cause of the mononuclear cell infiltration of the pancreas seen in Type I diabetes.

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AIDS incubation period

SIR—Jonas Salk (*Nature* **327**, 475–476, 1987) postulates that the long incubation period between infection and development of clinical AIDS (acquired immune deficiency syndrome) may be due to an immune response to the initial infection which, if boosted, would reduce the viral burden and prevent development of the clinical spectrum of AIDS.

An essential part of the hypothesis is that loss of CD4 cells is a consequence of both immune destruction of these cells by the host and by virus-induced cytopathicity; uninfected cells are coated with viral protein products and, as a result, are destroyed by antibody-dependent cell cytoxicity, leading to a net loss of CD4 lymphocytes. The destruction of uninfected CD4 cells in turn diminishes antibody-dependent cell cytotoxicity.

Professor Salk might have mentioned in support of his argument the known clinical situation in which repeated immune modulation continues after exposure to human immunodeficiency virus (HIV) infection. The striking example of this is haemophilia. Patients with severe haemophilia average at least one infusion of factor VIII concentration a week which contains not only factor VIII and variable amounts of other non-autologous proteins but also significant quantities of immunoglobulins. The rate of conversion of HIV infection to clinical AIDS in haemophilia is about 3–5 per cent of the infected population, much less than that in any other risk group. So far, there has been no adequate explanation of this ten fold factor. One possibility is that, in haemophilia, the incubation period will be longer than in other infected groups and this is supported by some mathematical models which predict incubation periods of five to fifteen years following blood-borne infection. Another possibility, however, is that repeated injections of factor VIII concentrates do in fact alter the immune response of haemophiliacs so that HIV protein products which attach to uninfected CD4 cells are more quickly cleared and/or that antibody-dependent cytotoxicity to HIV-infected CD4 cells is enhanced.

Whatever the mechanism, Salk's hypothesis is an attractive way of explaining the observed low incidence of AIDS in haemophiliacs; the availability of blood specimens from such patients makes it possible to test his hypothesis.

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Processing or inactivation of antimicrobial peptides

SIR—Three years ago while studying the skin secretions of *Xenopus laevis* we isolated and sequenced some of the peptides released on adrenaline stimulation. One was a undecapeptide with a sequence (see figure) that did not correspond to any known peptide or precursor at that time. The sequence remained unnoticed on the bulletin board in the laboratory until a recent News and Views column[1] disclosed our lack of imagination and the fact that it corresponds to an amino-terminal fragment of magainin II[2]. The large amounts of this small molecular form of magainin II in the skin secretion could be a result either of biosynthetic processing or of post-secretory proteolytic degradation.

Part of the normal biosynthetic process (in toad skin glands also[3]) is the removal by a carboxypeptidase of the basic residues that have served their purpose as cleavage signals. These basic residues, however, are still found at the carboxyterminus of the magainin fragment. Thus, our undecapeptide fragment of the 23 amino-acid magainin II is probably a post-secretory degradation product.

This kind of degradation may serve as a protective inactivation mechanism occurring on the surface of the cells of the toad. The antimicrobial effect of the magainins

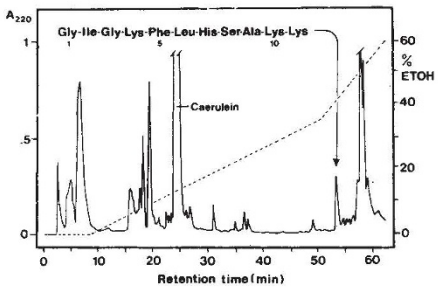

Fig. 1 Reconstituted ethanol washing of the skin of a toad injected subcutaneously with 50 μg of adrenaline, injected on a Vydac C_{18} column, (1 × 25 cm) and eluted with TFA/H_2O (0.1%) and a gradient of ethanol. The peptide indicated by the arrow, which was sequenced on an Applied Biosystems 470A sequencer, corresponds to residues 1–11 of magainin II[2].

has been connected to their ability to form amphiphilic alpha-helixes which can perturb membranes[1]. Cleavage of the magainins (magainin I also has a tryptic-like cleavage site in the middle of the molecule) results in the generation of two peptides both too small to span the membrane as an alpha-helix. The basic antimicrobial peptides of insects, the cecropins[4], can be cleaved and possibly inactivated by a similar mechanism.

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Antimicrobial peptides

SIR—Following my News and Views article[1] on the antimicrobial magainin peptides of Zasloff[2,3] I have become aware of a relevant publication of Giovannini *et al.*[4] which was published in April and which I failed to cite in my text. I apologize to the authors for this omission.

Giovannini *et al.*[4] report the detection and analysis of a wide range of peptides using skin secretions of *Xenopus laevis*. Two of these peptides, designated PGS and [Gly^{10},Lys^{22}]PGS have identical amino-acid sequences to, respectively, the magainins II and I described by Zasloff and co-workers[2,3]. It is noteworthy, however, that Zasloff[2] failed to detect the magainins in mucous-rich secretions from *X.laevis* skin.

Precise physiological roles for biologically-active peptides are hard to pin down[1]. Giovannini *et al.*[4] suggest granular gland secretions have a defensive role as have others before them — for example, Richter *et al.*[5], who also speculated more widely and considered a possible antibacterial activity associated with the need to combat infections that might befall *X.laevis* in its aqueous environment. Clearly, more experimental evidence is required before any definite conclusions can be reached concerning the functions of these peptides.

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