different definition of complexity applies to the so-called prion diseases, but, as described by C. Weissmann (University of Zürich), mouse mutant studies are again proving invaluable. Homozygous mice lacking the prion gene are still resistant to scrapie two years after infection. Interestingly, mice with hamster prion transgenes are susceptible to hamster prions but resistant to murine prions, suggesting that species homology is important, perhaps in provoking a conformational change to produce an infectious variant. There was no better illustration of the exquisite sensitivity of phototransduction than the remarkable 'back-of-the-envelope' calculation of J. Nathans (Johns Hopkins School of Medicine) showing that the potential energy expended in dropping a small coin one millimetre would translate into a discernible flash of light for the entire world's population.

Cancer is a complex genetic disease for which mouse studies have again come to the fore (D. Housman, Massachusetts Institute of Technology; N. Hastie, MRC Human Genetics Unit, Edinburgh). Homozygous male mice lacking α-inhibin develop bilateral testicular (and later adrenal) tumours, suggesting the existence of a novel signal transduction cascade involved in gonadal tumorigenesis (A. Bradley, Baylor College of Medicine). A growing number of hereditary cancer genes have been identified, including the gene for multiple endocrine neoplasia 2A (MEN2A), which B. Ponder (University of Cambridge) and colleagues have shown to be the *RET* oncogene. Ponder, "a slender, soft-spoken man with kind eyes" according to a recent magazine article (*Self*, October 1993, p. 166), described how certain *RET* mutations, even specific substitutions at a given codon, are associated with a given phenotype. Whether *RET* mutations also give rise to MEN2B or Hirschprung's disease, which was recently mapped to the same region of chromosome 10, remains to be seen, as does the identity of the hereditary breast and ovarian cancer gene (M-C. King, University of California, Berkeley).

Cancer development has been linked to the relaxation of imprinting, or parental allele-specific expression, which has been described for four mouse genes. D. Gottschling (University of Chicago) has analysed the silencing of genes at the telomere of yeast chromosomes—a phenomenon that may have significance for human disorders. The inactivation of *URA3*, for example, depends on both its proximity to the telomere and the presence of other loci. One of these, *SIR3*, is required for the basal silencing of genes, and, if overexpressed, is lethal to the cell. SIR3 may be the equivalent of mammalian MeCP proteins (A. Bird, University of Edinburgh). These nuclear proteins bind naturally to CpG dinucleotides and are thought to be important in controlling gene expression. Experiments are under way to mutate these genes in mice, which will allow comparison of the role of these proteins with DNA methyltransferase (R. Jaenisch, Whitehead Institute). S. Tilghman (Princeton University) has focused on the expression of a physically linked pair of imprinted genes, *H19* and *Igf-2*, which are expressed from the maternal and paternal chromosome respectively. These genes share common downstream enhancer factors, although whether they compete for such regulatory molecules is unclear. X-chromosome inactivation is associated with the expression of the XIST gene from the inactive X chromosome (M. Lyon, MRC Radiobiology Unit, Didcot). The *XIST* transcript is associated with the silent X (J.B. Lawrence, University of Massachusetts Medical Center), but its molecular mode of action remains a puzzle.

While new technology is urgently required in the sequencing realm, new methods are being developed to solve other 'ornery aspects' of human genetics, from the study of meiotic events in sperm (N. Arnheim, University of Southern California) to the application of deletion maps and classical genetics for pinpointing genes involved in sex determination (D. Page, Whitehead Institute). A technique called representational difference analysis allows the isolation of a DNA sequence that is unique between two otherwise identical samples (M. Wigler, Cold Spring Harbor Laboratory). The method has already been applied to pulling out probes at several mouse loci using inbred strains, and although more difficult, may prove useful in isolating human probes corresponding to hemizygous or homozygous deletions in tumours, as well as other types of rearrangement. □

Money matters

In last month's editorial (Vol. 5, 101–102; 1993), the US Army was said to have received a $210 appropriation for breast cancer research. This should, of course, have read $210 million. □