Discovery of Highly-Correlated Circadian Oscillations in Oral MicroRNA and Microbiome Levels Using Next Generation Sequencing of Human Saliva: Implications for Human Health and Disease

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MicroRNAs (miRNAs) are small non-coding RNAs that can regulate circadian gene expression. This study investigates the relationship of miRNA and microbiome levels to diurnal variations in human saliva to explore possible implications for sleep disorders. Human subjects (n=11) provided saliva samples at various times of day on repeated days. Identification and quantification of saliva miRNA and microbial content was performed using next generation sequencing, followed by statistical analysis. First a 2-way analysis of variance (ANOVA) was used in 2 independent sample sets to identify miRNAs and microbes that varied significantly according to the time of collection but not the day of collection. A subset of these miRNAs and microbes were then used in a third sample set to predict the time of collection using a multivariate regression. Strong and predictable changes with time of collection were apparent for 19 distinct miRNAs and 11 microbes out of all reliably quantified miRNAs and microbes. A model was developed from the miRNA data in the first 2 sample sets that was able to predict time of collection in the third sample set. The microbial data also showed a strong correlation with time of collection in the first two sample sets, but was not as accurate at predicting collection time in the third sample set. Highly significant correlations between several of the miRNAs and microbes were observed. Bioinformatic analysis of the best time predictor miRNAs indicated that most target at least one or more circadian genes and genes involving brain and immune function. This study suggests that there are highly-correlated circadian oscillations in oral miRNA and microbiome levels that have not been previously described and that some miRNAs are subjected to striking diurnal changes.

Awards Won:
Third Award of $1,000
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