

6. Barwick, J. L. *et al.* Trans-species gene transfer for analysis of glucocorticoid-inducible transcriptional activation of transiently expressed human CYP3A4 and rabbit CYP3A6 in primary cultures of adult rat and rabbit hepatocytes. *Mol. Pharmacol.* **50**, 10–16 (1996).
7. Kliewer, S. A. *et al.* An orphan nuclear receptor activated by pregnanes defines a novel steroid signaling pathway. *Cell* **92**, 73–82 (1998).
8. Blumberg, B. *et al.* SXR, a novel steroid and xenobiotic-sensing nuclear receptor. *Genes Dev.* **12**, 3195–3205 (1998).
9. Lehmann, J. M. *et al.* The human orphan nuclear receptor PXR is activated by compounds that regulate CYP3A4 gene expression and cause drug interactions. *J. Clin. Invest.* **102**, 1016–1023 (1998).
10. Bertilsson, G. *et al.* Identification of a human nuclear receptor defines a new signaling pathway for CYP3A induction. *Proc. Natl Acad. Sci. USA* **95**, 12208–12213 (1998).
11. Wrighton, S. A. *et al.* Demonstration in multiple species of inducible hepatic cytochromes P-450 and their mRNAs related to the glucocorticoid-inducible cytochrome P-450 of the rat. *Mol. Pharmacol.* **28**, 312–321 (1985).
12. Schuetz, E. G. & Guzelian, P. S. Induction of cytochrome P-450 by glucocorticoids in rat liver. II. Evidence that glucocorticoids regulate induction of cytochrome P-450 by a nonclassical receptor mechanism. *J. Biol. Chem.* **259**, 2007–2012 (1984).
13. Jones, S. A. *et al.* The pregnane X receptor: a promiscuous xenobiotic receptor that has diverged during evolution. *Mol. Endocrinol.* **14**, 27–39 (2000).
14. Savas, U., Griffin, K. J. & Johnson, E. F. Molecular mechanism of cytochrome P-450 induction by xenobiotics: an expanded role for nuclear hormone receptors. *Mol. Pharmacol.* **56**, 851–857 (1999).
15. Waxman, D. J. P450 gene induction by structurally diverse xenochemicals: central role of nuclear receptors CAR, PXR, and PPAR. *Arch. Biochem. Biophys.* **369**, 11–23 (1999).
16. Blumberg, B. & Evans, R. M. Orphan nuclear receptors—new ligands and new possibilities. *Genes Dev.* **12**, 3149–3155 (1998).
17. Pinkert, C. A., Ornitz, D. M., Brinster, R. L. & Palmiter, R. D. An albumin enhancer located 10 kb upstream functions along with its promoter to direct efficient, liver-specific expression in transgenic mice. *Genes Dev.* **1**, 268–276 (1987).
18. Schuetz, E. G., Schinkel, A. H., Relling, M. V. & Schuetz, J. D. P-glycoprotein: a major determinant of rifampicin-inducible expression of cytochrome P4503A in mice and human. *Proc. Natl Acad. Sci. USA* **93**, 4001–4005 (1996).
19. Kolars, J. C., Schmiedlin-Ren, P., Shuetz, J. D., Fang, C. & Watkins, P. B. Identification of rifampin-inducible P450IIIa4 (CYP3A4) in human small bowel enterocytes. *J. Clin. Invest.* **90**, 1871–1878 (1992).
20. Selye, H. Hormones and resistance. *J. Pharm. Sci.* **60**, 1–28 (1971).
21. Kolars, J. C., Benedict, P., Schmiedlin-Ren, P. & Watkins, P. B. Aflatoxin B1-adduct formation in rat and human small bowel enterocytes. *Gastroenterology* **106**, 433–439 (1994).
22. Bocherding, S. M., Baciewicz, A. M. & Self, T. H. Update on rifampin drug interactions. II. *Arch. Intern. Med.* **152**, 711–716 (1992).
23. Hebert, M. F., Roberts, J. P., Prueksaritanont, T. & Benet, L. Z. Bioavailability of cyclosporine with concomitant rifampin administration is markedly less than predicted by hepatic enzyme induction. *Clin. Pharmacol. Ther.* **52**, 453–457 (1992).
24. Burger, H. -J., Schuetz, J. D., Schuetz, E. G. & Guzelian, P. S. Paradoxical transcriptional activation of rat liver cytochrome P-450 3A1 by dexamethasone and the antiglucocorticoid pregnenolone 16 carbonitrile: Analysis by transient transfection into primary monolayer cultures of adult rat hepatocytes. *Proc. Natl Acad. Sci. USA* **89**, 2145–2149 (1992).
25. Hashimoto, H. *et al.* Gene structure of CYP3A4, and adult-specific form of cytochrome P450 in human livers, and its transcriptional control. *Eur. J. Biochem.* **218**, 585–595 (1993).
26. Ho, S. N., Hunt, H. D., Horton, R. M., Pullen, J. K. & Pease, L. R. Site-directed mutagenesis by overlap extension using the polymerase chain reaction. *Gene* **77**, 51–59 (1989).
27. Xie, W., Chow, L. T., Paterson, A. J., Chin, E. & Kudlow, J. E. Conditional expression of erbB2 oncogene in transgenic mice elicits striking hyperplasia in stratified epithelia, and up regulation of TGF $\alpha$  expression. *Oncogene* **18**, 3593–3607 (1999).
28. Yanagimoto, T., Itoh, S., Muller-Enoch, D. & Kamataki, T. Mouse liver cytochrome P-450 (P450IIIAM1): its cDNA cloning and inducibility by dexamethasone. *Biochim. Biophys. Acta* **1350**, 329–332 (1992).
29. Jelinek, D. F., Andersson, S., Slaughter, C. A. & Russell, D. W. Cloning and regulation of cholesterol 7 $\alpha$ -hydroxylase, the rate-limiting enzyme in bile acid biosynthesis. *J. Biol. Chem.* **265**, 8190–8197 (1990).
30. Kimura, S., Gonzalez, F. J. & Nebert, D. W. Mouse cytochrome P3-450: complete cDNA and amino acid sequence. *Nucleic Acids Res.* **12**, 2917–2928 (1984).

**Acknowledgements**

We thank K.-F. Lee for ES cells and his advice on ES cultures; Y. Dayn for her assistance in DNA and ES cell microinjections; A. Pierce, H. Juguilon, G. Nelson and I. Ong for technical assistance; J. Simon and M. Lieberman for assistance in photography; and E. Stevens and L. Ong for administrative assistance. W.X. is supported by Susan G. Komen Breast Cancer Foundation. M.D. is a C.J. Martin Research fellow of Australia. R.M.E. is an Investigator of the Howard Hughes Medical Institute at the Salk Institute for Biological Studies and March of Dimes Chair in Molecular and Developmental Biology. This work was supported by Mathers Foundation (R.M.E.), the Howard Hughes Medical Institute (R.M.E.) and grants from the NIH (P.S.G.).

Correspondence and requests for materials should be addressed to R.M.E. (e-mail: evans@salk.edu).

**correction**

**The protein kinase Pak3 positively regulates Raf-1 activity through phosphorylation of serine 338**

**Alastair J. King, Huaiyu Sun, Bruce Diaz, Darlene Barnard, Wenyan Miao, Shubha Bagrodia & Mark S. Marshall**

*Nature* **396**, 180–183 (1998)

In this letter, we stated that the isoform of p21-activated protein kinase (PAK) purified from rat spleen was Pak3. At the time of going to press, this was correct nomenclature for the rat isoform based on the SwissProt protein sequence database. However, under the restructuring of PAK nomenclature within this database (December 1998) the isoform we had previously purified has now been classified as Pak2. Although we were able to detect phosphorylation of the catalytic domain of Raf-1 (CR3) by the purified kinase, now identified as Pak2, we now note that experiments using recombinant protein (Fig. 3c, d) or DNA constructs (Fig. 4) all used *bona fide* Pak3 (murine) from a qualified source (R. Cerione laboratory). This suggests the potential involvement of various Pak isoforms in the regulation of Raf-1 activity through phosphorylation of Ser 338. □

**erratum**

**Turbulent convection at very high Rayleigh numbers**

**J. J. Niemela, L. Skrbek, K. R. Sreenivasan & R. J. Donnelly**

*Nature* **404**, 837–840 (2000)

In this Article the bold paragraph incorrectly stated that thermal transport had been investigated over the range  $10^6 \leq Ra \leq 10^7$ . It should have read 'Here we investigate thermal transport over eleven orders of magnitude of the Rayleigh number ( $10^6 \leq Ra \leq 10^{17}$ )'. □