

LETTER

Follicle-stimulating Hormone (FSH) Phosphorylation of Protein Kinase B (AKT) Remains Controversial

A recent report (1) concluded that follicle-stimulating hormone (FSH) via protein kinase A (PKA) activates protein phosphatase 1 (PP1) and sensitizes insulin receptor substrate 1 to tyrosine kinase phosphorylation, leading to protein kinase B (AKT) activation. However, the results do not support this claim. The evidence that constitutively active PKA phosphorylates AKT is missing in Fig. 5A although this was highlighted under “Results” and “Discussion.” Additionally, a collaborator on this report previously described that constitutively active PKA does not stimulate AKT (2). Moreover, it is claimed that PP1 knockdown inhibits AKT stimulation but Fig. 8C shows that FSH stimulates AKT in the absence of PP1. It is also stated that inhibition of PP1 with tautomycin “blocked FSH stimulation of AKT,” yet Fig. 8A shows that FSH strongly stimulates AKT in the

presence of the inhibitor. Critically, it is unclear how the percentages provided in Fig. 8 were calculated because no statistical analysis was performed; therefore, these data have no value. Finally, it is concluded that tautomycin prevents FSH and insulin-like growth factor 1 (IGF-1) synergism on AKT; however, the use of this inhibitor is controversial as it targets several phosphatases (3). For the above reasons, the publication (1) does not provide support for the involvement of PKA or PP1 on the activation of AKT by FSH.

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- 1 Law, N. C., and Hunzicker-Dunn, M. E. (2016) Insulin receptor substrate 1, the hub linking follicle-stimulating hormone to phosphatidylinositol 3-kinase activation. *J. Biol. Chem.* **291**, 4547–4560
- 2 Escamilla-Hernandez, R., Little-Ihrig, L., Orwig, K. E., Yue, J., Chandran, U., and Zeleznik, A. J. (2008) Constitutively active protein kinase A qualitatively mimics the effects of follicle-stimulating hormone on granulosa cell differentiation. *Mol. Endocrinol.* **22**, 1842–1852
- 3 Swingle, M., Ni, L., and Honkanen, R. E. (2007) Small-molecule inhibitors of ser/thr protein phosphatases: specificity, use and common forms of abuse. *Methods Mol. Biol.* **365**, 23–38

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