Project Title:	Neural Cell Networking Mediated by Circadian Clocks to Enhance Brain Repair Systems 晝夜節律鐘介導的神經細胞網路促進大腦修復系統
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Major Findings from the Period from July 2022 to June 2023:

In a year, the team has studied how circadian clock-mediate neural cell networking is changed in a neurodegenerative condition, excitotoxicity, and its consequences. It is reported that BMAL1 in hippocampal neurons and NSCs respond to glutamate excitotoxic conditions, which are frequently observed in neurodegeneration. Since BMAL1 is a crucial transcription factor in building circadian clocks, it is expressed in most cells, including neurons and NSCs. BMAL1 activities autonomously oscillate in cells but are also affected by external cues, followed by conveying information to neighbor cell clocks to synchronise them to new environments. Thus, BMAL1 can mediate cell-cell communications via clock synchronising mechanisms.

The research findings show that BMAL1 in hippocampal neurons—CA1 neurons and granular cells (GCs)—reduces its levels in excitotoxic lesions but involve different cellular processes, cell death and neurogenesis. Especially, GC BMAL1 communicates with NSC BMAL1 to convey GC damage information, thereby initiating NSC proliferation and differentiation. The findings support three points: 1) cell type-specific BMAL1 functions in excitotoxicity; 2) neuronal and NSC BMAL1 communicate to enhance neurogenesis; and 3) altered BMAL1 can be involved in detrimental or beneficial events depending on cell types.

Thus, it explains why targeting BMAL1 (clocks) for therapeutic purposes has to be cell type-specific rather than simply restoring all physiological rhythms.

(This work is currently under review at an international peer-reviewed journal.)

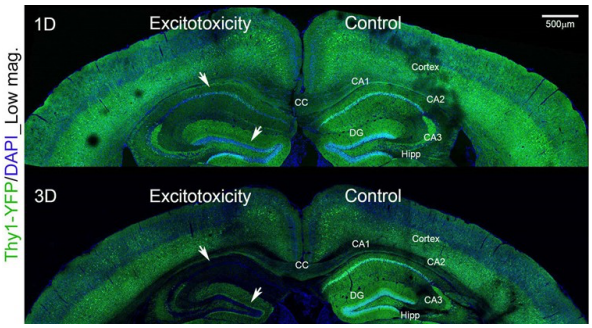

Fig 1. Neurodegeneration in excitotoxic hippocampal lesions of Thy-YFP-16 transgenic mice

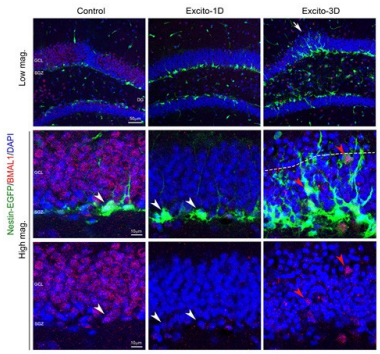

Fig 2. Reduced BMAL1 (red) in GCs results in induced EGFP+ NSCs (green) in excitotoxic DG lesions