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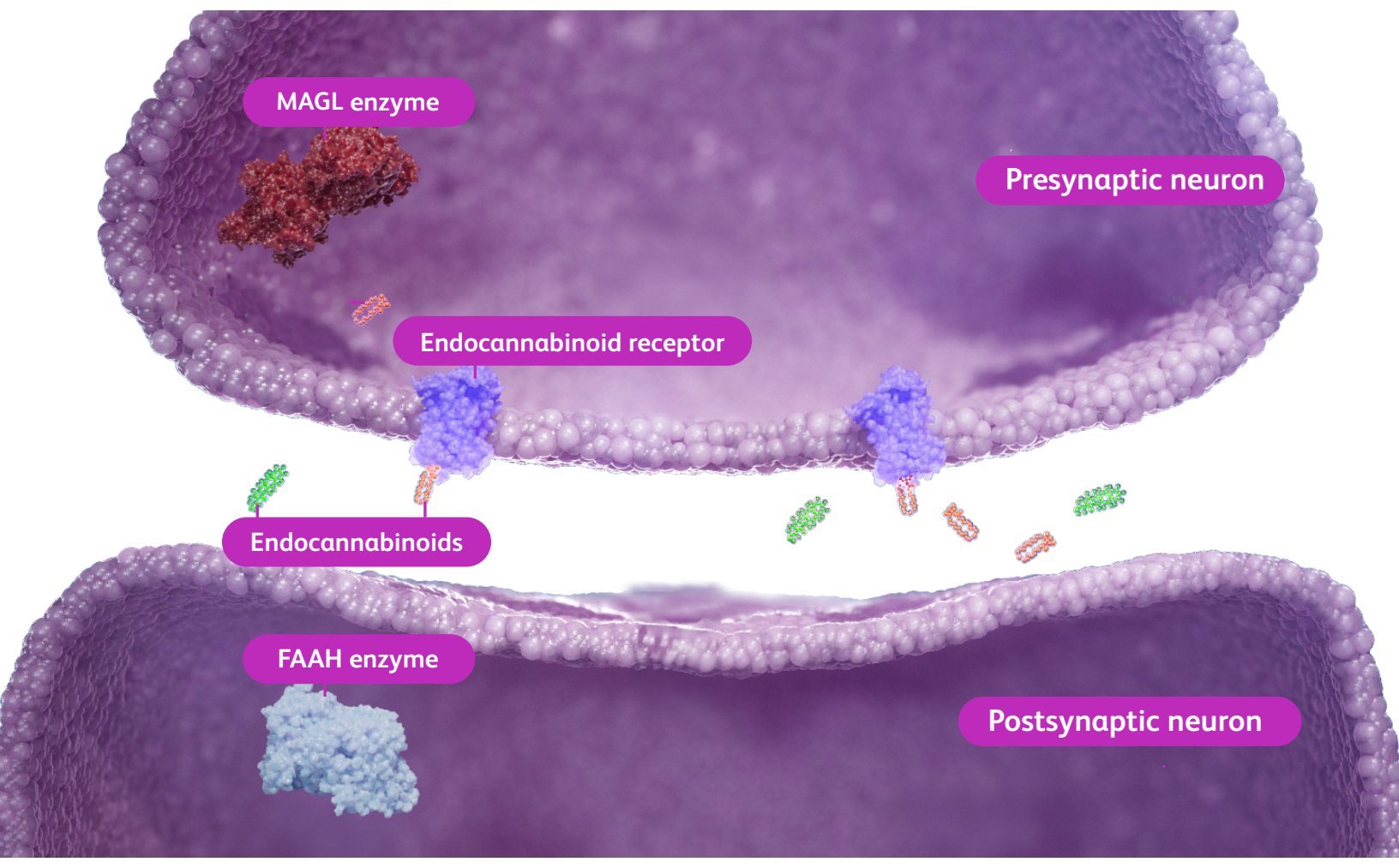
Endocannabinoid signaling and the role of FAAH and MAGL



The brain is a highly complex organ, and close regulation of signaling pathways is essential for healthy function.

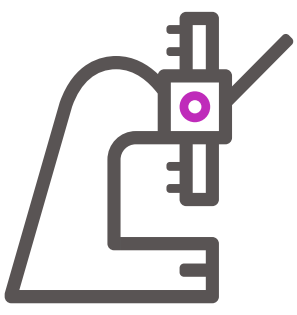
Endocannabinoids are important signaling molecules within the brain that help regulate neurotransmission, altering communication between neurons and keeping it at healthy levels. They also play a role in **reducing inflammation** in the brain and spinal cord, known as neuroinflammation.[1-3]

Fatty acid amide hydrolase (FAAH) and monoacylglycerol lipase (MAGL) are enzymes within cells in the central nervous system that **break down** the two main components of the endocannabinoid system. Normally, FAAH and MAGL maintain the right balance of endocannabinoids and their respective signaling within the brain.[4-6]

Excess neurotransmission in neurological diseases

Reduced levels of endocannabinoids result in higher-than-normal levels of neurotransmission causing **neuronal hyperexcitability**. Neuronal hyperexcitability is observed in many neurological conditions, including Alzheimer's disease agitation and multiple sclerosis spasticity.[7-9]

Research implications



Researchers are investigating ways to **increase brain endocannabinoids** to restore them to normal levels. This may reduce neuronal hyperexcitability and possibly protect brain cells from the harmful effects of neuroinflammation.

One method to achieve this may be to **inhibit the enzymatic activity of FAAH and MAGL**. Research suggests inhibiting both of these enzymes reduces the breakdown of endocannabinoids, facilitating signaling via their receptors and controlling neuronal hyperexcitability. This modulation of the endogenous endocannabinoid system could improve functional outcomes associated with multiple neurological conditions.

In addition, inhibiting FAAH and MAGL may also reduce neuroinflammation, thus contributing to neuroprotection.[10,11]

Bristol Myers Squibb is committed to rapidly advancing an innovative and diverse pipeline in neuroscience. With a deep focus on causal human biology, we are researching key pathways to slow or stop disease progression and treat symptoms to achieve the greatest possible outcomes for patients.

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