As a result, gene therapists are busy redesigning vectors, while other scientists are focusing on more traditional drug therapies for treating the disease.

An intriguing new suggestion for drug therapy is the use of aminoglycoside antibiotics to override premature stop codons on the CFTR gene – a class of mutations that account for approximately 5% of the cases of CF. Drs Marybeth Howard, Raymond A. Frizzell and David M. Bedwell at the University of Alabama (Birmingham, AL, USA) report that when the aminoglycoside antibiotic G-418 is administered to HeLa cells containing transfected CFTR genes with a premature in-frame ochre (UGA) stop codon in place of a codon for glycine, the cells expressed the full-length CFTR protein [*Nature Medicine* (1996) 2, 467–469]. Moreover, the full-length protein exhibited chloride channel activity. Such activity was not a foregone conclusion because the amino acid inserted in place of the stop codon was most likely not the glycine found in the wild-type protein.

All aminoglycoside antibiotics do not possess equal ability to suppress the premature stop codons. There was little or no full-length CFTR produced when the investigators used tobramicin and gentamicin – drugs frequently prescribed for lung infections in CF patients – in place of G-148. However, treatment with gentamicin caused chloride channel activity to appear. Undoubtedly many different aminoglycosides are available in pharmaceutical libraries. A systematic effort to sort through such compounds for those that are most efficient in suppressing premature stop codons might yield an important new class of compounds for treating some forms of CF.

Another promising approach is the design of chaperone molecules targeted to CFTR that will stabilize the biologically active conformation of the mutant protein. The major gene defect accounting for most cases of CF is the ΔF508 mutation, which allows the synthesis of a full-length CFTR protein but disrupts folding of the protein. The pre-Golgi protein synthesis machinery apparently recognizes the misfolded protein as aberrant and tags it for degradation. As a result, the plasma membrane is devoid of CFTR protein and chloride channel activity.

Dr Ron Kopito and coworkers (Stanford University, CA, USA) recently found that inclusion of 10% glycerol in the cell culture growth media induces the ΔF508 CFTR to fold correctly *in vivo* and results in the appearance of chloride channels [*J. Biol. Chem.* (1996) 271, 635–638]. Others had already shown that lowered temperatures also induce the mutant protein to fold into its functional conformation [Denning, G.M. *et al. Nature* (1992) 358, 761–764]. Drs Stephen J. Delaney and Brandon J. Wainwright at the Centre for Molecular and Cellular Biology at the University of Queensland (Brisbane, Australia) believe that these observations suggest that drugs acting as 'synthetic chaperones' might be found that could stabilize the wild-type conformation of the mutant CFTR molecule and restore chloride function to most CF patients [*Nature Medicine* (1996) 2, 392–393]. A molecular screen to uncover such molecules might produce an exciting and new class of therapeutics.

Robert W. Wallace

Scots search for slimmers' holy grail

Big may be beautiful for some, but obesity is now a common condition in all affluent countries, and it is now estimated that 10% of the UK population are frankly obese. There is good evidence that it is a chronic condition, and it is associated with a significantly higher mortality and morbidity resulting from an increased incidence of coronary heart disease, hypertension, stroke, type II diabetes, sexual dysfunction, colonic cancer, arthritis and pulmonary problems. A wide range of treatments has been tested, but none has been shown to produce a sustained loss in weight.

Scotland tops the world league for the incidence of heart disease in men, and this is attributable to factors such as the soft water, poor diet, smoking and alcohol consumption. Small wonder, then, that scientists at the Strathclyde Institute for Drug Research (SIDR), Glasgow, have become interested in this area. During their research into novel hypoglycaemic agents, they included different types of plant extract in the diet of mice. One plant was found to lower blood glucose but, to their surprise, there was a marked reduction in the weight of genetically obese, hyperglycaemic animals compared with controls. Initially they attributed this simply to loss of appetite, but the weight reduction was maintained when the animals began to eat normally – even when they began to eat more than the controls.

The active ingredient has now been extracted from the plant and found to be a small organic molecule with a molecular weight of less than 200. It has been synthesized and its activity confirmed *in vivo*. SIDR have filed a preliminary patent application and, according to Professor Alan Harvey, Director of SIDR, they are now looking for a commercial sponsor to allow them to accelerate the R&D programme for this agent in exchange for commercial rights.

The SIDR track record is impressive. Since it was set up in 1988, it has generated an extensive natural product library through developing a collaborative natural product network stretching from South America, across Africa to South-East Asia. It has also developed a series of ventures with industrial partners distributed almost equally between Europe, the USA and Japan and its total income for the financial year 1994 was more than £1.1 million.

David B. Jack