ROLE OF HSC70 PROTEIN IN MAINTENANCE OF ENDOPLASMIC RETICULUM CA^{2}+ HOMEOSTASIS

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Introduction. Intracellular calcium homeostasis is disrupted in many neuronal diseases and traumatic brain injuries resulting in endoplasmic reticulum (ER) stress [1]. ER stress and intracellular calcium homeostasis is a hub of signaling mechanisms that determine whether injured neurons will live or die. With survivable injuries neurons seek to restore normal function by several mechanisms including the upregulation of chaperones [2]. Hsc70 (aka Hsp73 and *HSPA8)* is one of such proteins, which is found to be highly concentrated in neurons. Unlike other chaperones in the HSP family Hsc70 is constitutively expressed and interacts with both cell cycle and apoptosis regulating proteins [3]. Therefore, we tested the hypothesis that Hsc70 regulates neural stem cell fate in response to changes intracellular calcium homeostasis. Currently little is known about the function of this novel chaperone or about the role of ER calcium homeostasis in neural stem cell fate determination and this work is the first to investigate this topic.

Materials and methods. Neural stem cells were isolated as neurospheres from 2 week old mice, plated on Matrigel (mouse extra cellular matrix) coated coverslips and differentiated in reduced serum [4]. Calcium homeostasis was challened by depleting ER stores with 50mM caffeine and ER stress was induced by glutamate (25^M for 24 hrs). Immunofluorescence using standard protocols was used to measure the levels proteins that indicate neural stem cell lineage, fate and stress response.

Results and discussion. Our results indicate that Hsc70 is present in neural stem cells and is responsive to ER stress to regulate development and differentiation.

Conclusions. Hsc70 may constitute a novel pathway for integrating intracellular calcium homeostasis and neural development.

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References.

1. Yoshida, H. (2006). ER stress and disease. The FEBS Journal. 630-658. doi:10.1111/j.1742-4658.2007.05639.x
2. Lindholm, D., Wootz, H., & Korhonen, L. (2006). ER stress and neurodegenerative diseases. Cell Death and Differentiation. 13, 385-392.
3. Liu, T., Daniels, C. K., & Cao, S. (2012). Comprehensive review on the HSC70 functions, interactions with related molecules and involvement in clinical diseases and therapeutic potential. Pharmacology and Therapeutics. 136, 354-374.
4. Babu, H., Claasen, J., Kannan, S., Runker, Palmer, T., & Kempermann G. (2011). A protocol for isolation and enriched monolayer cultivation of neural precursor cells from mouse dentate gyrus. Methods Article. DOI: 10.3389/fnins.2011.00089.