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In quest for finding the key regulators of the molecular mechanisms of long-term memory

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Contemporary understanding of memory formation relies on the concept of long-term synaptic plasticity, for which protein synthesis is a vital requirement. The best understanding of the synaptic plasticity comes from the studies of hippocampus, playing the central role in memory formation. Deterioration of hippocampal activity is associated with multiple forms of cognitive impairments and neurodegeneration. Despite extensive studies to elucidate mechanisms of memory traces formation and identity of the involved molecular factors is still elusive. Using the advantage of radial arm maze long-term spatial memory paradigm, we investigated protein turnover in mouse hippocampus during the learning. Utilizing quantitative proteomics, we identified 1592 proteins, exhibiting a complex picture of expression changes during memory formation. Variable linear decomposition enriched factors responsible for memory-related protein levels' at: The initial (167 proteins), the steep learning improvement (150 proteins) and final phases (123 proteins). Gene ontology and signaling pathways analysis revealed differential enrichment of: a) neurotrophic factors signaling pathways, proteins regulating synaptic transmission, microfilament assembly during the first day of learning curve; b) transcription and translation machinery, protein trafficking, metabolic activity and Wnt pathway during the steep phase of learning; c) cytoskeleton organization proteins at the final step. Network analysis of protein expression profiles revealed candidate key regulators of memory formation. Further, the role of two selected candidates was confirmed in synaptic plasticity. Summarizing, identification of the key regulators opens new horizons in understanding of memory formation molecular mechanisms, as well as in therapeutic targeting to shut down pathogenetic pathways of memory impairment.

Biography

I Michaelevski has completed his PhD in 2005 at Tel Aviv University and Post-doctoral studies from Weizmann Institute of Science and University of California, San Francisco as a Visitor Post-doctoral Fellow. He is an Independent Investigator from 2011 at Tel Aviv University and now in Ariel University. He is Head of the Molecular and Functional Neurobiology Laboratory.

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