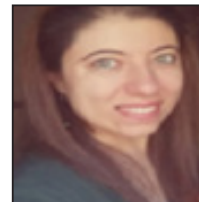


Speedy/RINGO as a neuroprotector in neurodegeneration

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Abstract

Statement of the Problem: Neurodegeneration is the progressive loss of function and structure of neurons that cause neuronal cell death. Although neurodegeneration is a multifactorial process, one of the main causative factors is elevated intracellular calcium levels which leads to apoptosis by inducing p53, thus negatively affecting two pathways: mitogenic extracellular signal-regulated kinase/mitogen activated protein kinase (ERK/MAPK) and survival phosphoinositide 3-kinase/protein kinase B (PI3K/AKT) pathways. Speedy/rapid inducer of G2/M progression in oocytes (Speedy/RINGO) is a cell cycle regulatory protein that increases survival of p53-positive mitotic cells by inhibiting the apoptosis. Moreover, we showed for the first time that this protein elicits p53-dependent anti-apoptotic effects in calcium-induced degenerated primary hippocampal neurons. **Methodology&Theoretical Orientation:** Our laboratory is currently investigating whether Speedy/RINGO exerts this anti-apoptotic function through ERK/MAPK and PI3K/AKT pathways. For this purpose, we used undifferentiated p53 and Speedy/RINGO-expressing neuronal-like neuroblastoma cells as preliminary model. **Findings:** Our previous investigations indicated that Speedy/RINGO protects neurons against calcium-mediated p53-dependent apoptosis without decreasing p53 levels. This finding implies that the anti-apoptotic effect of Speedy/RINGO is downstream of p53 activation, not directly on p53 itself. The most remarkable downstream targets of p53, in terms of generating an apoptotic effect on neurons, are ERK/MAPK and PI3K/AKT pathways. Within this context, silencing of the Speedy/RINGO gene significantly alters expression levels and phosphorylation states of certain members of these pathways. This leads to apoptotic death of neuroblastoma cells, likely due to the absence of Speedy/RINGO's regulatory function on these two pathways. **Conclusion & Significance:** Preliminary data indicates that Speedy/RINGO plays an essential role on the regulation of ERK/MAPK and PI3K/AKT pathways that directly affect the apoptotic state and survival rate of cells giving insights about molecular mechanism of Speedy/RINGO in neuronal survival. However, to understand the exact mechanism of Speedy/RINGO's anti-apoptotic function in neurons, studies is being performed in our laboratory both with in vitro degenerated primary neuron models.

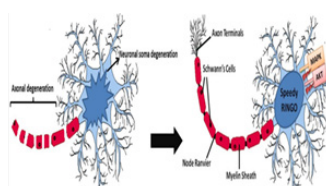


Figure 1: A schematic diagram for the proposed mechanism of anti-apoptotic action of Speedy/rapid inducer of G2/M progression in oocytes (Speedy/RINGO) on mitogen-activated protein kinase (MAPK)/extracellular signal-regulated kinase and phosphoinositide 3-kinase/protein kinase B (AKT) signaling cascades in degenerating neurons

Biography

Yesim Kaya works as a Research Assistant in Mugla Sitki Kocman University at Molecular Biology and Genetics Department. She completed two master's education. She has studied about "identifying the role of Speedy/RINGO on MAPK and AKT pathways intersection in neuroblastoma cells" during her second master education.

Publication

- Yildiz Unal A, Korulu S, Karabay A (2012) SpeedyRINGO inhibits calpain-directed apoptosis in neurons, *J Alzheimers Dis* 31:779-91.
- Sonkusare SK, Kaul CL, Ramarao P (2005) Dementia of Alzheimer's disease and other neurodegenerative disorders – memantine, a new hope. *Pharmacol Res* 51:1–17.
- Kaya Y, Yildiz A (2018) Speedy/RINGO: A Molecular Savior in Spinal Cord Injury-Based Neurodegeneration?, *Neuroimmunology and Neuroinflammation* 6:5.
- Huang H, Liu H, Yan R, Hu M (2017) PI3K/Akt and ERK/MAPK signaling promote different aspects of neuron survival and axonal regrowth following, rat facial nerve axotomy, *Neurochem Res* 42:3515-24.
- Golipour A, Myers D, Seagroves T, Murphy D, Evan GI, et al. (2008) The Spy1/RINGO family represents a novel mechanism regulating mammary growth and tumorigenesis, *Cancer Res* 68:3591-600.

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