tios greater than MORB have never been observed in arc terrains.

Anderson (8) now argues that a "correlation between ^{3}He and C suggests a recycling mechanism (IDP-rich sediments)," despite the facts that (i) He and CO_2 are both degassed from MORB and OIB lavas prior to and during eruption, so that concentrations of these gases in the original magmas are not known, and that (ii) no data exist for comparison of C and He concentrations in OIB magmas. He further argues (8) that there is no mechanism for material transport by mantle plumes. Be that as it may, Hiyagon's experiments (1) and the considerations detailed here show that there exists no mechanism for significant transport of extraterrestrial He and Ne into the source regions of hotspot magmas by subduction of IDPs in downgoing slabs.

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Response: I appreciate Harmon Craig's comment on my diffusion experiment (1) of solar He and Ne in IDPs in deep sea sediment as it gives me a chance to further examine the reliability of the experimental results.

The samples used in my diffusion experiment were not pure magnetite, but contained silicate minerals, clay minerals, and so on, which might also have contributed to control of oxygen fugacity. Furthermore, it is not certain whether the phase change could be accomplished within the relatively short heating duration of the experiment.

To answer this question, I conducted again the heating experiment under the same conditions as in the diffusion experiment and examined the run products as well as an the unheated sample with x-ray diffraction. I prepared three samples of a magnetic separate from Pacific Ocean sediment. The samples were wrapped with platinum foil, placed in a vacuum line, and heated in a molybdenum crucible at 500°C, 800°C, and 950°C for 2 hours. Partial decomposition of magnetite into a metallic phase is presumed to take place at 500°C according to Craig's suggestion, and at 800°C and 950°C the obtained diffusion data show linear correlations in the Arrhenius diagram. After cooling the furnace to room temperature, the samples were taken out from the crucible for analysis.

In the x-ray diffraction analysis, magnetite peaks were observed as major peaks together with many other peaks of silicate minerals. However, noticeable changes in the peaks were not observed among the samples; the intensities of the magnetite peaks were almost the same for all the heated samples and an unheated sample; no peaks of FeO, Fe_2O_3, or Fe were observed. The results suggest that magnetite remained as a major constituent of the magnetic fraction during the heating experiment, and that the effect of the phase change, if it occurred, may have been minimal under the present experimental conditions. The magnetite sample could have been self-buffered inside the platinum foil during the heating experiment, which could have prevented the magnetite from partial decomposition into iron within a few hours.

From these observations, I conclude that the release of solar gases from IDPs in my previous experiment was mostly a result of diffusion, and that phase changes of magnetite, if present, must have only a minor contribution to the gas release. An x-ray diffraction analysis, however, gives only qualitative information, and hence the possibility of a small amount of phase changes, pointed out by Craig, may not be ruled out completely. In any case, the results of the x-ray analysis further support the reliability of the diffusion data and support my conclusion that solar He and Ne would be lost from IDPs at shallow depths in the subduction system.

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Function of Maspin

We have examined the primary structure of the tumor-suppressing serpin, maspin, recently discovered by Z. Zou et al. (1). Unlike most serpins, maspin is most likely not an inhibitor, but may be a ligand-binding serpin, possibly of thymosin β_4.

Serpins are a highly diverse group of proteins -most of which are inhibitors of serine proteases. Some have evolved new functions, such as cortisol-binding globulin; others have no recognized function, such as ovalbumin. Although the amino acid sequences of serpins are diverse, certain regions are virtually invariant. The reactive center loop, situated near the COOH-terminus, is one of the highly variable regions and is the domain which binds to the active site of the serine protease. The sequences flanking the enzyme-binding site are highly conserved, such as the hinge region on the NH_2-terminal side of the reactive center.

This motif is important for the function of serpins as inhibitors, mutations within it interfere with inhibitory function (2), frequently resulting in the proteolysis of the serpin reactive center loop by proteases that would otherwise be inhibited.

A survey of serpin hinge regions (Table 1) shows that the non-inhibitors have diverged in sequence from the consensus at positions P14, and P12 to P8 [P-numbering according to Schechter and Berger (3)]. The equivalent region of maspin has also diverged from the consensus. In particular, the P8 to P12 residues share no homology with any known inhibitory serpin, thus maspin is probably one of the serpins that have evolved new functions.

What then might be the role of maspin? Both maspin (1) and thymosin β_4 (4) have been shown to suppress cell motility and tumor metastasis, but not to have any effect

Table 1. A comparison of the hinge region sequence of maspin with that of other serpins, inhibitory and non-inhibitory. The hinge regions of 21 serpins that have been demonstrated to be inhibitors and 5 serpins that, although well known, have not been shown to have any inhibitory activity were aligned by hand. The sequences were taken from C. J. Marshall (6). Abbreviations for the amino acid residues are as follows: 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.

Residue position	P17	P16	P15	P14	P13	P12	P11	P10	P9	P8
Consensus sequence	E	E/K	G	T	E	A	A	A	A	T
Absolute conservation in inhibitors (%)	100	55	100	77	61	94	72	55	55	77
Absolute conservation in noninhibitors (%)	60	60	80	20	80	20	40	20	0	20
Maspin sequence	E	D	G	G	D	S	I	E	V	P

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 β_4 (5).

Dubin *et al.* (5) postulated that an insertion (DIEDE) between strand 3B and helix G was responsible for binding thymosin β_4 in HLEI; the negatively charged residues would interact with thymosin β_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 cortisol-binding globulin and thyroxine-binding globulin from an α_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, α_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-P'1 peptide bond. Although it had been proposed that insertion of the hinge region into the β-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 β_4. We are examining this interesting possibility. In the example they give of equine leukocyte elastase inhibitor, however, binding of thymosin β_4 does not block its protease inhibitor activity. Thus, the question of whether maspin has protease inhibitor activity remains open.

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