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## SAŽETCI ABSTRACTS

SUPPLEMENT

3. – 6. listopada 2018.

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Alzheimerovoj bolesti  
(CROCAD-18)  
s međunarodnim sudjelovanjem

Novigrad, Hrvatska

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October 3 – 6, 2018

Croatian Congress on  
Alzheimer's Disease  
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with International Participation

Novigrad, Croatia

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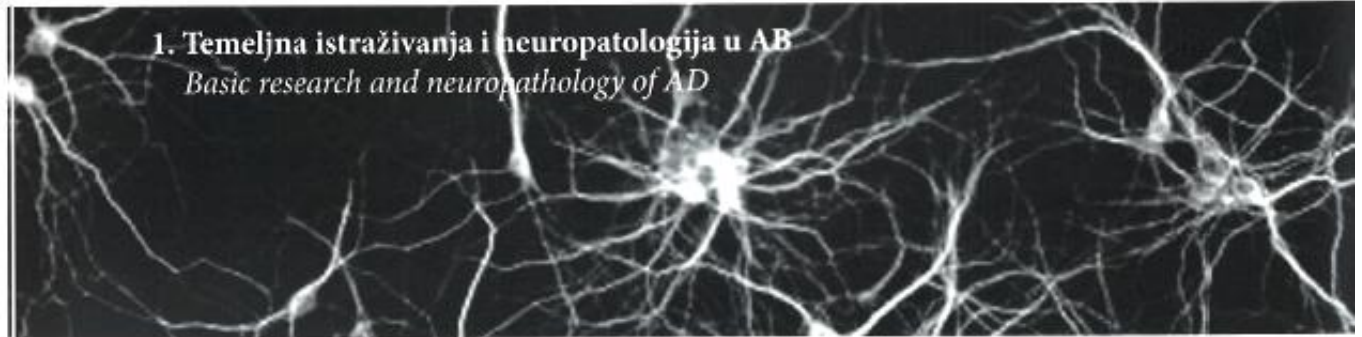
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Novigrad, Croatia

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## PROTEIN PHOSPHATASE INHIBITION BY OKADAIC ACID TREATMENT OF NEUROBLASTOMA SH-SY5Y CELLS INDUCES EXPRESSION OF HIGH MOLECULAR WEIGHT PHOSPHO-TAU-IMMUNOREACTIVE PROTEINS

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**Aim:** A key feature of Alzheimer's disease (AD) is aggregation of microtubule-associated protein tau in the neurofibrillary tangles (NFT) in the brain. NFT tau is characterized by abnormally high phosphorylation, which may result from the upregulated activity of protein kinases and downregulation of protein phosphatases.

**Methods:** To investigate tau under the condition of protein phosphatase impairment, we treated neuroblastoma SH-SY5Y cells with okadaic acid (OA), an inhibitor of protein phosphatases and analyzed total cell lysates with phospho-tau and total tau antibodies using immunoblot.

**Results:** In addition to the well-described 50-65 kDa tau isoforms, we observed that both undifferentiated and retinoic acid- and brain derived neurotrophic factor-differentiated SH-SY5Y cells treated with OA express high molecular weight protein species immunoreactive with anti-tau-pS202 and -pS396 antibodies. The apparent molecular weight of 100 kDa indicated a possibility of tau oligomer. In support, high molecular weight tau immunoreactive

proteins (HMW-TIP) were detected in a heat-stable fraction. However, we were unable to detect HMW-TIP using several anti-total tau antibodies, including a polyclonal anti-tau antibody. This could be due to protein truncation or epitope masking within the oligomer, or a possibility that HMW-TIP represents a tau-unrelated protein. DC11 antibody, which has been reported to recognize specific form of truncated tau, showed a pattern distinct from that of HMW-TIPs. Our biochemical characterization showed that HMW-TIP were stable under reducing conditions and in the presence of strong denaturing agents urea and guanidine, as well as upon alkaline phosphatase treatment.

**Conclusion:** In conclusion, we show that protein phosphatase inhibition by okadaic acid induces the appearance of HMW-TIP, which may represent tau oligomer or tau cross-reactive phospho-proteins.

**Keywords:** Alzheimer's disease, neurodegeneration, cell culture, tau protein, oligomerization