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Letter to the Editor

Aspects of UGT2B15 in the Human

To the Editor,

In their interesting and important new article on human UGT2B15, Divakaran et al. (2014) are to be congratulated for their determination to go beyond transcripts and to measure protein levels in a meticulous way.

These authors report an interesting post-natal sex difference in UGT2B15, with males expressing higher levels in the liver than females, as previously demonstrated by Court (2010). In our study (O’Shaughnessy et al., 2013), which was not mentioned in the Divakaran et al. (2014) publication, we observed no significant difference in hepatic UGT2B15 transcript between male and female fetuses at 11–21 weeks of gestation. This is despite the expression of androgen receptor (AR) transcript and protein in the human fetal liver and the plentiful circulating testosterone in the male human fetus at this time (O’Shaughnessy et al., 2007; 2013). It is very interesting that, despite the well-known sex-differentiating drive during the second trimester, this important hepatic enzyme does not show a sex difference until post-natal life. This later developmental onset of a sex difference in UGT2B15 may have important therapeutic implications. Furthermore, the fact that we (O’Shaughnessy et al., 2013) observed no effect of maternal smoking on fetal hepatic UGT2B15 expression (unlike UGT2B17 expression) does not mean that in utero exposure to cigarette smoke chemicals might not also perturb programming of post-natal UGT2B15. Unfortunately, there does not appear to be any existing literature on the effects of prenatal cigarette smoke exposure on these enzymes in the human liver in childhood or adult life.

Taken together, we now know from three well-powered studies that UGT2B15 expression is liver-predominant and climbs steadily from 5 weeks of gestation onwards (Divakaran et al., 2014; Ekstrom et al., 2013; O’Shaughnessy et al., 2013), indicative of an important role in fetal and then adult hepatic function. Furthermore, because of its role in fetal programming, a better understanding of the development of the human liver more generally, and its response to adverse exposure through maternal recreational drugs (including cigarettes and alcohol), is critical. This knowledge will be important in supporting population-based studies relating the in utero environment to subsequent adult health.

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References


Peter J. O’Shaughnessy

College of Medical, Veterinary and Life Sciences, Institute of Biodiversity, Animal Health and Comparative Medicine, University of Glasgow, Glasgow G61 1QH, United Kingdom

Paul A. Fowler

Division of Applied Medicine, Institute of Medical Sciences, University of Aberdeen, Aberdeen AB25 2ZD, United Kingdom

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