systems and mouse models have opened the way to further drug development, the fruits of which were also presented at the meeting in Boston.

NS3 is a popular target with research groups other than Boehringer Ingelheim's. Scientists at the Schering-Plough Research Institute, in New Jersey, for example, are developing their own inhibitor, and have just begun clinical trials with it. Meanwhile, Vertex Pharmaceuticals, a biotechnology company based in Cambridge, Massachusetts, has another anti-NS3 drug in the works. This substance, called VX-950, has been shown to block its target, at least in mice. The company hopes to test the drug in people next year. As John Thomson, the vice-president of research at Vertex, points out, just because Boehringer Ingelheim's compound has run into difficulties does not automatically dim the prospects of other protease inhibitors.

Meanwhile, others are attacking from different angles. Isis Pharmaceuticals, a biotech company based in Carlsbad, California, has seen encouraging results in patients given its "antisense" compound, which binds to the virus's genetic material and stops it reproducing. Other drugs highlighted in Boston tackle HCV's outer coat in an attempt to stop it binding to liver cells in the first stage of infection.

Among these is a compound from XTL Pharmaceuticals, based in Rehovot, Israel, which has just been tested on 25 chronic sufferers. The drug is a monoclonal antibody designed to lock on to, and block, one of HCV's outer features, called the E2 protein, which it needs to attach to its target cells. Roughly three-quarters of patients who received the compound saw a significant drop in their viral levels, with no serious side-effects. As a result. XTL is testing the drug in HCV-related liver-transplant patients, in whom it is hoped that it will prevent the infection of the transplanted organ by hidden reservoirs of the virus. The firm hopes to have the results of the trials before the end of next year.

In practice, it is unlikely that any one medicine will be enough to beat HCV. Just as with HIV—and, indeed, the existing interferon/ribavirin approach—a combination of drugs, attacking the problem from different angles, will probably be the most potent weapon. And as with AIDS, success in drugmaking will bring further difficulties. As Daniel Lavanchy, an infectious-disease specialist at the WHO, points out, existing treatments already cost $20,000, which puts them beyond the reach of most of the world's infected in developing countries. How much more will shiny new drugs, and the medical care needed to deliver them, add to the bill? While researchers struggle to find better ways to combat HCV, politicians will have an equally tough task—how to find the money to pay for them when they arrive. ■

Genetics

A blistering challenge

Genetics gets more complicated

THE official version of genetics is fairly straightforward. Genes are encoded in a molecule called DNA. This molecule is a double-stranded helix made from four different types of sub-molecule. These types are interchangeable, and can thus appear in any order in a strand. Reading the sub-molecules in groups of three (essentially, genetic "words") yields a message. The machinery of a cell can translate this message into a protein. And proteins are the molecules that do most of the work in a cell. Hence genes control cells. Hence, also, changing the order of the sub-molecules means that the message gets changed, and with it the protein.

Such changes are called mutations. Not all are detrimental. Some have no real effect, and are known as silent mutations. This is either because they cause no change in the composition of the protein that the gene encodes (some apparently different genetic words actually have the same meaning to the protein-making apparatus), or because the change they make has no effect on the protein's function. But if an effect is there, it will always be there unless it is masked by a second, undamaged copy of the gene in question. (There are two versions of most genes in an individual, one inherited from each parent.) That, at least, is the received wisdom. However, a study by Greg Gibson, Ian Dworkin and their colleagues at North Carolina State University, in Raleigh, suggests things may be more complicated and subtle than that. Working with the geneticists' favourite animal, the fruit fly *Drosophila*, Dr Gibson has pinpointed a series of so-called cryptic variations that have no effect on a protein's structure, but can nevertheless, if the circumstances are right, have a significant effect on the individual they belong to.

One of the genes in *Drosophila* is called Egfr. When this goes wrong, the wonky protein that results causes a fly's eyes to blister up, because too many photoreceptor cells are produced in them. In this case the blistering happens even if the other copy of the gene is healthy. In other words, a healthy gene cannot mask the blistering. That much is familiar to fly geneticists. However, the degree of blistering varies. Such variability could be due to environmental factors, but Dr Gibson suspected it might actually be due to minor variations in the healthy copy of the Egfr gene.

So much is known about fly genetics that a lot of these minor variations have already been identified, and lines of flies with particular versions of them bred routinely. The versions in question are called single-nucleotide polymorphisms (SNPs), because they involve substitutions of individual sub-molecules (nucleotides, as they are known technically) in the helix. In healthy flies, these substitutions have no perceptible effect. But when Dr Dworkin crossbred a range of fly lines each carrying a different silent SNP in the Egfr gene, with flies from a line that had a damaged Egfr gene, he found that the amount of blistering in the offspring varied significantly. More to the point, the variation was between lines, rather than within them, showing that the SNPs were somehow modifying the effect of the Egfr protein without modifying the protein itself.

How this happens is unclear. Probably, the SNPs are changing the amount of Egfr protein produced, by fine-tuning the way the gene's message is broadcast to the cell's protein-making apparatus. But whatever ▸▸

Who are you calling blistered?

its cause, it is a significant finding. A number of human diseases caused by damaged genes, such as cystic fibrosis and a range of cancers, have a similarly variable expression. It has long been suspected that in these cases, too, some sort of "cryptic" variation is to blame. But, before Dr Gibson's work, the existence of such variation was hypothetical. Now that the phenomenon has been exposed, it should be possible to find out how it works. That, in turn, may suggest ways of ameliorating these diseases by "turning down" some of the biochemical switches involved. And regardless of the practical consequences, Dr Gibson's work has shown that even genetic determinism is not the simple process that some of its proponents would have you believe. That alone is a lesson worth learning. ■

Deleting graffiti

The writing is off the wall

Researchers in Mexico have invented a new type of anti-graffiti paint

THE row over who will provide the anti-graffiti technology for Berlin's Holocaust memorial (see page 47) highlights a widespread and ancient problem. Even the Romans had to put up with slogans scratched on their fine new buildings by ungrateful locals. Ever since then, people have been struggling to deal with unofficial decorators who wish to express their opinions, or merely to catch the public eye.

Most existing anti-graffiti coatings work only a few times before they must be repainted; a nuisance when a newly cleaned surface gets redaubed almost immediately. But now, Víctor Castaño and his colleagues at the Autonomous National University of Mexico, in Santiago de Querétaro, believe they have a solution—a paint to which the daubings will not stick.

The group's research work has already led to one graffiti-proof coating, called Deletum 3000. But this is inconvenient to use as it has to be mixed just prior to use. The new product, Deletum 5000, which will be released in January, is a ready-mixed, and more effective, version, as Dr Castaño explained to the Nanotechnology in Crime Prevention and Detection conference held in London on October 28th.

Deletum 5000's special ingredient is silica. It is loaded with particles of the stuff that are but a few nanometres (billionths of a metre) across. These particles have had both oil-repellent and water-repellent molecules attached to their surfaces. Both are necessary, since the materials used by graffiti artists may be oil-based or water based. However, if merely mixed together, the two would end up repelling each other, and thus separating. By attaching them to the silica, this mutual loathing can be overcome and, as the paint dries, the changes that take place force the oil-and-water-proofing to the surface. The result is that most agents used by graffiti artists will not stick to that surface—and what does stick can be washed or brushed off easily.

Deletum 5000 can be painted on to concrete, brick, metal, plastic and wood. It is able to withstand repeated attacks. And it will last for ten years—twice as long as its predecessor. Also, because it can be applied as a very thin coating, it can be used to paint the surfaces of historic buildings without ruining the texture of the stone.

Protecting buildings may just be the start. A coating to which practically nothing adheres could provide maintenance-free surfaces in anything from restaurant kitchens to operating theatres. It could also get up-close and personal. Using his wife as a guinea pig, Dr Castaño has been testing a version of Deletum as a coating for nail varnish. Although, happily, it prevented the chipping that plagues fashion-conscious washers-up around the world, it was rather too permanent. Mrs Castaño wanted to change the colour of her fingernails more frequently than Deletum would allow. To placate her, Dr Castaño has now developed a solvent. ■

Mating preferences

Come into my beauty parlour

Female spiders are picky lovers

FREUD would have loved it: a tale of sexual cannibalism brought on by girls' youthful experience of older men. The only twist is that it is in spiders.

Eileen Hebets, of Cornell University in New York state, studies wolf spiders. Like the females of many other species of arachnid, female wolf spiders are as prone to eat a passing male as to mate with him. Indeed, in some species, the former generally follows the latter unless the male makes a speedy getaway. In wolf spiders, though, the girls make their preferences known before coitus, with extreme prejudice to any suitor to whom they take a dislike. What Dr Hebets wondered was exactly how they make their choice.

She reasoned that it might have something to do with looks—those, after all, are a criterion common to many species. Male wolf spiders do vary in appearance, particularly in the colour of their forelegs. Since the forelegs are used in the elaborate display by which a wolf spider indicates that he is a potential mate rather than (he hopes) a potential meal, Dr Hebets hypothesised that if any variation in appearance was likely to be important, it would be in the colour of a well-turned leg.

However, she carried the thought one stage further, wondering if a preference for a black versus a brown leg, assuming it existed, might be instilled in a young and impressionable female by reference to the sort of males she had met before she was, shall we say, truly interested in such matters herself. To test this idea, Dr Hebets turned to her make-up bag and brought out two shades of nail varnish (NailSlicks, midnight metal and bronze ice, as her paper

Fancy a lunch date?

in the *Proceedings of the National Academy of Sciences* quite properly describes in its materials and methods section, in case any other researcher wishes to replicate the experiment). She used these to alter the fashion sense of a clutch of male spiders.

In total, 81 young female spiders were exposed either to a number of males whose legs had been painted black, or to a number whose legs had been painted brown. When these females had matured, they were put, one at a time, into a box with a painted male, who may or may not have matched the sort of male they were used to.

The result was clear-cut. Being of a familiar type did not guarantee a male success and survival, but it brought pretty good odds with it. By contrast, being of an unfamiliar type resulted, in almost all cases, in a male becoming lunch.

As a control, Dr Hebets kept another batch of females away from contact with males until they were mature. These females did not seem to care about the colour of their suitors' legs. In spiders as in people, it seems, mating preferences are decided before sexual maturity.