Internship/research training at Department of Neuroscience, BMC Uppsala University

**Background:**
The mammalian circadian system with a periodicity of approximately 24hr is a complex hierarchical network which organizing around an ensemble of uniquely coupled cells comprising the principal circadian pacemaker in the suprachiasmatic nucleus of the hypothalamus. These circadian clocks anticipate environmental cycles and control daily rhythms in biochemistry, physiology, behavior and so on (Young et al., *Nat. Rev. Genet.*, 2001). Within cells, circadian oscillations are generated by a set of clock genes and their protein products together participate in auto regulatory feedback loops of transcription and translation to produce an oscillation with a period of about 24 hours (Takahashi et al., *Nat. Rev. Genet.*, 2008). In mammals, these clock genes including: *Clock*, *Bmal1*, *Per1*, *Per2*, *Cry1*, and *Cry2*.

**Aim:**
This project is aim to develop a mammalian cellular model using CRISPR/Cas9 technology and a firefly luciferase reporter. In recent years, real-time bioluminescence recording using firefly luciferase as a reporter has become a more and more popular technique for studying circadian rhythms in mammals. Once a reporter cell line is established, the dynamics of clock function can be examined through bioluminescence recording.

**Approach and methods:**
1) Cellular model culture: Human cancer cells;
2) Using cancer cells to generate the *Bmal1-Luc* or *Per2-Luc* reporter lines;
3) Checking with other cell types to ensure the procedure can be applied to other cell types.

**Significance:** Understanding the risks chemical exposure on the incidence and development of cancer are of high societal value.

**Societal impact (when applicable):** Our research is important for furthering our understanding of the interaction between exposure to chemicals and cancer progression.

**Ethical considerations (when applicable):** This project will only use human cancer cell lines which bought from ATCC and haven't got any developmental potency and no possibility to be cross contaminated to human subject.

**Starting date:** By agreement.

**Place:** Uppsala biomedicinska centrum (BMC), Uppsala University.
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