**University of Leicester**

**Future 50 PhD Scholarship**

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| **Project Referece** | GGB Chen |

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**Section 2 – *Project Information***

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| **Project Title** | Unravelling the role of sleep in cancer progression using *Drosophila* models | |
| **Project Highlights:** | 1. | International collaboration linking clinical and fundamental research |
| 2. | Novel investigation using latest genetics and behavioural techniques |
| 3. | Dual research strategies: patient genetic data and animal model |
| **Project Summary** | | |
| **Background:** Epidemiological data has indicated an association between sleep disruption and cancer. Yet research examining the underlying bi-directional causality remains absent. Recent findings have shown that sleep maintains healthy non-neuronal tissues via cellular mechanisms relevant to cancer development. Sleep is regulated partly by the circadian rhythm, an internal process that determines 24-hour sleep-wake profile. Previous research has demonstrated circadian disruption facilitates tumour progress. Nevertheless, the role of sleep *per se* in cancer development remains unclear.  Genetically altering sleep levels has become feasible in *Drosophila* in the past decade. Moreover, *Drosophila* male gonads (testis and accessory gland) have recently been successfully used to investigate the pathogenic molecular mechanisms mediated by the tumour associated genes (TAGs) in prostate and testicular cancers.  **Aim:** *The project will use the sleep-controlling neurogenetics to investigate the role of sleep in TAGs-derived Drosophila prostate and testicular cancer models*  **Project objectives:**   1. **Collecting patient sleep data:** Through collaboration with UHL oncologist, Dr Olubukola Ayodele, we will use sleep questionnaires to confirm the prevalence of sleep disruption in prostate and testicular cancer patients. 2. **Establishing TAG-derived cancer model:** Five evolutionarily conserved novel TAGs will be identified from the differentially expressed transcriptomes in prostate cancer tissue (Dr Shih-Chieh Lin, NCKU, Taiwan) or mined from GWAS studies for prostate or testicular cancers (Dr Chris Talbot, UoL). We will establish the cancer models by genetically up- or down-regulating *Drosophila* TAG orthologues. Tumour histology in male gonads (e.g., hyperplasia, hypertrophy and/or basal extrusion) will then be examined in the models. As positive controls, two existing models will be included: *RasV12* overexpressing accessory glands and *tut* mutant testis. 3. **Investigating bidirectional causality between sleep and cancer progress.** We will use automated sleep assays to verify sleep and circadian change in the cancer models. Both circadian rhythm and sleep will then be altered via manipulating neural activities of the sleep- and circadian-control circuits in the cancer models using opto/thermogenetics. The effect of altered sleep and circadian rhythm on tumour histology will then be verified. Additionally, we will examine the impact of sleep disrupting life-style behavior (i.e., shift work and blue screen exposure) on cancer development. | | |