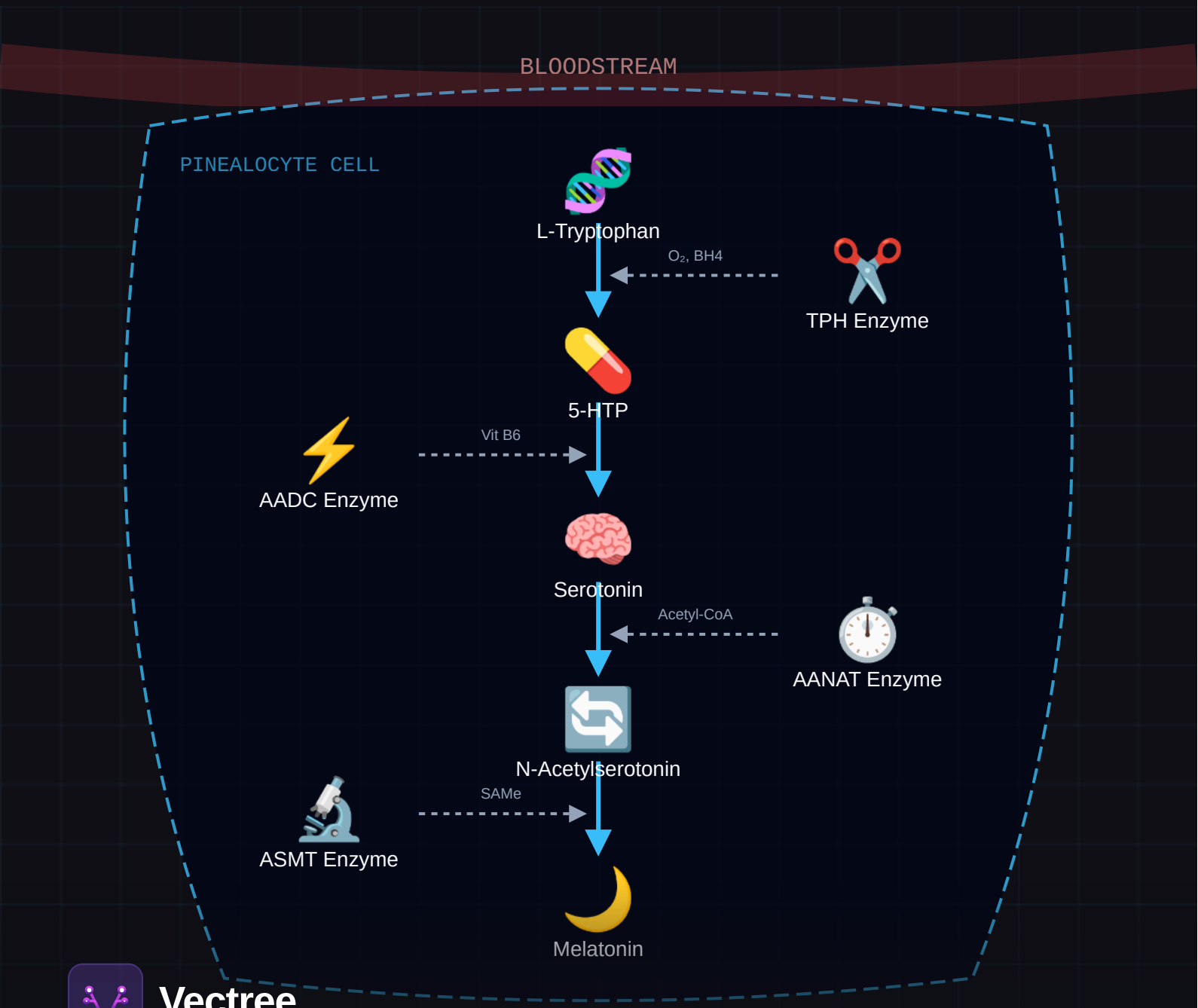

Vectree

Biochemical synthesis pathway of melatonin from tryptophan and serotonin

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VECTREE · KNOWLEDGE MAP

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L-Tryptophan

The synthesis of melatonin begins with L-Tryptophan, an essential amino acid. Because the body cannot synthesize it naturally, it must be absorbed from the diet and transported into the pineal gland via the bloodstream. Inside the pinealocyte cell, Tryptophan acts as the foundational building block for several critical neurotransmitters, including serotonin and eventually melatonin.

TPH Enzyme

Tryptophan Hydroxylase (TPH) is the first enzyme in the melatonin pathway. It catalyzes the addition of a hydroxyl group to the tryptophan ring, using oxygen and tetrahydrobiopterin as cofactors. This step converts L-Tryptophan into 5-Hydroxytryptophan (5-HTP) and acts as a critical regulatory checkpoint in serotonin production.

5-HTP

5-Hydroxytryptophan (5-HTP) is the direct biochemical precursor to serotonin in the melatonin synthesis pathway. Once synthesized by TPH, 5-HTP exists only briefly before it is rapidly decarboxylated. It is also popularly available as an over-the-counter dietary supplement capable of crossing the blood-brain barrier.

AADC Enzyme

Aromatic L-amino acid decarboxylase (AADC) is the enzyme responsible for converting 5-HTP into Serotonin. It achieves this by removing a carboxyl group from the 5-HTP molecule, relying heavily on Vitamin B6 as a coenzyme. Because AADC is highly active and abundant, 5-HTP is converted to serotonin almost as soon as it is formed.

Serotonin (5-HT)

Serotonin (5-Hydroxytryptamine) serves as a major intermediate in the melatonin pathway, famously known as a neurotransmitter regulating mood. During the day, serotonin accumulates and is stored in the pineal gland. When darkness falls, the sympathetic nervous system signals the pineal gland to begin converting this stored serotonin into melatonin.

⏱️ AANAT Enzyme

Serotonin N-acetyltransferase (AANAT) is the timekeeper enzyme and the rate-limiting step of melatonin synthesis. It attaches an acetyl group to serotonin to form N-Acetylserotonin, with its activity strictly controlled by light. Photoreceptors in the retina detect darkness to activate AANAT, while light exposure causes its rapid molecular destruction.

🔄 N-Acetylserotonin

N-Acetylserotonin (NAS) is the immediate precursor to melatonin, formed when AANAT acetylates serotonin. Interestingly, NAS is not merely an inactive intermediate; it activates TrkB receptors. This confers neuroprotective and antidepressant effects independent of both serotonin and melatonin.

🔬 ASMT Enzyme

Acetylserotonin O-methyltransferase (ASMT) catalyzes the final reaction in the pathway, converting N-Acetylserotonin into Melatonin. It transfers a methyl group from S-adenosyl methionine (SAMe) to the NAS molecule. Unlike AANAT, ASMT levels remain relatively constant throughout the day and night.

🌙 Melatonin

Melatonin (N-acetyl-5-methoxytryptamine) is the final product of this biochemical pathway, known as the hormone of darkness. It is rapidly released from the pineal gland into the bloodstream and cerebrospinal fluid. Melatonin synchronizes the body's circadian rhythms, signaling nighttime and preparing physiological systems for rest.