of the right upper extremity than to the left. This suggestion accords with neuroanatomical studies of the spinal cord in man, which suggest that the corticospinal tracts are larger on the right side of the cervical enlargement[5,6]. Many of these fibres originate in the left hemisphere (primarily those of the lateral corticospinal tract), and terminate in the right ventral horn of the cervical cord, where they innervate motor neurons governing the right upper extremity and related axial musculature. Moreover, electrophysiological studies of the primary motor map in non-human primates indicate that the somatotopic representation of the preferred paw is usually more extensive than that of the non-preferred paw[7]. Finally, volumetric measurements show that the right hand of right-handers is significantly larger than the left[8]. Based on what is known about trophic interactions between neurons and their peripheral targets[9], the larger size of the right hand also implies a greater amount of neural circuitry devoted to the governance of this extremity.

This conclusion is supported by other lines of evidence linking extraordinary performance to increased cortical representation. Examples are the remarkable amount of cortical space devoted to the rhinarium of pigs[10,11], the lips of sheep and goats[10], the tail of spider monkeys[12], the paws of raccoons[13,14], the whiskers of rats and mice[15], and the rays of star-nosed moles[16]. We suggest that hand preference in man is also instantiated by a greater amount of circuitry in corresponding neural centres. The gross measurements of the central sulcus that we have reported here argue for a detailed lateral comparison of the cytoarchitectonic areas along the entire human central sulcus.

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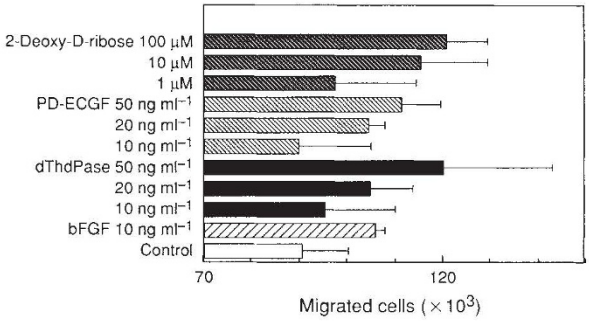
1. Coren, S. *The Left-Hander Syndrome: The Causes and Consequences of Left-Handedness* (Free Press, New York, 1992).
2. Penfield, W & Rasmussen, T. in *The Cerebral Cortex of Man* (MacMillan, New York, 1950).
3. Woolsey, C. N. *et al. J. Neurosurg.* **51**, 476–506 (1979).
4. Braak, H. *Architectonics of the Human Telencephalic Cortex* (Springer, New York, 1980).
5. Yakovlev, P. & Rakic, P. *Trans. Am. Neurol. Ass.* **91**, 366–367 (1966).
6. Nathan, P. W., Smith, M. C. & Deacon, P. *Brain* **113**, 303–324 (1990).
7. Nudo, R. J. *et al. J. Neurosci.* **12**, 2918–2947 (1992).
8. Purves, D., White, L. E. & Andrews, T. J. *Proc. natn. Acad. Sci. U.S.A.* (in the press).
9. Purves, D. *Body and Brain: A Trophic Theory of Neural Connections* (Harvard University Press, Cambridge, 1988).
10. Adrian, E. D. *Brain* **66**, 89–104 (1941).
11. Woolsey, C. N. & Fairman, D. *Surgery* **19**, 684–702 (1946).
12. Chang, H. T. *et al. Fedn. Proc.* **6**, 89 (1947).
13. Welker, W. I. & Campos, G. B. *J. comp. Neurol.* **120**, 19–36 (1963).
14. Johnson, J. I. in *Comparative Neurology of the Telencephalon* (ed. Ebesson, S.O.E.) 423–447 (Plenum, New York, 1980).
15. Woolsey, T. A. & Van der Loos, H. *Brain Res.* **17**, 205–242 (1970).
16. Catania, K. C. *et al. Nature* **364**, 493 (1993).
17. Zilles, K. in *The Human Nervous System* (ed. Paxinos G.) 752–802 (Academic, San Diego, 1990).

Angiogenic activity of enzymes

SIR — We have purified thymidine phosphorylase (dThdPase), an enzyme involved in pyrimidine nucleoside metabolism, from human placenta[1]. The activity of this enzyme has been reported to increase in several types of malignant tumours in man[1,2], but little is known about its precise physiological functions. We have shown that 120 amino acids of human dThdPase are identical to the sequence of platelet-derived endothelial cell growth factor (PD-ECGF)[3], and that recombinant PD-ECGF has dThdPase activity[4,5]. PD-ECGF was originally isolated as an endothelial cell mitogen from platelets[6]; it has chemotactic activity *in vitro* and angiogenic activity *in vivo*[7,8], but does not stimulate cell proliferation[9]. Here we show that dThdPase also has chemotactic and angiogenic activity.



Chemotactic activity of dThdPase. The number of BAE cells which migrate towards dThdPase, bFGF, PD-ECGF and 2-deoxy-D-ribose is shown. Values are the average ± s.d. of three determinations. The chemotaxis assay using BAE cells was performed as described[7]. Collagen coating of the upper wells was necessary for BAE cell adhesion. BAE cells (1×10^6 cells per well) were added to the upper wells and the compounds at the indicated concentrations in modified Eagles Medium supplemented with 1% fetal calf serum were added to the lower wells. For the control, the medium supplemented with 1% serum was added. The number of cells migrating to the lower surface of the filter was determined.

The figure shows that bovine aortic endothelial (BAE) cells migrated in response to PD-ECGF and dThdPase in a manner that was dose-dependent. We took two different approaches to investigate whether dThdPase has angiogenic activity *in vivo*. First, we investigated the effect of dThdPase on the developing vascular system of the chick chorioallantoic membrane (CAM assay) and found that recombinant PD-ECGF and purified dThdPase induce a dose-dependent angiogenic response. Second, we investigated the angiogenic activity of compounds in gelatin sponges implanted into a mouse subcutaneous pouch[10]. The haemoglobin content extracted from each sponge is a parameter of vascularization. The angiogenic response was evident at a dose of 10 μg basic fibroblast growth factor (bFGF) and dThdPase.

A competitive inhibitor of dThdPase, 6-amino-5-chlorouracil, almost completely inhibits the angiogenic effect of dThdPase, but does not significantly inhibit that of bFGF. These findings suggest that dThdPase itself is reponsible for the angiogenic activity, and that the dThdPase activity is indispensable for the angiogenic effect of dThdPase.

We thus examined the angiogenic activity of the degradation products of thymidine by dThdPase as well as 2-deoxy-D-ribose, a dephosphorylated product derived from 2-deoxy-D-ribose-1-phosphate. Angiogenesis was induced in 72% of the eggs by 6.7 ng (50 pmol) 2-deoxy-D-ribose. Thymidine, thymine, 2-deoxy-D-ribose-1-phosphate and D-ribose do not have significant angiogenic activity at the same dose as that of 2-deoxy-D-ribose.

In conclusion, PD-ECGF, dThdPase and 2-deoxy-D-ribose have chemotactic activity *in vitro* and angiogenic activity *in vivo*. PD-ECGF does not induce angiogenesis by direct stimulation of endothelial cell proliferation[9]. The enzymatic product(s) may stimulate the chemotaxis of endothelial and possibly other cells, causing angiogenesis: 2-deoxy-D-ribose may be one such product responsible for angiogenesis by dThdPase.

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1. Yoshimura, A. *et al. Biochim. biophys. Acta* **1034**, 107–113 (1990).
2. Pauly, J. L. *et al. J. nat. Cancer Inst.* **58**, 1587–1590 (1977).
3. Furukawa, T. *et al. Nature* **356**, 668 (1992).
4. Usuki, K. *et al. Biochem. biophys. Res. Commun.* **184**, 1317–1323 (1992).
5. Sumizawa, T. *et al. J. Biochem., (Tokyo)* **114**, 9–14 (1993).
6. Miyazono, K. *et al. J. biol. Chem.* **262**, 4098 (1987).
7. Ishikawa, F. *et al. Nature* **338**, 557–561 (1989).
8. Folkman, J. & Shing, Y. *J. biol. Chem.* **267**, 10931–10934 (1992).
9. Moghaddam, A. & Bicknell, R. *Biochemistry* **31**, 12141–12146 (1992).
10. Pesenti, E., Sola, F., Mongelli, N., Grandi, M. & Spreafico, F. *Br. J. Cancer* **66**, 367–372 (1992).