were doubts about the correctness of the KJU model, its use continued to suggest numerous experiments that yielded significant results. There was concern that the error was not in the model but in the contrary findings: for instance, in estimates of intracellular ion concentrations by indirect chemical means, superceded recently by direct measurements through ion-specific microelectrodes.

Finally, the model was beautiful, simple and reductionist: it made epithelial phenomena emerge from established properties of isolated cells. In contrast, the findings conflicting with the model were complex, intellectually unappealing and unconnected to work on isolated cells. Given a choice between what seemed to be a beautiful model and ugly findings, physiologists preferred the model. Now, many of the ugly findings that conflicted with the model can be explained by our newly-gained understanding of cross-talk. Beauty and truth are once more united! □

Trypanosoma cruzi: signals for transformation

from F.E.G. Cox

Trypanosoma cruzi is the causative organism of Chagas' disease, a disease that affects between 12 and 24 million people in South and Central America and causes considerable mortality and morbidity. The trypanosome is transmitted by numerous species of blood-sucking reduviid bugs. Trypanosomes in the trypomastigote form are taken up by the bug when it feeds and transform into epimastigote forms in the anterior part of the insect's gut. They then multiply by binary fission, building up vast numbers. Transmission becomes possible when the epimastigotes transform back into trypomastigotes again and pass into the hindgut where they are voided with the faeces to enter the victim through abrasions in the skin. The bugs live for long periods and, having become infected, remain infective for life, so providing a continuous threat to all those who might subsequently be bitten.

The signals that trigger these transformations have not yet been definitely identified but it seems certain that the membrane surface of the epimastigote form recognizes signals provided by the intrinsic or extrinsic contents of the insect's gut. The membrane surface is very complex and contains polysaccharides, lipopolysaccharides and glycoproteins. The carbohydrate components can be identified using lectins[1], and peanut butter agglutinin can be used to extract galactose-terminal glycoproteins[2]. Monoclonal antibodies can also be used to identify glycoproteins[3]. The tools with which to study the signals responsible for transformation in the bug are therefore available.

It has been suggested that the lectins already identified in the insect gut might regulate the morphogenesis of the trypanosome[4]. One of the molecules possibly involved has now been identified[5] in a letter that has just appeared in *Nature* (Sher, A. & Snary, D. **300**, 639; 1982). Epimastigotes do not readily transform into trypomastigotes (a problem that has also troubled workers using African trypanosomes) and Sher and Snary[5] devised a technique whereby epimastigotes enclosed within Millipore chambers were transplanted subcutaneously into mice, left in position for 7 h, withdrawn and transferred to an appropriate culture medium. In these conditions, epimastigotes transform into trypomastigotes, a change that does not occur if the *in vivo* 'programming' is not carried out. Using this technique, Sher and Snary were able to investigate the inhibitory effects of six monoclonal antibodies against epimastigote surface components and one lectin, wheat germ agglutinin. The substances to be tested were introduced into the culture media containing 'programmed' epimastigotes and the proportion transformed calculated.

The experiments showed that only one of the monoclonal antibodies inhibited transformation from the epimastigote to the trypomastigote form. The antibody had already been shown to be directed against a cell-surface glycoprotein with a molecular weight of 72,000 (ref.3). It does not affect the longevity or motility of the epimastigote, only its ability to transform into a trypomastigote. The lectin had no inhibitory effect. The results suggest that in the midgut of reduviid bugs there exists a substance, or substances, which reacts with the 72,000-molecular weight glycoprotein on the epimastigote surface and inhibits transformation into the trypomastigote form. Whether or not this is one of the lectins previously described has yet to be determined.

The significance of these findings is that they provide a clue as to why epimastigotes are inhibited from transforming into trypomastigotes. The inhibition probably serves two purposes — to accumulate epimastigotes in the midgut until such time as a relatively large proportion can transform into trypomastigotes, so ensuring the infection of a new host; and to retain a number of untransformed epimastigotes for later transformation and infection. Parasites need to be retained in the midgut because the nutritional conditions are more favourable there than in the hindgut.

From an epidemiological point of view the findings are very interesting. Many bugs can transmit *T. cruzi* but not all do so equally well and it is possible that the potential to act as a reservoir of infection also varies. Susceptibility and the ability to transmit the infection may be tied up with the interactions between surface molecules and insect products and as there are quantitative and qualitative differences between the surface components of different strains of *T. cruzi*[6] it may well be that a full understanding of Chagas' disease will depend on developments at the molecular level. The findings may also be significant in other situations; in leishmaniasis, for example, lectins have also been shown to bind to the surfaces of the parasites and the capacity to bind to vary between species and strains[7]. Monoclonal antibodies, at present largely the tool of immunologists, may become equally important to epidemiologists. □

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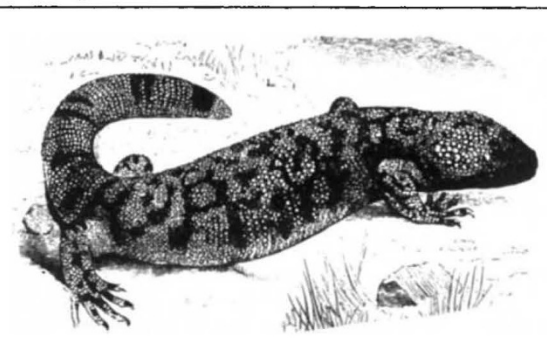

100 years ago

THE SONORAN HELODERM

(*Heloderma suspectum*)

At least one form of lizard is endowed with the faculty of producing a poisonous bite. The possessors of these formidable weapons of defence are the members of the genus *Heloderma* of naturalists, one species of which was long ago described from Mexico under the appropriate name *Heloderma horridum*. This lizard has not only grooved teeth, after the manner of many of the poisonous serpants, but likewise highly developed salivary glands, which issue at the bases of the teeth with the evident purpose of carrying poisonous saliva into the grooves.

From *Nature* **27**, 153; December 14, 1882.

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