Dissertations

Novel Progestin Signaling Molecules in the Brain: Distribution, Regulation and Molecular Mechanism of Action

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Abstract
Progesterone regulates female reproduction in many ways, yet it is still unclear how signals are conveyed through nuclear and extranuclear receptors. The traditional notion was that progesterone binds classical progesterone receptors to alter gene transcription. This view has been challenged by the discovery of additional progesterone signaling molecules important for progesterone actions in non-neural cells. In granulosa cells, the progesterone receptor membrane component 1 (Pgrmc1) mediates progesterone effects by forming a receptor complex with binding partner, Serpine mRNA binding protein 1, but it is unknown whether these molecules function similarly in the brain. To begin to address these issues, I investigated the neural role of Pgrmc1 in female mouse brain, rat brain and in neural cells. By examining the neuroanatomical localization, hormonal regulation, and colocalization of Pgrmc1 within key neurons in the neural control of ovulation, Pgrmc1 emerged as a candidate signaling molecule likely to mediate progesterone functions. Furthermore, Pgrmc1 levels regulate the expression of several diverse genes and signaling pathways in neural cells. Taken together, these results demonstrate that Pgrmc1 function is likely to impact diverse neural functions.