214–215 Nucleic Acids Research, 1998, Vol. 26, No. 1

A database of germline p53 mutations in cancer-prone families

Z. Sedlacek[1,3], R. Kodet[2], A. Poustka[3] and P. Goetz[1,*]

[1]Institute of Biology and Medical Genetics and [2]Institute of Pathological Anatomy, Second Medical School, Charles University, V uvalu 84, 150 06 Prague 5, Czech Republic and [3]Division of Molecular Genome Analysis, Deutsches Krebsforschungszentrum, 69120 Heidelberg, Germany

Received October 7, 1997; Accepted October 8, 1997

ABSTRACT

We created a comprehensive database covering all published cases of germline p53 mutations. The current version lists 580 tumours in 448 individuals belonging to 122 independent pedigrees. The database describes each p53 mutation (type of the mutation, exon and codon affected by the mutation, nucleotide and amino acid change), each family (family history of cancer, diagnosis of Li–Fraumeni syndrome), each affected individual (sex, generation, p53 status, from which parent the mutation was inherited) and each tumour (type, age of onset, p53 status—loss of heterozygosity, immunostaining). Each entry contains the original reference(s). The database is freely available and can be obtained from http://www.lf2.cuni.cz

INTRODUCTION

Somatic mutations in the p53 tumour suppressor gene have been described in a variety of human cancers (1). Mutations have, however, also been found in the germline of individuals from cancer-prone families (2,3), as well as in isolated patients affected by cancer at a young age, or suffering from sarcomas or multiple tumours (4,5). A large fraction of the cancer-prone families with germline p53 mutation conform to the criteria of Li–Fraumeni syndrome (6), a rare familial autosomal dominant cancer syndrome characterised mainly by early-onset sarcomas, brain tumours, premenopausal breast cancer, leukaemias and adrenocortical tumours.

The spectrum of manifestations in individuals carrying germline p53 mutations is very broad in terms of penetrance, tumour type, tumour location and age of onset. The collection of a larger set of data is thus necessary to establish correlations between the nature and location of germline p53 mutations and their phenotypical consequences. Such genotype–phenotype correlations, including figures for age-, sex- and site-specific cancer risks for carriers of diverse mutations, may in turn improve the counselling and preventative approaches undertaken to aid the affected families. In addition, increased cancer predisposition due to a germline mutation in the p53 tumour suppressor gene is a useful model for studying the general processes of carcinogenesis.

Reports of germline p53 mutations have accumulated rapidly over the past 6 years. Because the currently available databases of mutations in the p53 gene (7–9) either exclude germline mutations or contain only incomplete data, we created a comprehensive database of published cases of germline p53 mutations. In addition to listing all mutations, the database includes detailed information about the families, affected individuals, and characteristics of tumours. It therefore provides a powerful means for correlating between various aspects of germline p53 mutations and for comparing with somatic p53 mutations in sporadic tumours.

DESCRIPTION OF THE DATABASE

The current version of the database includes all germline p53 mutations reported in sufficient detail in the literature until August 1997. It lists 580 tumours in 448 individuals belonging to 122 independent pedigrees. The database will be updated regularly.

The database describes each p53 mutation (type of the mutation, exon and codon affected by the mutation, nucleotide and amino acid change), each family (family history of cancer, diagnosis of Li–Fraumeni syndrome), each affected individual (sex, generation, p53 status, from which parent the mutation was inherited) and each tumour [type, age of onset, p53 status (loss of heterozygosity and immunostaining)]. Each entry contains the original reference(s). For easy comparison, each individual included in the database has an identifier, most often the pedigree number, used in the original report. Individuals affected by cancer which were shown experimentally not to carry a germline p53 mutation are not listed, as well as affected individuals belonging to a branch of the pedigree where a germline p53 mutation was excluded (phenocopies).

AVAILABILITY

The database is freely available and can be obtained via the World Wide Web from http://www.lf2.cuni.cz . It is in Excel 5.0 format and can be loaded as an Excel file or tab delimited text file. The

*To whom correspondence should be addressed. Tel: +420 2 24435990; Fax: +420 2 24435994; Email: petr.goetz@lfmotol.cuni.cz

legend to the database can be loaded as a Word 6.0 file or plain text file. The database may be cited by referencing this article.

ACKNOWLEDGEMENTS

We thank Tomas Sladek and Jan Vejvalka for help with the WWW applications and Nina Heiss for critical reading of the manuscript. This work was supported by grants No. 9463 from the Czech Grant Agency and No. 10-0947-P01 from Deutsche Krebshilfe.

REFERENCES

1 Greenblatt,M.S., Bennett,W.P., Hollstein,M. and Harris,C.C. (1994) *Cancer Res.*, **54**, 4855–4878.
2 Malkin,D., Li,F.P., Strong,L.C., Fraumeni,J.F., Nelson,C.E., Kim,D.H., Kassel,J., Gryka,M.A., Bischoff,F.Z., Tainsky,M.A. and Friend,S.H. (1990) *Science*, **250**, 1233–1238.
3 Srivastava,S., Zou,Z., Pirollo,K., Blattner,W. and Chang,E.H. (1990) *Nature*, **348**, 747–749.
4 Malkin,D., Jolly,K.W., Barbier,N., Look,T.A., Friend,S.H., Gebhardt,M.C., Andersen,T.I., Borresen,A.L., Li,F.P., Garber,J. and Strong,L.C. (1992) *N. Engl. J. Med.*, **326**, 1309–1315.
5 Toguchhida,J., Toshikazu,Y., Dayton,S.H., Beauchamp,R.L., Herrera,G.E., Ishizaki,K., Yamamuro,T., Meyers,P.A., Little,J.B., Sasaki,M.S., *et al.* (1992) *N. Engl. J. Med.*, **326**, 1301–1308.
6 Li,F.P. and Fraumeni,J.F. (1969) *Ann. Intern. Med.*, **71**, 747–752.
7 Hainaut,P., Soussi,T., Shomer,B., Hollstein,M., Greenblatt,M., Hovig,E., Harris,C.C. and Montesano,R. (1997) *Nucleic Acids Res.*, **25**, 151–157 [see also this issue (1998) *Nucleic Acids Res.* **26**, 205–213].
8 De Vries,E.M.G., Ricke,D.O., De Vries,T.N., Hartmann,A., Blaszyk,H., Liao,D., Soussi,T., Kovach,J.S. and Sommer,S.S. (1996) *Hum. Mutat.*, **7**, 202–213.
9 Cooper,D.N. and Krawczak,M. (1993) *Human Gene Mutation*. BIOS Scientific Publishers, Oxford.