adult epidermis in a corresponding fashion. A second example is that of mutations such as *engrailed*[6] and the segmentation mutations isolated and described by Nusslein-Volhard and Wieschaus[7] which alter the pattern of all segments in a homologous fashion. These mutations affect all segments of the embryo, and in a few cases all segments of the adult. Moreover, they generally result in deletion of a particular portion of the segment and in mirror image duplication of the remaining portion. Again, as in the case of homeotic mutations, these mutations result in phenotypes which may be described as the replacement of one cell pattern by another. Also, like the homeotic mutations, they alter the cell pattern of the embryo, and hence affect cells which have not undergone extensive proliferation.

Whether mutations which result in the replacement of one cell pattern by another are more likely to be relevant to the process of positional signalling than mutations which simply eliminate homologous portions of cell pattern is anybody's guess. Similarly, it is difficult to assess whether mutations which alter cell pattern in precise ways in the absence of extensive proliferation are of more interest than mutations which cause the elimination of proliferating cells. In the case of the *decapentaplegic* complex, further descriptions of mutant phenotypes at the cellular level may help to bolster the argument that this gene complex plays a specific part in positional information. But ultimately, the validity of this argument, or lack thereof, may only be apparent after all the hard work is done — when we understand the molecular roles of the *decapentaplegic* gene products. □

Synthetic peptides as the basis for future vaccines

from John Beale

MOST antigenic determinants of proteins are thought to be conformational rather than sequential; they depend upon the three-dimensional folding of the molecule rather than on the linear sequence of amino acids. Jim Bittle and his colleagues provide in this issue of *Nature*, p.30, an example of the importance of the primary amino acid sequence for foot-and-mouth disease virus (FMDV). They synthesized peptides corresponding to several regions of the virus polypeptide VP1 and found that one of them, corresponding to amino acids 141–160, when coupled to keyhole limpet haemocyanin (KLH) and given with an adjuvant, produced neutralizing antibodies to FMDV and protection against challenge in animals. Another peptide, containing amino acids 201–213 of VP1, also produced neutralizing antibodies. This is an exciting result for both theoretical and practical reasons.

The fact that alteration of conformation by denaturation or enzymatic digestion greatly changes antigenicity suggests that most antigenic determinants of proteins are conformational rather than sequential. For foot-and-mouth disease, for example, the viral peptides derived from either infected cells or disrupted virus have lost most of their immunogenicity; genetically engineered VP1 is also of low immunogenicity[1]. However, several recent lines of evidence suggest that small synthetic peptides having the sequence of antigenic determinants on a protein will, in fact, react with antibody to the intact native antigen and in some instances will neutralize its biological activity.

Langbeheim, Arnon and Sela[2], for example, found that a 20 amino acid peptide corresponding to amino acids 89–108 of the coat protein of MS2 phage, when coupled to a carrier, induced antibodies in animals which neutralized the phage and were as effective as antibody to the intact phage or the coat protein. The neutralization test involved the use of goat antiglobulin which may have produced neutralization without the primary antibody binding to a specific neutralizing site. Peptides representing other regions of the coat protein were ineffective. Similar results come from synthetic peptides corresponding to the antigenic determinant regions of diptheria toxin[3] and the natural cyanogen bromide immunizing fragment of the M protein of type 24 *Streptococcus pyogenes*[4]. Success with hepatitis B virus has also been achieved by several groups, although protection in chimpanzees has not yet been reported (see A. Zuckerman *News & Views* **295**, 98; 1982). Attempts to reproduce the native conformation of the antigenic determinant by producing a cyclic peptide[5] did not yield an antigen clearly superior to the linear peptides[6].

The situation with influenza virus is more confused. Studies of variants using monoclonal antibodies and X-ray crystallography[7] have provided very precise information about the amino acid sequences and the antigenic sites, so the effectiveness of synthetic peptides would be confidently predicted. In the event, although antibodies raised against several KLH-linked synthetic peptides could react with influenza haemagglutinin, they did not react with the previously delineated antigenic sites[8]. Moreover, antibodies raised against the haemagglutinin did not react with the synthetic peptides. These results suggest conformation of the molecule is important.

A key question is whether synthetic peptides can form the basis for a practical vaccine. The results so far obtained have great promise. Peptides with differing specificities might even be coupled to a single carrier protein to give a multivalent vaccine. Problems still remain to be solved, however, some applicable to all vaccine candidates and others more specific to particular vaccines. For foot-and-mouth disease, a synthetic vaccine would have to compete with existing vaccines which are produced by highly developed technology and are very efficient and cheap. Nonetheless, existing vaccines have some problems. First, safety: a number of outbreaks of foot-and-mouth disease have been associated with failures of the inactivation process. The most recent outbreaks in Jersey, and on the Isle of Wight, almost certainly derived from such an accident, as was shown by careful analysis of the molecular characteristics of the virus which showed striking identity between vaccine strains and strains isolated from outbreaks (ref.9 and see J. Brooksby *News & Views* **293**, 431; 1981). Clearly, a synthetic peptide overcomes these problems, but in truth, safety is not a problem if formalin is avoided as an inactivating agent. This chemical has well established limitations for viral inactivation but when acetyl ethyleneimine is substituted there are no problems with inactivation of FMDV. A second consideration is effectiveness. There are several problems for existing vaccines; first, antigenic variability. One of the reasons for suspecting that the two regions on VP1 would be effective immunogens was that they vary in amino acid sequence from strain to strain. New synthetic peptides will be required for each strain but the process of cloning and sequencing the VP1 in order to identify new peptides to synthesize should be simple. Indeed, a number of new peptides might be made ahead of time. Some strains grow poorly in cell culture and are poor vaccine strains for this reason, whilst others are very unstable or are poor strains for less clearly defined reasons. These problems may well be solved by the use of synthetic peptides. Similarly, all foot-and-mouth disease virions are relatively unstable, especially at below *p*H 5.0 and at ambient temperatures; again synthetic peptides are likely to be superior because they are more stable. The existing vaccines are effective after a single dose when given with an adjuvant, usually absorption to aluminium hydroxide and saponin for cattle and an oily adjuvant for pigs. So far, the vaccines prepared from VP1 produced

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in *Escherichia coli* have proved less effective than existing vaccines. Thus, even after two doses, antibody levels are much lower than after a single dose of conventional whole-virus vaccines. Synthetic peptides are reported by Bittle *et al.* to be far more effective than VP1 but this comparison is a bit unreal for two reasons: first, the VP1 they used was prepared by SDS treatment and polyacrylamide gel electrophoresis which is a denaturing step and may hide the sites in VP1 reacting with antipeptide sera or with native virions. Also, VP1 is a relatively small protein, whereas the synthetic peptide was coupled to KLH, one of the most immunogenic carrier proteins in the immunologist's repertoire. The results of coupling VP1 produced by genetic engineering to a similar immunogenic carrier would have been a more valid comparison. Perhaps the most encouraging feature, however, was the almost equally good results they obtained from a single dose using aluminium hydroxide compared with Freunds adjuvant. The dose schedule and duration of immunity are important aspects of vaccine development. As noted earlier for foot-and-mouth disease vaccine, because of the difficulty of mustering animals for vaccination, protection is required from a single dose, but two to three doses may be given each year. For many other vaccines a two-dose primary schedule can be followed by booster doses over a period of years. The performance of vaccines based on synthetic peptides in these respects will need study, but there is no reason to suppose they will prove less efficient than existing killed vaccines.

The feasibility and economics of synthetic peptide vaccines are difficult to judge. The situation for foot-and-mouth disease, where there is an existing relatively cheap vaccine, is very different from that of hepatitis B, for example, where the vaccine is very expensive and can be made only on a limited scale. Another key factor will be the degree of purity of the peptides required. Lerner and his colleagues did not make any special efforts to purify the peptides that are produced by the Merriefield solid-phase synthesis. Plainly it will be essential to establish that the effects are due to a peptide truly of the sequence deduced from DNA sequencing. The degree of purity ultimately required will doubtless vary according to the application. It will be necessary to have a synthetic process that consistently produces the same product — no doubt the spur of a practical application will lead to improved methods and reduced costs. The size of the peptide to be made will be a key factor. Another important element requiring more research is the carrier. In the present experiments with FMDV, KLH was used but it seems certain to be superseded because of supply problems. The addition of a carrier such as KLH negates some of the advantages of a defined synthetic vaccine and problems of hypersensitivity to the carrier may occur when repeated injections are necessary. Clearly there are alternative carriers, such as tetanus toxoid or poly-DL-lysine, and this is an important matter for more research.

Similarly, there will be a need for an adjuvant. Aluminium hydroxide is a clinically acceptable adjuvant for man and it is encouraging that it worked for FMDV. The question of the adjuvant is linked to the requirement for a carrier and the best combination will need to be reassessed. Knowledge about adjuvants is at present a dark area of immunology.

The work of Bittle *et al.* is a significant step along the road to synthetic vaccines. It opens up exciting possibilities for vaccine development which should be vigorously pursued. □

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The internal evolution of Venus and the galilean satellites

from Sean C. Solomon

THE solid planets and satellites of this Solar System display a great diversity of surface features. The Moon and Mercury and many of the icy satellites of Jupiter and Saturn have heavily cratered terrains that have been little altered for billions of years. Jupiter's moon Io has been continuously resurfaced over periods of millions of years by vigorous volcanic eruptions fuelled by the dissipation of huge solid-body tides. The Earth has a lithosphere underlying the ocean basins that is recycled by plate tectonics over a period of about 100 million years. Despite their differences, all these bodies have been shaped by common physical processes during their formation and subsequent evolution. A continuing challenge, made evident by the many new results on the internal and surface evolution of planets and satellites presented at the 13th Lunar and Planetary Science Conference*, is to understand how these common processes have produced the observed diversity of Solar System objects.

Particular interest at the conference was focused on Venus and the galilean satellites of Jupiter, all objects of recent scrutiny by US and Soviet spacecraft.

Dramatic new results have come from Venera 13 and 14 which landed on Venus on 1 and 15 March respectively (V.L. Barsukov and Yu. A. Surkov, Vernadsky Institute of Geochemistry and Analytical Chemistry; and see *News and Views* **296**, 607; 1982). Most notable are the chemical analyses of compositions of Venus soils, derived by X-ray fluorescence, that indicate similarities to a high-potassium alkali basalt at Venera 13 and a terrestrial oceanic tholeiite at Venera 14. On Earth tholeiites, because they comprise the upper igneous crust of all ocean basins, are the most common volcanic rock type. Discovery of such basalts on Venus supports the hypothesis that the major-element compositions of the two planets and their respective mechanisms for the formation and eruption of basaltic magma are similar.

Detailed comparisons of Venus and Earth with respect to planetary composition, mechanical properties and tectonic evolution were also presented. The bulk density of Venus, after correcting for the effects of compression, is generally estimated to be about one per cent less than that of the Earth[1]. The difference is often explained in terms of a slightly different composition for the two planets[1,2]. K.A. Goettel (Washington University) suggested that Venus may have a bulk density at standard conditions equal to or greater than that of the Earth. Such a result would hold if internal temperatures are significantly higher for Venus than for Earth at comparable depths and if Venus has a thicker layer of basaltic crust[3]. The required higher temperatures may occur, however, only if Venus has no analogue to terrestrial plate recycling [4]. If Goettel's suggestion is correct, then cosmochemical models for inner planet formation will require revision.

There is much debate over whether some version of plate tectonics operates on Venus. The issue has broad implications for our understanding of heat transfer and surface evolution on silicate planets. H. Spetzler, I.C. Getting (CIRES, University of Colorado) and H. Mizutani (University of Nagoya) have made a new contribution in a theoretical formulation for brittle failure in silicate planets based on stress corrosion theory and the interaction of growing cracks. Including the effects of

*The 13th Lunar and Planetary Science Conference was held at the Lyndon B. Johnson Space Center, Houston, Texas on 15–19 March 1982.

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