our models; Arg^{16} is conserved betwen HNP-3 and NP-3b, and in the HNP-3 crystal structure this Gu forms a hydrogen bond with Thr^{18} (equivalent to Asp^{18} of NP-3b). In each of our three hypothetical membrane-bound models the Arg^{16} side chain can be repositioned so that its methylene groups contact lipid tails while its Gu group binds lipid head groups. Perhaps in NP-3b the Arg^{16} Gu maintains a salt bridge with Asp^{18} within the hydrophobic lipid environment. Such intramembrane salt bridges have precedence (*32*). Despite the high degree of defensin sequence variation, the flexibility of Arg side chains and plasticity of the membrane suggests that the different defensins could all interact with membranes in an identical manner.

All three of the hypotheses are consistent with the observation that a membrane potential is required for defensin activity (*8, 9*). In the wedge model the net negative charge on the inside of the cell drives the cationic wedge into the bilayer. In the pore models the potential is required to pull some of the Arg side chains completely across the membrane. All three models also rationalize the observed biphasic binding kinetics (*5*), in which the first step is predominantly electrostatic (Arg side chains with head groups) and the second of a more hydrophobic nature with lipid functions that are initially cryptic (hydrophobic dimer surface with lipid tails).

Defensin shares more in structural characteristics with small toxins that act by binding to specific receptor proteins than with other lytic peptides. Defensin's overall dimensions, positive charge, β sheet, and disulfide bonds are reminiscent of various snake, scorpion, and spider toxins (*33*) that function not by permeabilizing the membrane, but by binding molecules such as the acetylcholine receptor. Although similar to these, the defensin structure is quite different from other membrane-permabilizing peptides. The constrained, disulfide cross-linked structure, common to defensins and the small toxins, may reflect a requirement to maintain a stable and compact conformation to avoid digestion by proteases.

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20. Secondary structure was defined with the program DSSP (*21*). The first β strand, residues 4 to 6, is followed by a type VI turn (*22*) formed by residues 6 to 9, the third residue of which, Pro^8, is preceded by a cis peptide bond. Residues 9 to 11 are extended but without backbone hydrogen bonds. Then residues 11 to 14 form a type II turn with a hydrogen bond between 11 O and 14 N. At residue 15, the chain continues with a long β strand and then forms a type I′ hairpin at residues 22 to 25. The final β strand consists of residues from Gly^{24} through the carboxyl terminus. The β sheet is twisted in the usual sense (*23*), and this twist is exaggerated by a β bulge (*24*) formed by residues 17, 18, and 29.
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26. The GPNP sequence does not seem to be an exception: the Thr and Tyr that replace Arg^6 and Glu^{14} in GPNP do not seem to disrupt the structure, but rather fill the same volume as the Arg and Glu side chains in HNP-3; also a hydrogen bond can probably be formed between GPNP Thr^6 $O\gamma^1$ and Tyr^{14} Oη.
27. NMR studies on NP-5 (*28, 29*), which show a β hairpin formed by residues 19 to 28 and a type I′ turn formed by residues 22 to 25, in general agreement with the HNP-3 crystal structure. The crystal structure of HNP-3 differs, however, from the NMR structure in details. For example, the crystal structure includes a third β strand formed by residues 4 to 6. This strand has not been described for NP-5, although inspection of stereo figures in (*29*) indicates that the NMR conformation in this region is similar to that in HNP-3 crystals.
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39. Abbreviations for the amino acid residues are A, Ala; C, Cys; D, Asp; E, Glu; F, Phe; G, Gly; H, His; I, Ile; K, Lys; L, Leu; M, Met; N, Asn; P, Pro; Q, Gln; R, Arg; S, Ser; T, Thr; V, Val; W, Trp; and Y, Tyr.
40. Defensin amino acid sequence: HNP-1, HNP-2, and HNP-3, M. E. Selsted, S. S. L. Harwig, T. Ganz, J. W. Schilling, R. I. Lehrer, *J. Clin. Invest.* **76**, 1436 (1985); HNP-4, C. G. Wilde, J. E. Griffith, M. N. Marra, J. L. Snable, R. W. Scott, *J. Biol. Chem.* **264**, 11200 (1989); GPNP, M. E. Selsted and S. S. L. Harwig, *Infect. Immun.* **55**, 2281 (1987); NP-1, NP-2, NP-3a, NP-3b, NP-4, and NP-5, M. E. Selsted, D. M. Brown, R. J. DeLange, S. S. L. Harwig, R. I. Lehrer, *J. Biol. Chem.* **260**, 4579 (1985); and RatNP-1, RatNP-3, and RatNP-4, P. B. Eisenhauer *et al.*, *Infec. Immun.* **57**, 2021 (1989). The RatNP-2 sequence was determined by P. B. Eisenhauer, M. E. Selsted, and colleagues.

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Cross-Regulatory Interactions Between the Proneural *achaete* and *scute* Genes of *Drosophila*

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The *achaete* (*ac*) and *scute* (*sc*) genes of *Drosophila* allow cells to become sensory organ mother cells. Although *ac* and *sc* have similar patterns of expression, deletion of either gene removes specific subsets of sensory organs. This specificity was shown to reside in the peculiar regulation of *ac* and *sc* expression. These genes are first activated in complementary spatial domains in response to different cis-regulatory sequences. Each gene product then stimulates expression of the other gene, thus generating similar patterns of expression. Therefore, removal of one gene leads to the absence of both proneural gene products and sensory organs in the sites specified by its cis-regulatory sequences.

THE CUTICLE OF *DROSOPHILA* CARries many sensory organs (SOs). The *achaete* (*ac*) and *scute* (*sc*) genes are necessary for cells to become sensory organ mother cells (SMCs) (*1*). In the imaginal discs that give rise to the adult epidermis, *ac* and *sc* are expressed in groups of cells called the proneural clusters, which delimit the sites where SMCs will develop (*2*). Although these genes are expressed in similar