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A miracle (miR-196a) in the fight against Huntington's disease

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Huntington's Disease (HD) is a genetic disease and caused by a mutation in Huntingtin gene, leading to neuro-pathological symptoms. To date, there is no effective medicine for HD. Based on previous studies, transcriptional regulation is impaired during the progression of HD, and regulation of microRNA (miRNA) is one of affected mechanisms. Since HD leads to dysfunction of gene regulation and one miRNA could target to multiple pathways, it suggests miRNA could be one potential treatment for HD. In my laboratory, we identified one potential miRNA, miR-196a, from HD transgenic monkeys and found the neuro-protective effects of miR-196a on HD in cell, transgenic mouse and HD patient-derived induced pluripotent stem cell models. miR-196a could not only improve molecular, neuro-pathological and behavioral phenotypes in transgenic mouse models, but also suppress pathological aggregates in neurons derived from HD patients. Furthermore, we also investigate molecular mechanisms of miR-196a and show miR-196a could enhance cellular morphology, intracellular transport, synaptic plasticity, neuronal activity, learning and memory both *in vitro* and *in vivo*. In addition, miR-196a could work through binding to 3' untranslated region of *RAN* binding protein 10 (*RANBP10*) to suppress the protein expression, further enhancing the assembly of β -tubulin. Most importantly, overexpression of *RANBP10* led to worse neuronal morphology and severer pathological phenotypes in the HD transgenic mouse model, suggesting that miR-196a enhances neuronal morphology through suppressing *RANBP10* to provide neuro-protection in HD. These results suggest the important role of miR-196a on HD and might provide a new insight of therapeutic strategy for HD.

Biography

Shang-Hsun Yang is an Associate Professor in Department of Physiology at National Cheng Kung University, Taiwan. He has completed his BSc at National Chung Hsing University in 1998, MSc at National Taiwan University in 2000 and PhD at Emory University, USA, in 2008. His research interests focus on the regulation of microRNAs on HD.

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