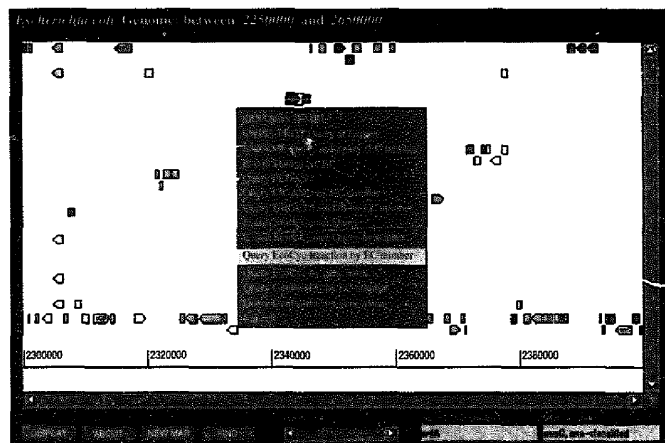


## Genomes with a view

Genome Navigator (<http://www.mping-berlin-dahlem.mpg.de/~andy/GN/>) is a Web-based visual interactive display and query resource for a number of genomes

including human, mouse, *Saccharomyces cerevisiae*, *Escherichia coli* and *Helicobacter pylori*. It graphically displays maps from a level of chromosomal bands,



A segment of the *E. coli* genome with a menu of available external data sources. Selected object (*nrDA*) above the menu is marked by a black border.

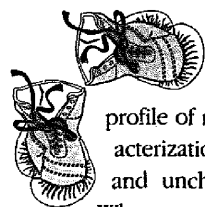
clones and markers, down to coding sequences, and allows users to zoom and to navigate the genomes, and query other data sources for additional information on any of these elements.

DerBrowser (a Java applet) is employed as a universal tool to present physical, genetic, comparative and other types of maps. A user can select any map object and poll external databases for more data. The list of data sources currently includes Whitehead/MIT, GDB, CEPH-Genethon Infocline, CHLC, Human Transcript Map, and several human chromosome-specific databases: EUGIB, SGD, YPD, MIPS, GeneQuiz, SRS, SWISS-PROT, ENZYME, NCBI, PEDANT, DBGET/LinkDB, EcoCyc, GenProtEC, *E. coli* Genetic Stock Center and TIGR. (Up-to-date references to these servers are available at the Genome Navigator site.)

For the well-studied genomes, such as *S. cerevisiae* and *E. coli*, this flexible system not only delivers a convenient positional view of any genomic region, but also provides an easy and transparent access to structural, functional, metabolic pathway and strain information.

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'It's a Knockout!' provides an update of some of the latest mouse knockouts in TBASE (Refs 1, 2). The column provides a concise phenotypic profile of novel mutants, and renders their complete characterization directly accessible to Web users via unique and unchanging accession numbers (TG-nnn-nn-nnn). Where possible, interesting knockouts will be grouped according to gene families, application or phenotypic similarities.

## It's a Knockout!

Successful gene targeting continues to furnish valuable mouse models that recapitulate various pathogenic mechanisms underlying human disease syndromes. Such a model is provided by *Pxr1*-null mice (TG-000-04-527) for the cerebrotendinous syndrome of Zellweger. Besides the absence of morphologically distinguishable peroxisomes, *Pxr1* knockouts exhibit intrauterine growth retardation, neonatal hypotonia and lethality, as well as impaired neuronal migration and apoptosis<sup>1</sup>. Likewise, embryos heterozygous for the

*Cbp* allele (TG-000-04-532), encoding a transcriptional transactivator essential to several transcription factors, are partly reminiscent of the Rubinstein-Taybi syndrome with respect to skeletal anomalies<sup>2</sup>. A putative model is described for the renal salt-wasting syndrome pseudohypoaldosteronism<sup>3</sup> by transgenic mice harboring the  $\alpha$  subunit of amiloride-sensitive epithelial sodium channel on an  $\alpha$ ENaC-null background (TG-000-04-578), while disruption of the *Fbn1* gene encoding fibrillin 1 (TG-000-04-557) causes cardiovascular

complications and early demise, phenocopying the vascular profile of Marfan syndrome<sup>4</sup>. Aberrant placental vasculogenesis is noted in *Vhlb*-null mice (TG-000-04-577), lacking the von Hippel-Lindau syndrome homolog<sup>5</sup>, while targeting of the murine X-linked *Aldyh* gene (TG-000-04-579) leads to biochemical alterations similar to those encountered in human X-linked adrenoleukodystrophy<sup>6</sup>. Interestingly, *Plcd1* knockouts (TG-000-04-575) have massively enlarged cystic kidneys, pancreatic ductal cysts and pulmonary hypoplasia, and mimic a mutation detected in human autosomal dominant polycystic kidney disease<sup>7</sup>. Finally, conditional targeting and loss of *Apc* function, accomplished by Cre-loxP-mediated recombination, provides a model of familial adenomatous polyposis coli, which allows chronological evaluation of colorectal adenoma formation<sup>10</sup>.

An enhanced double-knockout model is concurrently published by two independent groups<sup>11,12</sup> for assessing the pathogenesis and therapeutic interventions employed in Duchenne muscular dystrophy (DMD). *mdx* mice harbor a nonsense mutation in the dystrophin gene that eliminates dystrophin expression, and show many of the cellular and biochemical features of the early myopathic phase of DMD (Ref. 13). Importantly, *mdx* mice exhibit mild weakness, have normal life spans

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and do not develop the devastating myofibrosis and cardiomyopathy encountered in DMD. Moreover, single utrophin-deficient knockouts (TG-000-04-563, TG-000-04-566) have only subtle derangements at the neuromuscular junctions of skeletal muscle, characterized by reduced density of acetylcholine receptors and postsynaptic folding<sup>14,15</sup>. It has been postulated that utrophin and dystrophin act synergistically, and that the former can compensate for dystrophin deficiency more effectively in *mdx* mice than DMD patients. Indeed, analysis of *mdx*:utrophin mutants (TG-000-04-573, TG-000-04-582) reveals that, although synaptic development remains unaltered, double knockouts die prematurely of severe progressive muscular dystrophy, exhibit neuromuscular and myotendinous aberrations, and abnormally coexpress myosin heavy chain isoforms within a fiber, thus contributing a more accurate murine model of human DMD (Refs 11, 12).

Inactivation of the *Dazla* gene leads to infertility in homozygous null mice of both genders (TG-000-04-536), and unveils its critical involvement in the development and survival of germ cells in both ovary and testis. Although fertile, *Dazla* heterozygous males (TG-000-04-535) still exhibit reduced sperm counts and visible aberrations when compared with their wild-type counterparts<sup>16</sup>. Male infertility is also noted in *Hsp70-2*-null mice (TG-000-04-540) deficient in heat shock protein

70kDa2 owing to an ensuing arrest of primary spermatocytes in meiosis I. Further analysis suggests that HSP70-2 might act as a molecular chaperone in the assembly of a functional CDC2-cyclin B1 complex in pachytene spermatocytes during this phase of spermatogenesis<sup>17</sup>. Albeit fully fertile, *Ptgfr*-null females (TG-000-04-539) are devoid of prostaglandin F receptors and fail to deliver normal fetuses at term, because of a failure of the corpora lutea to terminate progesterone production<sup>18</sup>. Conversely, *Cebpb*-null female mice (TG-000-04-560) deficient in CCAAT/enhancer binding protein  $\beta$  are unexpectedly sterile: their granulosa cells fail to transgress to the luteal stage, resulting in perturbed ovarian follicle development and infertility<sup>19</sup>.

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# BOOKS



## In love with maize

### Mutants of Maize

by Gerald M. Neuffer, Edward H. Coe and Susan R. Wessler

Cold Spring Harbor Laboratory Press, 1997. US\$100.00 pbk (xii + 468 pages)  
ISBN 0 87969 444 0

I confess to having loved maize only. The reason I agreed to review the charming and informative picture book *The Mutants of Maize* is so that I wouldn't have to suffer the indignity of paying for a copy. All plant geneticists and all science libraries should own this book, or the CD-ROM.

The heart of *The Mutants of Maize* is Chapter 2 (about a third of the book) in which each of the 19 maize chromosomes is explored, stopping approximately every eight map units to focus on diagnostic phenes characterizing the

mutant alleles that define the genes. For example, at *tassel seed2* (on chromosome 1, short arm at position 24 i.e. 1S-24) is a photograph of a bizarre tassel, the male flower, covered with heavy female seeds and adorned with silks, so the plant looks as though it has a 'broken neck'. This photograph is one of four on the page. Two map units away (and on the next page) are photographs of seedling leaves of homozygotes-recessive mutants at *high chlorophyll fluorescence3* (1S-26) taken under long-wave UV light; the figure legend describes how the red glow derives

from build up of intermediates because the PSII complex of the chloroplast thylacoid membrane is missing. Phenotypes for 21 genes are highlighted on chromosome 1, all in 23 pages.

Some of the genes located on chromosome 1 have a special meaning to me. *Rough sheath2* (1S-56) is currently the object of much competition and squabbling because it probably controls the expression of class1 homeobox genes; the photograph is beautiful. The dominant mutant phenotype, vestigial glume (mutant allele *Vg1-R*, 1L-85), which is so clearly displayed here, I know to be caused by programmed cell death because of research in my laboratory. The photograph of a D8 plant (*d8* gene, 1L-132) shows the results of being unable to respond to the plant growth hormone gibberellic acid, and I know the strange alleles of this gene extremely well; there are alleles that confer subtle dwarfism but remain completely unresponsive to the

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