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PARP1 dependent long-term memory acquisition

Unexpectedly, a post-translational modification of DNA-binding proteins, initiating the cell response to single-strand DNA damage, is also required for long-term memory acquisition in a variety of learning paradigms. Our findings disclose a molecular mechanism based on PARP1-Erk2 synergism, which may underlie this phenomenon. A stimulation induced PARP1 binding to phosphorylated Erk2 in the chromatin of cerebral neurons caused Erk-induced PARP1 activation, rendering transcription factors and promoters of immediate early genes (IEG) accessible to PARP1-bound phosphorylated Erk2. PARP1 inhibition, silencing, or genetic deletion abrogated stimulation-induced Erk-recruitment to IEG promoters, IEG expression and LTP generation in hippocampal CA3-CA1-connections. Moreover, a predominant binding of PARP1 to single-strand DNA breaks, occluding its Erk binding sites, suppressed IEG expression prevented the generation of LTP. These findings suggested that Erk-induced PARP1 activation mediates IEG expression implicated in synaptic plasticity and in long-term memory acquisition which deteriorates in senescence when aged cerebral neurons accumulate DNA single-strand breaks. These findings may be also implicated in a PARP1 dependent mechanism associated with reward-related memory retrieval.

Biography

M Cohen-Armon received BSc in Chemistry (*cum laude*) and DSc in Biophysics & Electrophysiology from the Technion, Israel. From 1992 – present, she is holding Academic position in Faculty of Medicine, Dept. of Physiology and Pharmacology at the Tel-Aviv University of Life Sciences. In 2001, she was a Visiting Researcher in the Lab of Learning and Memory, Columbia University, New York, in collaboration with Late Prof. James Schwartz. She is an Academic Editor in *PLOS ONE* and *Am. J. of Alzheimer's Disease & Other Dementias*. In 2004, she along with Prof. Schwartz first reported on a mechanism in the chromatin that is required for long-term memory acquisition during learning. Their finding was reported in *Science*, and was accompanied by Press Release in USA and Israel. She has carried out research in various other fields including human solid cancer cells and at present, her applied research on PJ34 is supported by Novartis.

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