CHRONOFLOW: Integrated circadian transcriptomic, microRNA, and proteomic profiling of the choroid plexus in relation to blood-cerebrospinal fluid barrier function and glymphatic rhythmicity

Why are sleep, day–night rhythms, and efficient brain cleansing so important for mental and neurological health? In our project, we will explore how the biological clock operates in one of the brain's lesser-known yet critically important structures—the **choroid plexus**. This organ produces **cerebrospinal fluid (CSF)**, which not only cushions the brain but also helps remove toxic metabolic waste. This process is supported by the **glymphatic system**—a kind of "waste disposal" network in the brain that works most efficiently during sleep.

Although we know that the human body follows a daily (circadian) rhythm—for example, sleep at night and activity during the day—we still lack understanding of how these rhythms are regulated within the choroid plexus and how they affect CSF composition and immune processes in the brain. In particular, we are interested in whether fluctuations in CSF production can influence the brain's "cleaning efficiency" and whether they may be linked to inflammation or the development of neurodegenerative diseases.

The project will use two research models: **laboratory rats** (to study daily changes in the choroid plexus, CSF, and brain) and a **human-derived choroid plexus epithelial cell line** known as HIBCPP, which allows us to investigate molecular mechanisms underlying the circadian function of the **blood–CSF barrier**. Special attention will be paid to small regulatory molecules called **microRNAs**, which may act as precise "switches" in the biological clock.

We will also assess **blood–CSF barrier permeability** (based on the CSF/serum albumin ratio), CSF composition at different times of day, microglial activation, and markers of inflammation and oxidative stress in the cerebral cortex—as indirect indicators of the brain's clearance efficiency.

Our research will help to better understand how biological rhythms support brain homeostasis and self-cleansing. The findings may also identify new therapeutic targets and optimal timing for delivering drugs that reach the brain via the CSF, for example in the treatment of neurodegenerative disorders. The project addresses an important knowledge gap by integrating three interconnected elements—the **choroid plexus**, **CSF**, and **glymphatic system**—within the framework of circadian regulation, while also considering potential **sex-related differences**.