The colourful behaviour of garter snakes

AMONG other things, evolutionary biologists dream of finding a full explanation for the high levels of genetic diversity found in natural populations. One popular idea is that such variation might be related to the complexity of the environment. According to theory, the conditions under which environmental heterogeneity might favour the maintenance of genetic variability are likely to be less restrictive if individuals select those niches or habitats in which they are fittest; in other words, perhaps genes can 'choose' habitats.

In the case of defence against predators, it has been suggested that selection might favour particular combinations of colour pattern and behaviour leading to a build up of genetic correlations between the two. Many studies have been carried out to try to find evidence for such correlations between behaviour and morphology; some have apparently been successful, though few of them have been claimed to demonstrate a genetic basis.

On page 542 of this issue, Edmund Brodie reports the existence of genetic correlations between morphology and antipredator behaviour in natural populations of the garter snake (*Thamnophis ordinoides*) in coastal Oregon. This species is highly polymorphic with regard to colour pattern (see figure). Individuals also differ in their behavioural response to predators in ways which include sprint speed, endurance, antipredator display and the number of reversals during flight. Brodie has shown that these behaviours are not mutually exclusive but that the degree to which they are present in an individual depends to an extent on its colour-pattern phenotype.

This correlation does indeed seem to have a genetic basis. But it is not clear whether it results from pleiotropy (genes with multiple effects) or linkage disequilibrium (the nonrandom association of alleles at different loci), although Brodie favours the latter. It will be fascinating to see which one of these alternatives is supported by future research.

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well as for binding to class I MHC. This degree of competition is unique to the class I-restricted killer system and may explain why epitopes (peptide fragments) able to stimulate class I-restricted CTL are found less frequently than those able to induce class II-restricted T cells. It may also explain why efficient delivery to the cytoplasm is vital if peptides are to be effective CTL immunogens *in vivo*.

Neither access to the normal pathway of presentation nor competition with other peptides presents such formidable hurdles to the induction of a class II-restricted response. Class II molecules specialize in presenting peptides derived from antigens that come from outside the cell, and endocytosed peptides or proteins readily gain access to the compartment in which association takes place. Unlike the class I pathway, where there are no obvious cues to distinguish self from foreign proteins inside the cell, selective uptake of antibody-bound or aggregated antigen may serve to concentrate foreign antigens relative to self proteins in the endosomes, and competition for class II association is thereby avoided, at least to some extent.

Because so many proteins compete on an equal footing for class I presentation, epitopes able to stimulate CTL responses may be present in only a few antigenic complexes at the surface of an infected cell. Only CTL with high-affinity receptors will be able to respond, a point that is of some relevance to vaccinating with peptides. An acid test for the physiological relevance of killer cells that have been raised by peptide immunization is their ability to lyse target cells expressing the natural antigen endogenously. Unlike the peptide-specific CTL that can be induced by using high concentrations of peptide in culture[5], the effector cells described by Deres *et al.* pass this test.

In spite of the promise of this approach, the rarity of physiologically relevant class I-restricted epitopes raises questions over the usefulness of attempting immunization with peptides. The problem of infrequent epitopes is further compounded by the polymorphism of MHC molecules, which means that each binds a different range of peptides. If an immunogen as complex and foreign as influenza cannot be presented by some class I alleles[6], peptide vaccines will have to be carefully tailored to individual MHC alleles. This might not be completely impractical, as some class I alleles occur frequently in the population. Even so the rarity of epitopes is such that non-responsiveness is likely to occur if epitopes from only a single protein were used. For example, when hen ovalbumin is presented as an endogenous antigen, H-2^d and H-2^k mice fail to mount a CTL response[7]. It may be possible to provide a useful level of protection in an outbred population with peptide vaccines. But to achieve this a carefully designed cocktail of peptide epitopes, derived from all subunits of the pathogen, would probably have to be used. □

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