Hypothesis:

Alterations in biological clocks due to a high calorie diet and/or chronodisruption forms the basis of lifestyle disorders such as NAFLD/NASH. Nocturnin (Noct) is a metabolically relevant circadian clock output and a key regulator of hepatic lipid metabolism. Under experimentally induced chronodisruption, Noct can possibly function as a player in NASH pathology that needs scrutiny. We hypothesize that experimentally induced CD in mice can account for alterations in Noct oscillations and drawing meaningful correlations with NASH pathophysiology. Hepatoprotective effects of melatonin in NASH have been widely reported by research groups and from our laboratory. Melatonin and Nocturnin interactions in NASH pathophysiology is also hypothesized herein. Additionally, alterations in miRNA and altered synergy of metabolic genes in circadian dysregulation are privy to the said pathophysiological changes in NASH. Since, miRNA: gene networks are crucial but are minimally explored in NASH, it is hypothesized that deciphering the intricacies of a miRNA: Noct axis shall help in decoding the epigenetic control of Noct in NASH.

Aim of the Study

To investigate possible regulation of Nocturnin in experimental models of NASH wherein endocrine and epigenetic regulators have been put to scrutiny.

Objectives:

Objective 1.

To investigate H and/or CD mediated alterations in Nocturnin oscillations in NASH pathology.

in silico functional analysis of Nocturnin (Noct), hepatic *Noct* oscillations in mice and HepG2 cells have been studied herein.

Objective 2.

To investigate the possible melatonin- Nocturnin synergy.

Molecular docking studies between melatonin and NOCT, merits of exogenous melatonin and its effects on hepatic Noct oscillations were studied. A detailed study on melatonin-mediated changes in Noct

Objective 3.

To investigate the epigenetic regulation of Nocturnin in CD induced NASH pathology.

In silico algorithms and target prediction softwares to establish role of miR-122 in NASH. This was followed by its manipulation in hepatic miR-122 and its consequences on Noct rhythmicity were assessed. All rhythmic data were scrutinized by CircWave analysis.