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Re: Hadh2 and 3-hydroxyacyl-CoA dehydrogenase

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TO THE EDITOR: To investigate the impact of maternal diabetes on oocyte metabolism and meiotic maturation, Ratchford et al. (10) reported changes in 3-hydroxyacyl-CoA dehydrogenase II (Hadh2) activity in oocytes after treatment with 5-aminoimidazole-4-carboxamide-1-β-D-ribofuranoside or after administration of human chorionic gonadotropin, respectively (as shown in Figs. 3*A* and 4*A* of Ref. 10). These data were obtained by performing β-hydroxyacyl-CoA dehydrogenase (BOAC) assays (6), in which acetoacetyl-CoA served as the substrate. Using this substrate, these authors actually measured the combined activities of Hadh2 and 3-hydroxyacyl-CoA dehydrogenase in the oocytes, since the reduction of acetoacetyl-CoA by NADH could be effectively catalyzed by both of these distinct dehydrogenases (3, 4, 12).

The term BOAC, an abbreviation favored by some groups in the past (6, 8), has been updated to 3-hydroxyacyl-CoA dehydrogenase (HADH) (OMIM[1] 601609). According to the conventional usage, Hadh2 is an abbreviation for 3-hydroxyacyl-CoA dehydrogenase II (4, 14, 15). Moreover, the terms *HADH2* and 3-hydroxyacyl-CoA dehydrogenase II have recently been replaced by *HSD17B10* and hydroxysteroid (17β) dehydrogenase 10 (HSD10), respectively, as approved designations for the gene and gene product (OMIM 300256) (5).

HSD10, a multifunctional enzyme (1, 13, 14), is a member of the short-chain dehydrogenase/reductase family (1, 3) but not the 3-hydroxyacyl-CoA dehydrogenase family, which consists of 3-hydroxyacyl-CoA dehydrogenases and long-chain 3-hydroxyacyl-CoA dehydrogenase (OMIM609016) (11, 14).

The report (10) stated that "a lack of Hadh2 activity may impart early developmental problems, leading to embryo lethality," and further concluded that, in oocytes from diabetic mice, "activities of Hadh2 and Gpt2, two enzymes activated by AMPK, were significantly less in these oocytes." The identity of this Hadh2 activity is ambiguous. For scientific accuracy, the distinction between Hadh2 and 3-hydroxyacyl-CoA dehydrogenase is essential.

For the purpose of specifically measuring intracellular Hadh2 activities, branched-chain acyl-CoA thioesters, instead of acetoacetyl-CoA, should be used as the substrate in either the forward (7) or reverse reaction (9). In contrast to 3-hydroxyacyl-CoA dehydrogenase catalyzing the third reaction of straight-chain fatty acid oxidation spiral (2, 12), HSD10 (formerly Hadh2) functions in isoleucine and steroid metabolism (1, 13, 15). In our opinion, it is most likely that, in addition to the 3-hydroxyacyl-CoA dehydrogenase activity, the HSD10 (formerly Hadh2) activity is also relevant to the metabolism and meiotic maturation of oocytes.

GRANTS

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[1] OMIM, Online Mandelian Inheritance in Man, a database of the National Center for Biotechnology Information, US National Library of Medicine.

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