

ly, it has been suggested that the presence of chrysolmelidial in the secretion of *P. versicolora* may be artifactual, resulting from a decomposition of plagiodial (6). Our analysis indicated the presence of plagiolactone in the secretion. Contrary to Duffield and Wheeler's statement, this agrees well with other published accounts, including the one by Meinwald *et al.* (6-8).

Until such time as aqueous fractions of the defensive secretions of these larvae are assayed, we are forced to assume, as have many others (2-6, 8), that there is a strong causal relationship between the biological

activity of the larval defensive secretions and the nonaqueous compounds they contain.

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Histones and Metal-Binding Domains

Jeremy M. Berg (1) describes potential metal-binding domains in nucleic acid-binding proteins. These metal-binding domains consist of sequences Cys-X₂₋₄-Cys-X₄₋₁₅-His-X₂₋₈-Cys. Berg also cites the fact that proteins known to bind ions have short sequences of the form Cys-X₂₋₄-Cys, Cys-X₂₋₄-His, or His-X₂₋₃-His. A well-known DNA-binding protein, histone H3, also has the conserved sequence Cys-Ala-Ile-His from residues 110 to 113 (2). The nucleosome octamer has two histones of each kind of four histones. These histones are organized about an axis of symmetry, such that these conserved sequences on each histone H3 oppose each other (3). The apposition of these two histone H3 sequences would generate a structure potentially able to coordinate a metal ion, namely 2(Cys-Ala-Ile-His).

It has been proposed that the two histones H3, in the nucleosome, interact through the formation of an interchain disulfide bond (3). The suggestion that the two copies of histone H3 may interact through the coordination of metal ions raises the possibility that other types of

interactions may occur within nucleosomes. The availability of different forms of interaction may also have implications for nucleosome structure and flexibility.

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20 May 1986; accepted 29 October 1986

Response: Saavedra points out the occurrence of the sequence Cys-X₂-His in histone H3 and suggests that these residues are potentially involved in binding a metal ion between two H3 subunits. Such a sequence would not have been detected by the search algorithm I described (1) and, indeed, a general search for such short sequences would undoubtedly pick up many sequences

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28 July 1986; accepted 30 October 1986

not involved in metal binding. However, as Saavedra notes, these residues do indeed lie at the H3 dimer interface as demonstrated by observations with disulfide-linked H3 dimers (2) and by the 3.3 Å resolution electron density map of the histone octamer (3). The involvement of residues from individual polypeptides in binding metal ions and stabilizing an oligomer is well preceded by the Zn²⁺-based insulin hexamer (4). However, it must be kept in mind that with histone H3, as with the proteins identified by the previous search, the sequences noted are potential metal-binding sites. Demonstration of the actual role(s) of metal binding in these systems will require careful experimental investigation.

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21 November 1986; accepted 24 November 1986

Response: Histones and Metal-Binding Domains

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Science **234** (4783), 1589.

DOI: 10.1126/science.234.4783.1589-a

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