Identification of Neuronal Autophagy Regulators with iKAP and THANATOS

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Abstract: Objective Autophagy is a promising therapeutic target against neurodegenerative diseases, which are characterized by protein accumulations in neurons. The purpose of this study is to identify important kinases involved in neuronal autophagy. Methods we developed a novel network-based algorithm, in silico Kinome Activity Profiling (iKAP), to computationally infer significantly regulated kinases by isomers, which induce autophagy in different manners, from the quantitative phosphoproteomic data. And these annotated autophagy regulators induced by isomers were identified in the THANATOS database, which contains 191,543 proteins potentially associated with autophagy in 164 eukaryotes. Results MAP2K2 and PLK1 were well validated that MAP2K2 might be essential for the induction of autophagy, whereas PLK1 plays a potential role in the maturation of autophagosomes. Conclusion The combined use of iKAP and THANATOS will be a powerful approach to identify the key regulators in neuronal autophagy, which would provide suggestions to the research or drug discovery in neurodegenerative disease.

Keywords: neurodegenerative diseases, autophagy, iKAP, THANATOS