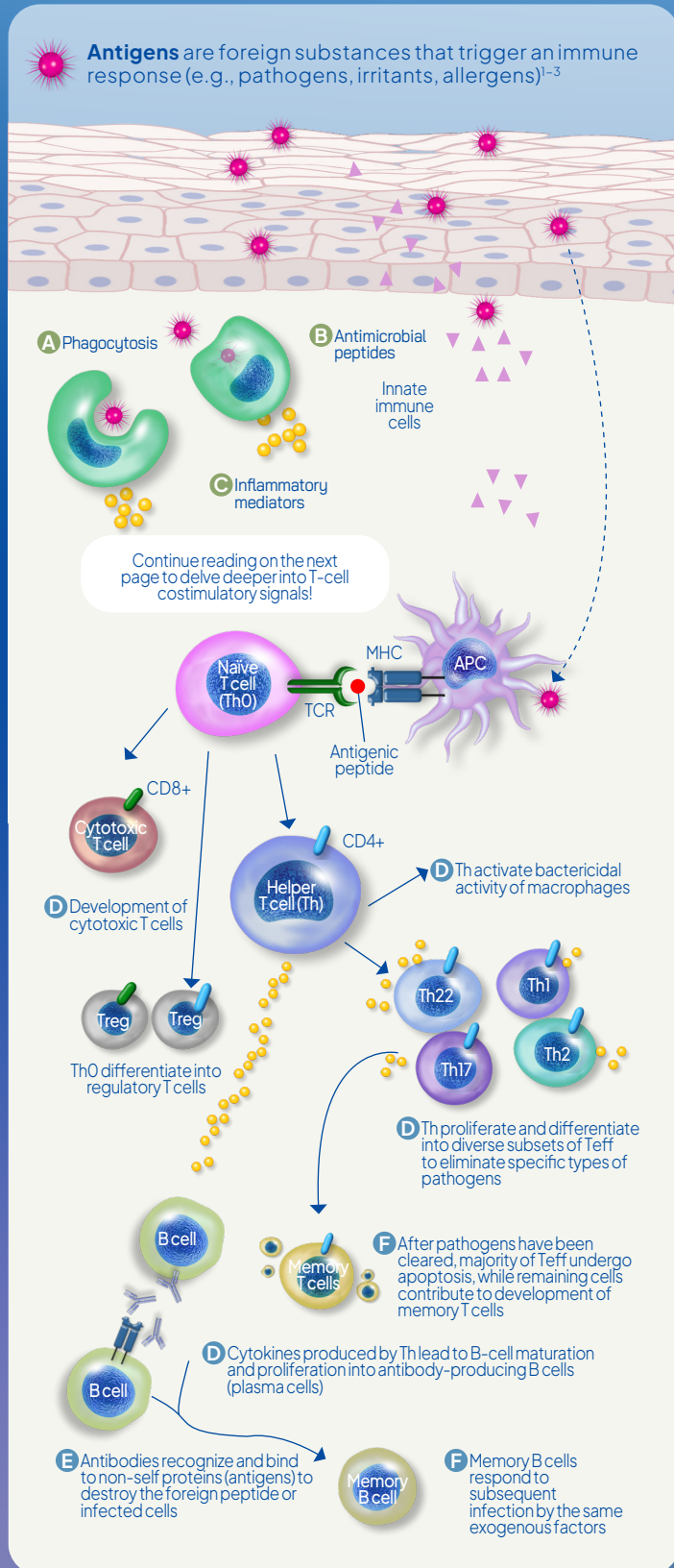


Basic Guide to Key Concepts of Immunology

The immune system has 2 fundamental lines of defense: innate & adaptive immunity¹



Innate immunity

Rapid and short-lived | Nonspecific¹

Nonspecific and direct response¹

- A** Phagocytosis (digest and kill exogenous factors)
- B** Production and release of antimicrobial peptides
- C** Induction of inflammatory mediators (e.g., cytokines, chemokines, neuropeptides, eicosanoids)

Key cells of the innate immune system^{1,2}

- **Macrophages:** phagocytosis, antigen presentation
- **Neutrophils:** phagocytosis, degranulation (against bacterial and fungal infection)
- **Basophils, mast cells:** degranulation, release of inflammatory mediators (in response to allergens)
- **Monocytes:** differentiation into macrophages and dendritic cells to elicit immune response
- **NK cells:** tumor rejection, destruction of infected cells, release of perforin and granzymes which induce apoptosis

Antigen Presenting Cells (APCs)¹⁻⁴

(A link between innate and adaptive immune response)

Antigen presenting cells process and present the antigens using MHC molecules to train immune cells¹⁻³

- **Professional APCs** (dendritic cells, macrophages, Langerhans cells, B cells) present antigenic peptides using **MHC II and costimulatory molecules**^{1,3}
- **Nonprofessional APCs** (ILCs, fibroblasts, epithelial cells, endothelial cells) present antigenic peptides using MHC I; **do not typically express MHC II and costimulatory molecules**^{2,3,5-8}

Adaptive immunity

Delayed but long-lasting | Pathogen-specific¹

Pathogen-specific response^{1,2}

- D** Generation of pathogen-specific immunologic effector pathways that eliminate specific pathogens or pathogen-infected cells
- E** Recognition of specific non-self antigens
- F** Development of immunologic memory that eliminates a specific pathogen in subsequent exposure

Key cells of the adaptive immune system^{1,2,9,10}

- **T cells** originate from bone marrow and mature in the “T”hymus
Details on T cells are on the next page
 - Naïve T cells (Th0)
 - Effector T cells (T_{eff}) including helper T cells (Th), regulatory T cells (Treg), and cytotoxic T cells
 - Memory T cells
- **B cells** develop in “niche” – a complex microenvironment created by the stromal cells of the bone marrow
 - B cells
 - Plasma cells

Details on B cells are not covered in this infographic

APC, antigen-presenting cell; CD, cluster of differentiation; ILC, innate lymphoid cell; MHC, major histocompatibility complex; NK, natural killer; TCR, T-cell receptor.
1. Modlin RL, et al. Innate and adaptive immunity in the skin. In: Goldsmith LA, et al. eds. *Fitzpatrick's Dermatology in General Medicine*, 8e. The McGraw-Hill Companies; 2012:105–126. Accessed June 11, 2024. Available from: <https://accessmedicine.mhmedical.com/content.aspx?bookid=392§ionid=41138688>; 2. Marshall JS, et al. *Allergy Asthma Clin Immunol*. 2018;14(Suppl 2):49; 3. Eiz-Vesper B, Schmetzer HM. *Transfus Med Hemother*. 2020;47(6):429–431; 4. Gaudino SJ, Kumar P. *Front Immunol*. 2019;10:360; 5. Narinyan W, et al. *Biomedicines*. 2022;10(11):2828; 6. Hargrave KE, et al. *Int J Biochem Cell Biol*. 2022;153:106331; 7. Amersfoort J, et al. *Nat Rev Immunol*. 2022;22(9):576–588; 8. de Haan A, et al. *Transplantation*. 2000;69(8):1637–1644; 9. Raphael I, et al. *Cells*. 2020;9(3):531; 10. Cano RLE, Lopera HDE. Chapter 5. In: Anaya JM, et al. eds. *Autoimmunity: From Bench to Bedside* [Internet]. El Rosario University Press; July 18, 2013. Accessed July 23, 2024. Available from: <https://www.ncbi.nlm.nih.gov/books/NBK459471/>.

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Basic Guide to Key Concepts of Immunology

T-cell costimulatory pathways that lead to T-cell activation and differentiation

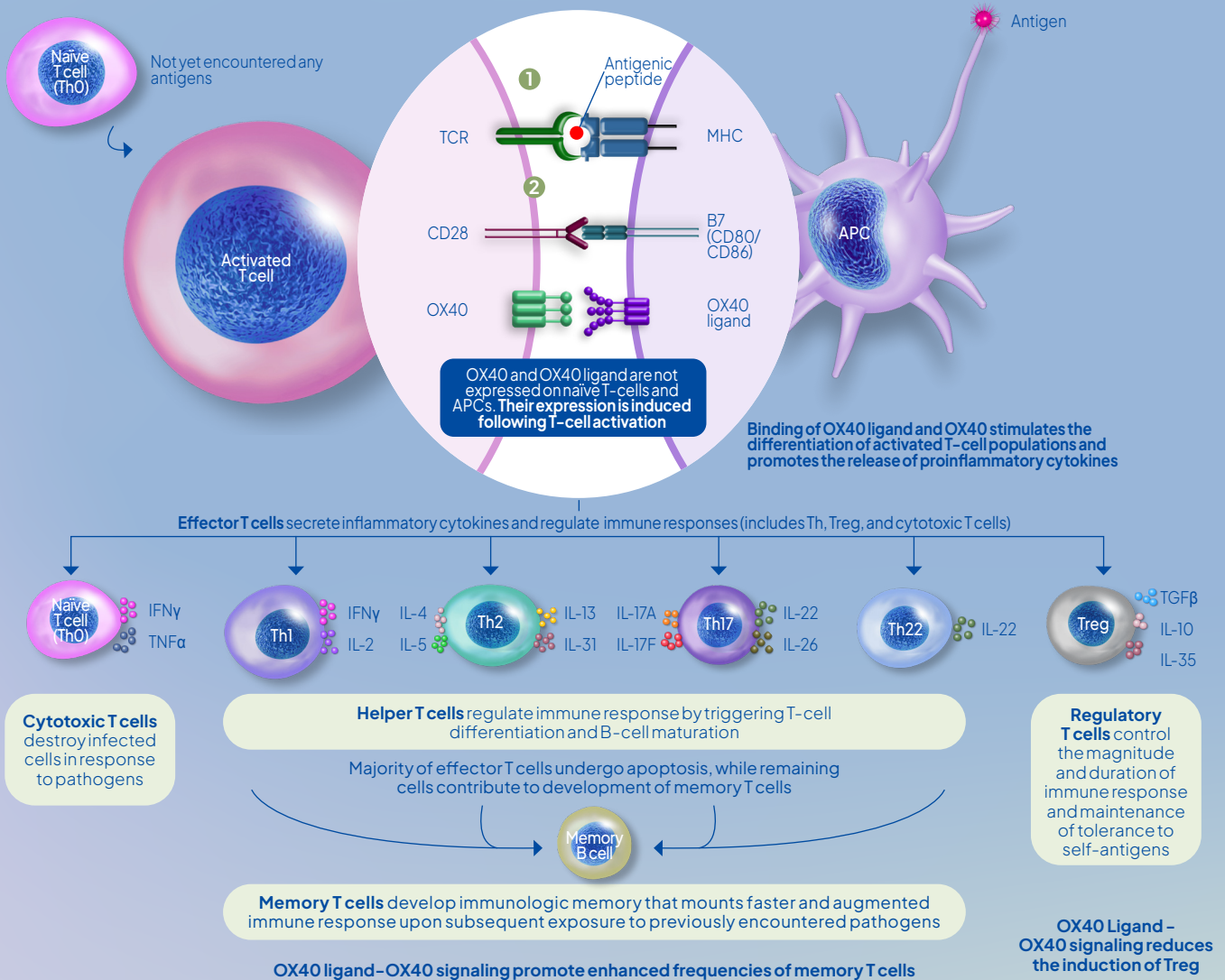
T-cell activation by APCs require **2 signals**¹⁻³:

- Primary Stimulatory Signal** via TCR binding antigenic peptides presented by MHC molecules on APCs
 - TCR on **naïve CD4+** T cell binds to peptide-**MHC II** complex, leading to maturation of **helper T cells**
 - TCR on **naïve CD8+** T cell binds to peptide-**MHC I** complex, leading to maturation of **cytotoxic T cells**
 - **Sustained TCR-MHC signaling is crucial to effectively activate and maintain signal transduction**
- Secondary Costimulatory Signal** via receptor-ligand pair expressed on APC and naïve T-cell surfaces
 - Signaling molecules (e.g., CD28/CD80, CD28/CD86) have been identified
 - **Costimulatory molecules, such as OX40 Ligand and OX40, control the downstream immune responses**

OX40 Ligand and OX40 are not expressed on naïve APCs and T cells. Their expression is induced following T-cell activation. Factors that determine the level of expression include:⁴

- T-cell receptor signals
- CD28-B7.1/2 costimulatory interactions
- Adaptive cytokines (e.g. IL-1, IL-2, TNF)
- Innate cytokines (e.g. IL-18, IL-33, TSLP)

T-cell activation and differentiation via primary and secondary costimulatory signals^{1,3-9}



APC, antigen-presenting cell; **CD**, cluster of differentiation; **CTLA-4**, cytotoxic T-lymphocyte-associated protein 4; **IFN γ** , interferon gamma; **IL**, interleukin; **MHC**, major histocompatibility complex; **TCR**, T-cell receptor; **TGF β** , transforming growth factor beta; **Th**, helper T cell; **TNF**, tumor necrosis factor; **Treg**, regulatory T cell; **TSLP**, thymic stromal lymphopoietin.

1. Modlin RL, et al. Innate and adaptive immunity in the skin. In: Goldsmith LA, et al. eds. *Fitzpatrick's Dermatology in General Medicine*, 8e. The McGraw-Hill Companies; 2012:105-126. Accessed June 11, 2024. Available from: <https://accessmedicine.mhmedical.com/content.aspx?bookid=392§ionid=41138688>; 2. Goronzy JJ, Weyand CM. *Arthritis Res Ther*. 2008;10 Suppl 1:S3; 3. Tai Y, et al. *Front Pharmacol*. 2018;9:642; 4. Croft M, et al. *Immunol Rev*. 2009;229(1):173-191; 5. Fujita T, et al. *Immunol Lett*. 2006;106(1):27-33; 6. Sadrolashrafi K, et al. *Cells*. 2024;13(7):587; 7. Guttman-Yassky E, et al. *Br J Dermatol*. Published online June 5, 2024; 8. Tau GZ, et al. *J Immunol*. 2001;167(10):5574-5582; 9. Raphael I, et al. *Cells*. 2020;9(3):531.

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