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Reply to Lechin *et al.*

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We thank Dr. Lechin for his commentary on plasma serotonin (5-HT) and pulmonary hypertension (PHT). We are very aware of the literature concerning plasma 5-HT and the association of plasma 5-HT with PHT and, indeed MacLean *et al.* have reviewed this area recently (see MacLean, *TIPS*, 20, 471–509, 1999; MacLean *et al.*, *Br. J. Pharmacol.*, 131, 161–168, 2000).

Despite this there is actually more recent evidence that suggests that it is not so much the rise in plasma 5-HT that promotes PHT but the increase in its transport into the pulmonary vascular smooth muscle cells (see Eddahibi *et al.*, *J. Clin. Invest.*, 108, 1141–1150, 2001). Indeed, 5-HT transporter inhibitors reduce experimental PHT (Eddahibi *et al.*, *Am. J. Resp. Crit. Care Med.*, 165, A748, 2002), and are being considered for clinical trials in PPH. As your own work demonstrates, a rise in plasma 5-HT alone is not sufficient for the development of PHT. Future research will certainly need to clarify the relationship between the serotonin transporter and plasma 5-HT. In addition, it is widely felt that the literature pertaining to plasma 5-HT levels is misleading. Reported levels are much higher than physiologically normal 5-HT levels due to platelet contamination. This is due to the concentration gradient between plasma and platelets. Plasma free 5-HT is normally extremely low, around 0.7 nmol L^{-1}, when measured accurately (Beck *et al.*, *Biochem. Biophys. Res. Comm.*, 196, 260–266, 1993); whilst platelet levels are well over 100 fold higher (Maurer-Spurej *et al.*, *Br. J. Haematol.*, 116, 604–611, 2002). Hence, even slight disruption of the platelets causes erroneous results. It should be advised that urine HIAA excretion be measured as well as plasma 5-HT levels. We do, however, acknowledge that the role of free plasma 5-HT is an interesting area requiring further consideration.