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Preface

Special issue

Reproductive steroids and growth factors play critical roles in the development of the CNS and in the normal adult brain. It is often assumed that their effects are independent, because reproductive steroids and growth factors bind to distinct receptors, but recent studies have shown that some effects of reproductive steroids and growth factors are mediated by common signal transduction pathways. In addition, it has been demonstrated that some reproductive steroids, such as estrogen, influence growth factor expression by transcriptional regulation. This field is rapidly developing: more examples of growth factors that are regulated by gonadal hormones, and new mechanisms for steroid-growth factor interactions, are identified each year.

The recent growth in this field makes it timely to review some of the most striking examples of reproductive hormone-growth factor interactions. Of the many examples for reproductive hormone-growth factor interrelationships, some of the most extensive studies have focused on estrogen and brain-derived neurotrophic factor (BDNF) or estrogen and insulin-like growth factor-1 (IGF-1). This special issue of *FIN* provides a set of reviews of these interactions that explore them in different brain regions and in different contexts, and analyze them at the cellular, systems, and behavioral levels.

These reviews provide insight into the mechanisms underlying the diverse effects of estrogen: some actions may be dependent on growth factors. Conversely, the reasons growth factors may have multiple actions in the CNS could be due to the dependence on estrogen for some of their effects. This perspective is important not only to clarify normal CNS function but also to address clinical issues, such as the relationship between estrogen and neuroprotection, or estrogen and Alzheimer's disease.

This topic was initially developed as a symposium titled "Growth Factors as 'Second Messengers' for Reproductive Hormones" for the annual meeting of the Society for Behavioral Neuroendocrinology at Austin, Texas, in June, 2005, co-organized by Andrea Kudwa (University of Virginia, USA) and Helen Scharfman (Columbia University and Helen Hayes Hospital, USA). The symposium provided a forum for investigators with different backgrounds, and studying different brain areas or behaviors, to provide

their perspectives. The interest in the presentations led to the suggestion that even more investigators become involved by generating a series of reviews that reflected the content of the presentations. This special issue provides the opportunity to share the perspectives of the contributors throughout the neuroscience community, in order to stimulate further progress in this area of research.

As was the case for the symposium, the first reviews in this special issue discuss examples of reproductive hormone-growth factor interactions that involve estrogen. The first topic involves estrogen and its relationship to BDNF, a subject with widespread implications because of the diversity of action of both estrogen and BDNF in the CNS.

Helen Scharfman and Neil MacLusky (University of Guelph, Canada) present an overview of estrogen-BDNF interactions in hippocampus and raise the importance of neuropeptide Y (NPY), a target of BDNF and estrogen that has robust functional effects in hippocampus. Farida Sohrabji and D.K. Lewis (Texas A&M University, USA) describe dependence on BDNF regulation by estrogen on brain region and age. They also raise the hypothesis that BDNF mediates the neuroprotective effects of estrogen, a perspective with important clinical implications. Cordian Beyer (University of Tübingen, Germany) reviews the ways estrogen controls the development and survival of mid-brain dopamine neurons. In this system, actions of estrogen appear to depend not only on BDNF but also on glial-derived neurotrophic factor (GDNF).

Following the organization of the Society for Behavioral Neuroendocrinology symposium, the next articles in this special issue involve the role of estrogen or progesterone with IGF-1. Luis-Miguel Garcia-Segura (Institute of Cajal, Madrid, Spain) describes the cooperativity of estradiol and IGF-1 in development, neural plasticity, neurogenesis, and neuronal survival. Anne Etgen (Albert Einstein School of Medicine, USA) reviews the evidence that the control of female reproductive behavior by estradiol and progesterone is dependent on IGF-1 signal transduction. The mechanisms for these coordinated actions are instructive because they demonstrate that reproductive steroids and growth factors may interact in many ways: (1) they can depend on neurons as well as on glia, (2) reproductive hormones can exert

transcriptional control on growth factor levels, (3) specific receptor interactions, such as the interaction between estrogen receptor α and IGF-1 receptors, may exist.

The contributors sincerely appreciate the consideration of this topic as a special issue in *Frontiers in Neuroendocrinology*. We are indebted to Jon Levine, who as editor has provided the opportunity and time to make this special issue possible. His editorial comments have allowed the transition from symposium to publication to proceed as efficiently and effectively as possible.

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