

Our New DNA Sequencing Service

Only Performs to the Highest Levels

Automated DNA Sequencing - *de novo* or confirmatory

A range of automated DNA sequencing services is now available from R&D Systems. This is in addition to our long standing manual sequencing service. We are flexible enough to cater for almost any project or budget. Sequences varying from tens of bases to several kilobases can be resolved.

You can provide:

- ▶ Single strand DNA
- ▶ Double strand DNA
- ▶ Amplification products
- ▶ Prepared template or transformed bacteria

Absolute confidentiality is guaranteed and we work to your deadlines.

For further information on R&D Systems' Automated DNA Sequencing Service call us today.

Technical Service

Belgique/België: 078 11 04 68. Danmark: 80 01 85 92.
 Deutschland: 0130 110169. France: 05 90 72 49.
 Nederland: 060 225607. Norge: 800 11033.
 Sverige: 020 79 31 49.

Europe
 R&D Systems Europe Ltd., UK
 Tel: +44 (0)1235 531074
 Fax: +44 (0)1235 533420

USA and Canada
 R&D Systems, Inc., MN, USA
 Tel: 1-800-343-7475
 Fax: 612 379-6580

R&D
 SYSTEMS
 1-800-343-7475

CNTF and endogenous psychoses?

Sir — Takahashi *et al.*¹ recently reported in *Nature Genetics* a null mutation in the human *CNTF* gene that is not causally related to neurological diseases. We have genotyped 352 unrelated Caucasian individuals (178 females, 174 males; mean age \pm SD: 44.2 \pm 17.2 years) for this mutation. The sample comprised 205 neurological patients, 41 healthy controls (well matched for age and sex) as well as 106 psychiatric inpatients.

We found a frequency of the mutant allele of 0.122 in the control group and of 0.144 in our patients with neurological diseases, confirming the previous results that the allele frequency is not significantly elevated in neurological patients. However, for psychiatric patients we found a significantly (chi-square test, $P < 0.05$) increased mutant allele frequency of 0.241. The distribution of the single genotypes in controls vs. neurological vs. psychiatric patients was as follows: normal: 75.6% vs. 72.7% vs 54.7%; heterozygote mutant: 24.4% vs 25.9% vs 42.5%; homozygote mutant: 0.0% vs 1.5% vs 2.8%.

More than 66% of our psychiatric patients suffered from endogenous psychoses such as schizophrenia, schizotypal and delusional disorders (ICD-10 F2) and mood affective disorders (ICD-10 F3). The three homozygous mutation carriers of the psychiatric group suffered from manic-depressive disorder, hypochondriacal depression and periodic catatonia, respectively. The latter represents a subtype of schizophrenic psychosis with considerable familial inheritance.

We conclude that a reduced level of neurotrophic factors may

represent a predisposing factor which together with other noxae such as environmental effects or other genetic defects, might lead to disturbed development and function of the CNS. On the other hand it is possible that a disorder involving the lack of a neurotrophic disorder (such as *CNTF*) might underlie a specific subgroup of psychiatric diseases. Neurodevelopmental deficits, disturbances of the cell migration and dysconnections of neuronal and glial structures are possible pathomechanisms for psychiatric disorders, mainly psychoses²⁻⁴. Associations have been found between variants in another neurotrophic factor gene (*NT3*) and schizophrenia^{5,6}. Our results support these findings. The fact that the mutations are found in healthy persons as well could be due to the strong pleiotropia and redundancy among neurotrophic factors⁷.

Johannes Thome¹
 Johannes Kornhuber¹
 Alessandra Baumer²
 Michael Rösler¹
 Helmut Beckmann¹
 Peter Riederer¹

Departments of ¹Psychiatry and
²Human Genetics
 University of Würzburg,
 Fuchsleinstraße 15, 97080 Würzburg,
 Germany

1. Takahashi, R. *et al.* *Nature Genet.* **7**, 79-84 (1994).
2. Jakob, H. & Beckmann, H. *J. Neural Transm.* **65**, 303-326 (1986).
3. Jones, P. & Murray R.M. *Br. J. Psych.* **158**, 615-623 (1991).
4. Weinberger, D.R. & Lipska B.K. *Schizophr. Res.* **16**, 87-110 (1995).
5. Nanko, S. *et al.* *Acta Psychiatr. Scand.* **89**, 390-392 (1994).
6. Hattori, M. & Nanko, S. *Biophys. Res. Comm.* **208**, 513-518 (1995).
7. Korsching, S. *J. Neurosci.* **13**, 2739-2748 (1993).