OMIM passes the 1,000-disease-gene mark

On 2 February 2000, OMIM reached 1,000 gene entries containing at least one allelic variant (AV) identified as the cause of, or associated with, a recognizable human phenotype.

OMIM, the on-line version of Mendelian Inheritance in Man[1,2], is a catalogue of human genes and genetic disorders that aims to be comprehensive, authoritative and timely. It is based on the periodical biomedical literature, and has been authored since the early 1960s and available on-line since 1987 (http://www.ncbi.nlm.nih.gov/omim). The cataloguing of AVs as subentries of gene entries was initiated in 1988. Each AV subentry is given a unique 10-digit number: the 6-digit number of the gene followed by 4 digits, beginning with 0.0001 for the first AV.

An effort has been made to list at least one AV for every gene with disease-related mutations, but only selected additional AVs are included according to the following criteria: (i) the first or first few AVs reported; (ii) common mutations in particular populations, such as the *BRCA1* mutation in Ashkenazi Jews (113705.0003); (iii) mutations in a gene causing different disorders, for example *RET*, causing Hirschsprung disease (164761.0014), multiple endocrine neoplasia type IIA (164761.0001) or type IIB (164761.0013) and familial medullary thyroid carcinoma (164766.0025); (iv) mutations in the same gene causing a phenotype with different modes of inheritance, such as recessive (139250.0001) or dominant (139250.0007) isolated growth hormone deficiency; (v) regulatory mutations such as that in the promoter in androgen-sensitive haemophilia B (306900.0001); 4 unusual mutation mechanisms such as the LINE insertion in *F8C* (306700.0022); (vii) distinctive types of mutation, such as the partial inversion of *F8C* in severe haemophilia A (306700.0067); or (viii) mutations in historical pedigrees, such as the Peutz-Jeghers syndrome pedigree reported in 1921 (602216.0014). OMIM has 450 entries with 5 or more AVs, 210 with 10 or more, 5 with 100 or more, and only 1 with more than 300, the *HBB* entry (141900).

In addition to disease-causing mutations, the AVs include 69 selected polymorphisms with some phenotypic association. Examples include the Duffy blood group associated with resistance to malaria (110700.0001) and the AV of *CCR5* associated with resistance to HIV infection (601373.0001).

There is also an effort to catalogue all distinct phenotypes related to a particular gene. There are 1,429 phenotypes associated with the 1,014 genes with AVs (as of 15 March 2000). If one excludes the 69 genes with only polymorphisms, there are, on average, 1.4 phenotypes per gene. We also determined the number of gene entries with AVs that contain the listed keywords (Table 1), reflecting the range of organs and systems represented among the 1,429 phenotypes. The frequency of the different mutation types recorded as 0.0001 is not different from that of all mutation types in the Human Gene Mutation Database[3] (http://www.uwcm.ac.uk/uwcm/mg/hgmd0.html). On 15 March 2000, the total number of AVs in OMIM under the 1,014 genes was 7,989; the total number of mutations recorded in the comprehensive HGMD was 20,864.

OMIM will continue to grow and be of increasing importance after the completion of the sequencing of the human genome. It contributes to the annotation of the human sequences, and is the only comprehensive record of the links between altered DNA sequence and disease phenotypes.

Table 1 • Categories of phenotypes associated with genes with allelic variants

Keywords	No. of gene entries	Keywords	No. of gene entries
cancer	58	stomach	25
eye	98	intestine	55
ear	42	colon	67
heart defect	115	vascular	88
mental retardation	168	skin	308
developmental delay	62	immune	85
skeletal	214	psychiatric	21
kidney	202	diabetes	98
lungs	115	hypertension	66
genital	24	obesity	39
brain	271	asthma	18
endocrine	71	neurologic	154
urinary	137	CNS	61
hand	148	newborn	97
liver	345	child	283

Data as of 15 March 2000.

Acknowledgements

We thank the members of the OMIM staff and colleagues at the National Center for Biotechnology Information, who maintain the OMIM database in an easily accessible form. The authoring and editing of OMIM at Johns Hopkins University are funded by the National Human Genome Research Institute.

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1. McKusick, V.A. *Mendelian Inheritance in Man. Catalogs of Human Genes and Genetic Disorders* (Johns Hopkins University Press, Baltimore, 1998).
2. Hamosh, A., Scott, A.F., Amberger, J., Valle, D. & McKusick, V.A. *Hum. Mutat.* **15**, 57–61 (2000).
3. Krawczak, M. & Cooper, D.M. *Trends Genet.* **13**, 121–122 (1997).