Poster Abstract Submission

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Research Title	ROCK1 antagonizes the Melatonin-induced production of BACE-1 in SHSY5Y human neuroblastoma cells

Abstract:

Alzheimer's disease (AD) is the most common neurodegenerative disorder associated with reduced sleep quality and characterized by aggregation of amyloid β peptides (Aβ) in the brain. Melatonin is a neuroprotective hormone which improves circadian rhythm disruptions by enhancing sleep quality and reducing Aβ production. Recent studies indicated that melatonin suppresses Rho-kinase associated protein (ROCK) 1 and ROCK 2 activities in diabetic nephropathy. ROCK1 and ROCK2 are serine/threonine kinases that share 65% similarity in their amino acid sequences and 92% identity in their kinase domains. ROCKs are the principal downstream effectors of the small GTPases and their inhibition reduce Aβ production. BACE1 (beta-site amyloid precursor protein cleaving enzyme 1) is required for the generation of all monomeric forms of Aβ, including Aβ42 which aggregates into bioactive conformational species and likely initiates toxicity in AD. However, the precise mechanisms exhibited by melatonin on Aβ production have not been fully elucidated. In this study, we aimed to determine whether melatonin attenuates the production of Aβ through ROCK1/ROCK2 signaling using human neuroblastoma cell line SHSY5Y. Western blot analysis showed that melatonin (3mM, 24h) significantly increased the expression of BACE-1 in these cells. Interestingly, the silencing of the ROCK1 gene (siPool) in these same conditions enhanced the effect of melatonin on BACE-1 production. However, the knockdown of ROCK2 was without a significant effect on the expression of BACE-1 in melatonin-treated cells. Together our data indicate that the melatonin-induced production of BACE-1 is antagonized by ROCK1 in our model. Further investigation is warranted to decipher the signaling pathway of melatonin through ROCK1 and ROCK2. These findings may crystallize the ROCK1/2 dynamics as novel therapeutic targets for Alzheimer disease.