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In vitro studies of metabolic hormone signaling and central control of fertility

L. David Jaramillo[1], Kathryn Smedlund[2], Jennifer W. Hill[3*]

[1]3000 Arlington Avenue, The University of Toledo, Toledo OH 43615

[2]Research Associate, 3000 Arlington Avenue, The University of Toledo, Toledo OH 43615

[3]Professor, Department of Physiology and Pharmacology, 3000 Arlington Avenue, The University of Toledo, Toledo OH 43615

Email: JenniferW.Hill@utoledo.edu

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Central control of puberty and fertility is inextricably linked to energetic status, though several decades of studies have shown that the cell populations and mechanisms regulating this physiology are diverse yet highly redundant. Release of prostaglandin E2 (PGE2) from astrocytes, a major non-neuronal population, has been shown to mediate gonadotropin releasing hormone (GnRH) neuron pulsatile activity (the last central effector of the hypothalamic-pituitary-gonadotropin (HPG) axis). Furthermore, astrocyte specific deletion of insulin receptor in murine models results in delayed onset of puberty and decreased reproductive fitness. Our work aims to use murine derived primary astrocyte (PMA) cultures to identify key metabolic signaling molecules/receptors and intrinsic molecular signaling pathways responsible for astrocyte release of PGE2 in vitro. Currently, treatments of primary astrocytes with insulin or insulin-related growth factor-1 (IGF-1) at various concentrations and time points are not able to consistently induce elevated PGE2 signals in comparison to vehicle as measured by ELISA. Interestingly, by using several inhibitors known to be downstream of insulin or IGF-1 receptor, we have identified key pathways for basal or intrinsic PGE2 release from astrocytes. These studies, with in vivo results in mind, suggest that maintenance and experimental conditions for PMA cultures are likely not ideal for reproducible experiments, yet underscore the potential for studying signaling mediating PGE2 release. Ongoing and future studies aim to explore various cell media conditions to sync astrocyte cultures and achieve greater sensitivity to treatments.

Keywords: Astrocyte, Prostaglandin, Fertility, Reproduction, Metabolism

