Mathematical Modeling of Circadian Rhythms, Tumor Growth, and Radiotherapy

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The goal of this project is to study how to effectively utilize circadian rhythms in aiding drug delivery against tumor growth. Circadian rhythms are 24-hour cycles in physiological processes, such as cell growth and sleep/wake. In a number of studies, researchers have shown that disruption of the circadian clock can increase or decrease the cell population growth rate. The model presented in El Cheikh et al.[10] is the first step in developing a multiscale model for the interaction between the circadian clock and the cell cycle. Another paper, written by Checkley et al.[11], discussed a mathematical model for cancer cell population growth and simulated its reaction to a combination of therapies.

In this project, we aim to integrate these two models and analyze the best time of day to administer therapies to cancer patients. We hypothesize that by taking into account the phase of circadian rhythms in healthy and cancer cells, appropriately timed therapies will be more effective in killing cancer cells while being less toxic to healthy cells. We will implement our model in MATLAB and conduct simulations to explore the complex interactions between the cell cycle, the circadian clock, and tumor growth. Combined circadian rhythm/cell population and drug PK-PD models can be a helpful tool for chronotherapy of cancer patients. Thus, this project will help provide a foundation to develop more personalized and effective treatments specific to each patient's circadian phase and tumor properties.

[10] El Cheikh, R., Bernard, S., & Khatib, N. E. (2014). Modeling circadian clock–cell cycle interaction effects on cell population growth rates. *Journal of Theoretical Biology, 363*, 318-331. doi:10.1016/j.jtbi.2014.08.008

[11] Checkley, S., Maccallum, L., Yates, J., Jasper, P., Luo, H., Tolsma, J., & Bendtsen, C. (2016). Bridging the gap between in vitro and in vivo: Dose and schedule predictions for the ATR inhibitor AZD6738. *Scientific Reports, 6*(1). doi:10.1038/srep16545