Published in final edited form as:

Mol Cell Endocrinol. 2008 August 13; 290(1-2): 1. doi:10.1016/j.mce.2008.05.012.

Foreword for the Special Issue on "New Insights into Estrogen Signaling and Actions in the Brain"

Darrell W. Brann and Virendra B. Mahesh [Guest Editors]

Rapid advances regarding the function and mode of actions of estrogens have resulted in the recognition that estradiol has a far greater role in biology than just its well known actions in the regulation of reproductive function. Its role in neuroprotection, synaptic plasticity, memory and learning has been a subject of intense investigation in the past decade, and its potential beneficial effects in delaying and ameliorating the effects of neurodegenerative disorders continues to be an important area of research. There is also extensive evidence that estrogens act via a rapid nongenomic mechanism of action as well as the classical genomic mechanism. This special issue attempts to provide current information on a number of aspects of estrogen signaling and actions in the brain.

The first four articles address the question of estrogen signaling. Dr. Darrell Brann's group describes a novel estrogen-receptor interaction protein PELP-1 that is implicated to mediate estrogen nongenomic and genomic signaling in many tissues in the body, including the brain. Dr. Paul Mermelstein's group has presented evidence for the role of caveolin associated proteins in the action of ER- α and ER- β . Dr. Martin Kelly's group has discussed the estrogen response element (ERE) dependent and ERE-independent actions of estrogens via protein-protein interactions with transcription factors and non-genomic pathways. To further determine the role of ERE-dependent and ERE-independent pathways in estrogen action, Dr. Jon Levine's group has generated an ER- α null mouse model with an ER- knockin mutation where ER- α cannot bind DNA but retains activity in the ERE-independent pathway, that has yielded very interesting insights.

The next two articles address the important question whether estrogens, androgens and progestins are present in the brain solely via peripheral circulation or whether they can be synthesized *de novo* in the brain. Dr. Suguru Kawato's group has presented compelling evidence of the presence of aromatase enzymes in glutamatergic neurons in CA1, CA3 and dentate gyrus and shown evidence for a role of estrogens in memory related synaptic plasticity. Dr Paul Micevych's group has provided evidence that the synthesis of progesterone, a very important hormone in reproductive function is regulated by estrogens in the brain.

Finally, the last two articles deal with the action of estrogens. Since mitochondria are very important in cellular life and death decisions and estrogens have been shown to be neuroprotective, Dr. James Simpkins's group has demonstrated an important regulatory role of estrogens in mitochondrial function. Because of the possibility of beneficial effects of estrogens in Parkinson's disease, Dr. Therese DiPaolo's group has used a mouse model of Parkinson's disease to study the beneficial effects of estrogenic drugs.

In conclusion, this special issue provides an exciting compilation of “state of the art” minireviews in the area of estrogen signaling and actions in the brain, which we hope will prove beneficial to scientists and layman alike, and help propel future advances in this important area of research.