of it. The data in the references cited in the letters of Cross *et al.* and Anderson *et al.* appear to be satisfied by the SS model. Our work cites numerous references containing data compatable with the DS model. Important new information provided by our X-ray structure determination of the ion complexes of gramicidin concern the nature of ion coordination in the channel, including identification of binding sites, occupancy factors and unusual carbonyl □ cloud ion coordination. Consequently it seems appropriate to reexamine the observations cited in the Andersen *et al.* letter in terms of the DS structure. We feel that resolution of the disparity between our X-ray results and those of Wallace and between our interpretation of the NMR results and those of Cross is a prerequisite to understanding data from other sources for which interpretation is far more subjective.

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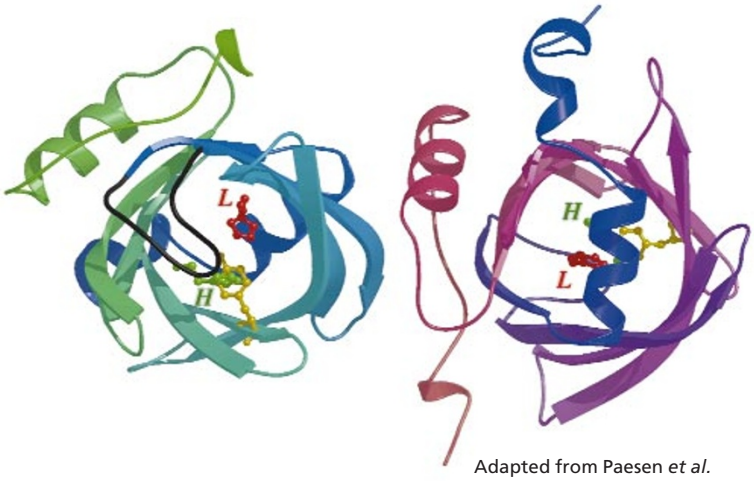
Mopping up histamine

Histamine triggers responses in capillary walls that facilitate the passage of inflammatory cells and repair factors from the blood into damaged tissues. As a result, local inflammation occurs, followed by wound healing. This histamine-induced response is part of a defense system mounted by some animals against blood-sucking arthropods. Ticks and certain other insects, which remain attached to their hosts for extended periods of time ranging from minutes to days, have a variety of soluble proteins in their saliva that remove histamine from the feeding site and therefore diminish the host's response.

An understanding of how these histamine-binding proteins (HBPs) function is important for a variety of reasons. For example, one serious side effect of a tick's feeding process can be the transmission of pathogenic microorganisms to the host. These opportunistic pathogens may take advantage of the anti-inflammatory action of the tick's HBPs. But not only tick-borne pathogens find curbing a histamine response useful — many people use drugs that block histamine receptors to treat allergic reactions. Greater knowledge of the molecular properties of HBPs could allow these proteins to be used in new therapies to curb the ill effects of histamine by an alternative route.

Recently, Paesen and colleagues reported the isolation and characterization of three histamine binding proteins (HBP1-3) from the tick *Rhipicephalus appendiculatus* and presented the crystal structure of HBP2 (*Mol. Cell* **3**, 661-671, 1999). *In vitro*, all three HBPs bind histamine tightly and specifically and, *in vivo*, these proteins compete with histamine receptors for the ligand.

HBP2 is a 171-residue protein that is an eight-stranded anti-parallel □-barrel with an □-helix (colored purple in the right image) at one end of the barrel, and a tongue-shaped loop (colored black in the left image, which shows a different orientation of the protein) at the other. Two histamine molecules, shown in red and green, are bound within the □-barrel at two sites, a high affinity site (labeled H) and a low affinity site (labeled L). Interestingly, the short helix and the tongue-shaped loop block the openings of the barrel, suggesting that conformational changes in these regions could be necessary to allow entry or exit of the ligands and thus could conceivably play a role in the high affinity of HBPs for histamine. *Hwa-ping Feng*



Adapted from Paesen *et al.*