LED-Based Photobiomodulation (PBM) Platform for Standardized Neuronal Maturation With a TICT-Based Fluorescent Readout

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Translational research on neurodegenerative diseases is constrained by the cost, long timelines, and variability of generating mature neuronal assay substrates, which also limits scalable production of homogeneous neurons for therapeutic applications. This project integrates two complementary solutions into a single workflow: an LED-based photobiomodulation (PBM) platform to accelerate and standardize neuronal maturation, and TICT (twisted intramolecular charge transfer) fluorescent probes that enable sensitive amyloid-ß (Aß) measurement as a quantitative readout. First, LED PBM (460, 520, 630 nm) was optimized in human SK-N-SH cells and hiPSC-derived brain organoids by tuning wavelength, exposure time, and energy density. Red light and sequential RGB irradiation significantly increased neuronal maturation markers, including MAP2 (up to 10-fold), TUBB3, and NeuN, indicating more consistent maturation across cultures. PBM reduces dependence on expensive biochemical inducers and enables large-area, uniform irradiation to improve reproducibility. Second, low-molecular-weight TICT "turn-on" Aß probes were designed and synthesized. Upon Aß binding, the lead probe produced up to a 154-fold fluorescence increase, enabling high signal-to-noise quantification. The probes detected Aß not only in cells but also directly in the culture medium, allowing non-destructive quality control using small media samples during large-scale cell manufacturing. Overall, PBM serves as an assay-enabling maturation standardization system, while the TICT probe provides an Aß-associated quantitative readout for maturation. This integrated platform supports scalable, reproducible production of mature neurons for cell therapy and offers a practical foundation for standardized neuronal assays.

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