p53 and APC gene mutations: software and databases

Christophe Béroud and T. Soussi¹,*

Hôpital Necker Enfants Malades, U383 INSERM, Paris, France and ¹U301 INSERM 27 rue J. Dodu, 75010 Paris, France

Received October 7, 1996; Accepted October 8, 1996

ABSTRACT
A large number of different mutations in the APC and p53 tumor suppressor genes have been identified in various types of cancer. This substantial increase since our previous reports can enable analyses which were not previously possible. In order to capture all these new data, the software permitting analysis has been improved. This report describes the various improvements since the second release of the database.

INTRODUCTION
We have previously described a generic software which allows the entry and analysis of mutations in any gene of interest. This software was used for the creation and the analysis of mutation databases for the p53 gene (1), the APC gene (2), the fibrilin gene (3) and the VHL gene (C. Béroud, unpublished data).

Since the last release in 1995, each database has been updated and several improvements have been included in the software that is now freely available through the use of a runtime that does not require any royalties to ACI. The p53 database (6000 mutations, September 1996) and the APC database (1000 mutations, September 1996) can be used for molecular epidemiology in order to draw some precise link between carcinogen exposure and specific mutational events.

Although the p53 gene is usually inactivated by missense mutations, 10% of the mutations are small frameshift mutations (insertions or deletions). An exhaustive analysis of these frameshift mutations has been performed recently (4). Most of them do not occur at random position as they are found at specific DNA sequences which are known to be associated with DNA polymerase infidelity: monomeric base runs, adjacent or non-adjacent repeats of short tandem sequences, palindromes or homocopolymer runs.

The huge increase of p53 mutations which have been included in the database now allows more precise evaluation of the pattern of p53 mutations. For a given cancer type such as breast or lung cancer, analysis can be performed for distinct histologic group or specific mutational events.

In the APC gene, an inverse situation is observed with >95% of the alterations corresponding either to frameshift or to nonsense mutations. Huang et al. have investigated the influence of the replication error phenotype (RER) on the pattern of APC mutations (5). Although the frequency of APC mutations is similar in RER and non-RER tumors, there is a significant excess of frameshift mutations in the RER cases. This observation suggests first that the mechanism involved in APC mutation is different in these two tumor types. Second, the genetic instability associated with the RER phenotype is directly involved in APC mutation and has a direct role in tumor formation. Recent studies have confirmed that some clinical feature such as ophthalmic or dental lesions (6,7).

AVAILABILITY
The program was developed with the 4thDimension (4D) package from ACI (version 5.5.1). This version generates a compiled program which can be used either on MAC (680xx or PowerMac) or IBM computer (486 or Pentium). Furthermore, the compilation integrates the runtime of 4thDimension that alleviate the need of any other software. This standalone software has a size of 4 Mo. The p53 database and the APC database have a size of 10 Mo and 3 Mo, respectively. The software and the databases are now freely available. They can be obtained from T. Soussi (100721.1244@CompuServe.com). Ten formatted floppy disks are necessary for sending the full version of the database and the software. Solid support such as Syquest cartridge (44 Mo, 88 Mo or 200 Mo) or Jaz cartridge (1 Go) can also be handled. Both databases are also available as Microsoft Excel files (two formatted floppy disks are necessary). The software and the databases will be available on the web during mid-1997.

ACKNOWLEDGMENTS
This work was supported by grants from the Association de Recherche sur le Cancer, Ligue Nationale contre le Cancer (Comité de Paris), Ligue Nationale contre le Cancer (Comité National) and MGEN.

REFERENCES

* To whom correspondence should be addressed at present address: UMR 218 du CNRS, Institut Curie, Pavillon Trouillet Rossignol, 26 rue d’Ulm, 75231 Paris cedex 05, France. Tel: +33 1 442 34 65 11; Fax: +33 1 442 34 67 25; Email: thieerry.soussi@curie.fr