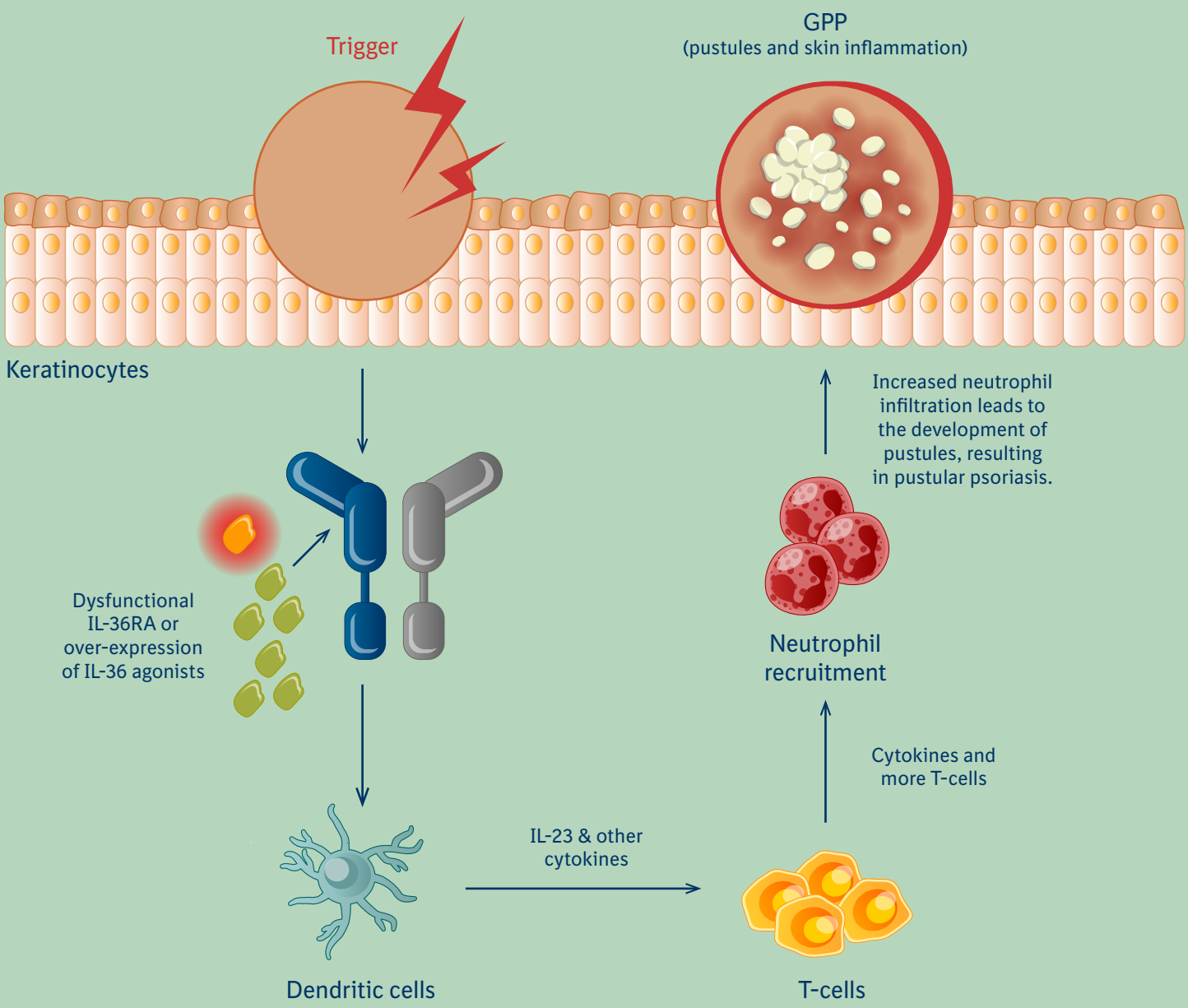
IL-36 PATHWAY INHIBITION

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



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

Uncontrolled inflammatory signalling, 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)** and **palmoplantar pustulosis (PPP)** – types of pustular psoriasis.[2,5-8]



While **pustular psoriasis** and **plaque psoriasis** are distinct conditions, driven by separate underlying pathways, crosstalk between these pathways can sometimes lead to a vicious **cycle of inflammation** and **mutually reinforced disease.**[2,7,9-11]

Boehringer Ingelheim is committed to transforming the lives of people living with autoinflammatory diseases, such as pustular psoriasis, through understanding how faults occur in the immune system and developing treatments to blunt an overactive inflammatory response, block further damage and repair damage caused.

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 signalling and the immune response

References:
1. Ngo Vu L, *et al. PNAS*. 2018;**115(22)**. **2.** Gabay C, *et al. J Leukoc Biol.* 2015;97(4):645-52. **3.** Ganesan R, *et al. mAbs*. 2017;9:1143-54. **4.** Bassoy EY, *et al. Immunol Rev.* 2018;281:169-78. **5.** Marrakchi S, *et al. N Engl J Med.* 2011;365:620-8. **6.** Sugiura K, *et al. J Invest Dermatol.* 2013;133:2514-21. **7.** Furue K, *et al. Acta Derm Venereol.* 2018;98(1):5-13. **8.** Johnston A, *et al. J Allergy Clin Immunol.* 2017 July;140(1):109–120. **9.** Schön M, *et al. Front Immunol.* 2018;9:1323. **10.** Pfaff CM, *et al. Sci Rep.* 2017;7:15631. **11.** Liang Y, *et al. Curr Opin Immunol.* 2017;49:1-8.