on cell adhesion. Maspin, as noted by Zou et al., has a structure that is 43% identical to that of equine leukocyte elastase inhibitor (HLEI) which, as well as inhibiting elastase, also binds thymosin $\beta_4$ (5).

Dubin et al. (5) postulated that an insertion (DIEDE) between strand 3B and helix G was responsible for binding thymosin $\beta_4$ in HLEI; the negatively charged residues would interact with thymosin $\beta_4$. Maspin has a similar sequence, DVEDE, inserted in an equivalent position.

This suggests that maspin may be a ligand-binding serpin that evolved from an HLEI-like serpin in a similar fashion to the evolution of cortisold-binding globulin and thyroxin-binding globulin from an $\alpha_1$-antitrypsin-like serpin (6).

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Response: We reported the discovery of a serpin called maspin, which is produced in mammary epithelial cells, but absent in invasive breast cancer and in lymph node and distant metastases (1). Maspin has tumor-suppressing properties; it inhibits tumor cell invasion through Matrigel and tumor formation by tumor transfectants that express maspin in nude mice. We proposed that these properties could result from protease inhibitor activity and cited structural similarities of maspin with the prototypic serpin, $\alpha_1$-antitrypsin.

Hopkins and Whisstock suggest that maspin may not be a protease inhibitor because of particular amino acid substitutions in the hinge region of the molecule, a peptide stretch located 9 to 15 residues from the NH$_2$-terminal of the P1-P1' peptide bond. Although it had been proposed that insertion of the hinge region into the $\beta$-sheet A was essential for protease inhibitor activity (2), current reports (3) of the crystallographic structure of antichymotrypsin suggest that this insertion may not be essential. Thus it is not established that a particular conformation involving the hinge region is a universal requirement for inhibitory serpins. To determine the functions of maspin, solving the x-ray crystal structure of the protein is of key importance, as is identifying the target protease, or ligands, or both that are associated with maspin in the cell.

Hopkins and Whisstock also propose that maspin may be a ligand-binding serpin and that its ligand may be thymosin $\beta_4$. We are examining this interesting possibility. In the example they give of equine leukocyte elastase inhibitor, however, binding of thymosin $\beta_4$ does not block its protease inhibitor activity. Thus, the question of whether maspin has protease inhibitor activity remains open.

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16 May 1994; accepted 15 June 1994

AAAS–Newcomb Cleveland Prize

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The AAAS–Newcomb Cleveland Prize is awarded to the author of an outstanding paper published in Science. The value of the prize is $5000; the winner also receives a bronze medal. The current competition period began with the 3 June 1994 issue and ends with the issue of 26 May 1995.

Reports, Research Articles, and Articles that include original research data, theories, or syntheses and are fundamental contributions to basic knowledge or technical achievements of far-reaching consequence are eligible for consideration for the prize. The paper must be a first-time publication of the author's own work. Reference to pertinent earlier work by the author may be included to give perspective.

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The award will be presented at the 1996 AAAS annual meeting. In cases of multiple authorship, the prize will be divided equally between or among the authors.
Response
Ruth Sager

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