**A Novel Method For Reducing The Liver Toxicity Of A Liver Damaging Agent And Treating Liver Disease And Disorders By Altering The Circadian Rhythmicity Of Microbes In The Gut Microbiome**

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Summary:

The human intestine carries a vast and diverse microbial ecosystem associated with a host of physiological conditions ranging from obesity and diabetes to autism and mental health. Like its human host, the intestinal microbiota undergoes circadian oscillations manifested in changes in composition and biogeography.

The human circadian clock adjusts physiological processes to diurnal environmental variations through the coordination of transcriptome oscillations in the peripheral tissues. In each individual cell the rhythmic transcriptional program is carried out by a network of transcription factors. These transcription factors determine the fraction of genome undergoing oscillating expression, in a tissue specific manner. As a result, up to 20% of the tissue’s total transcriptome and up to 50% of the transcript in the body consist of oscillating elements, which in turn determine the diurnal pattern of cellular and organismal activity.

The labs of profs. Elinav and Segal have discovered that the diurnal microbial behavior drives global programming of the host circadian transcriptional, epigenetic, and metabolite oscillations. Disruption to the microbiome rhythmicity not only abrogates normal chromatin and transcriptional oscillations of the host, but also incites genome-wide de novo oscillations in both intestine and liver.

Hepatic drug detoxification and hepatotoxicity are strongly tied to the liver’s homeostatic diurnal variation. This in turn means that through the identified host-microbiome diurnal interface we can modulate and treat different liver conditions associated with disruption of the microbiota and circadian clock.

**Consequently, there is a strong need for the development of novel methods for analyzing and modulating the gut microbiota composition and oscillations for the treatment of liver disease and toxicity.**

The groups of Prof. Eran Elinav and Prof. Eran Segal have discovered that oscillations in the gut microbiome population and biogeography can affect transcriptional oscillations in different organs, which in turn determines their activity. The microbiome effect on diurnal organ activity can be used to treat different conditions by manipulating the gut microbiome.

Applications and Advantages:

* **A method for treating liver disease by altering gut microbiota oscillations which can supplement and augment other therapeutic methods.**
* **Analysis of the gut microbiome’s composition, oscillations, and metabolome can help improve ongoing treatment regimens.**

Technology's essence:

The Elinav-Segal research teams discovered that the host’s gut-microbiome influences rhythmic host physiology beyond the intestine by driving systemic metabolic rhythms and programing of transcriptional oscillations in the liver. This finding can be used in a number of ways to treat different liver diseases and drug toxicities: first, by administering different agents such as antibiotics, probiotic, polyamines or fecal transplants to alter the circadian rhythmicity of an individual's gut microbiome, thereby reducing the toxicity of the liver damaging agent. Second, by analyzing the circadian rhythms of specific gut microbes, the applied treatment regimen can be modified for better results.