

terms, or if they were saying different things it was only because they were talking about different things".

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## Enlarged family of putative helicases

SIR—I read with great interest T.C. Hodgman's correspondence<sup>1</sup> on the amino-acid motifs present in a superfamily of 21 proteins involved in nucleic-acid recombination/replication, comprising six separate families of related pro-

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	I	Ia	II	III	IV	V	VI							
p68	7	GVAQTSGKTLSEYL	20	LVLAP--TRELAQQVQVA	56	YLVLEADREHL	--DMGFEPQIRK	84	ETKRCDEL	10	AMGHGDKSQQE--RDWVLEEK	6	LJATDVASRG	(4)
eIF-4A	58	AQAGSGTKRTATFA	15	LVLAP--TRELAQQTQKV	56	MFVLDEADREHL	--SRGFGKQIYD	81	NTRKRVDEL	10	VSMHGMQDQKE--RDVIMBEFR	6	LITTLDLALG	(3)

Conserved motifs of p68 and eIF-4A aligned to match the six families identified by Hodgman. As in Hodgman's figure (see *Nature* 333; 578), hyphens represent gaps introduced during the alignment and the number of amino-acid residues between motifs is shown to the left of each motif.

teins, to which I can now add a seventh, and the first higher eukaryotic, family.

Visual inspection of the deduced amino-acid sequences of eIF-4A, a translation initiation factor<sup>2</sup>, and p68, a nuclear protein that may be a helicase<sup>3</sup>, readily revealed the presence of all six of Hodgman's motifs in the two proteins, which share 32% amino-acid identity. As the figure shows, they also both possess the additional motif (here called Ia) between motifs I and II that Hodgman noted in a subset of the superfamily known to interact with DNA. In p68 and eIF-4A motifs II and III are fused and the gap between motif III and IV is atypically large, perhaps in compensation, because the gap between the II/III boundary and the start of domain IV is within the range of the other six families. The 92 residues of the motifs constitute 23% of the eIF-4A coding sequence and yet contain 41% of the total amino-acid identities with p68. Within the 92 residues, p68 and eIF-4A share 54% identity; outside the motifs they show only 24% identity.

The recruitment of this family of two new related proteins to the superfamily broadens its scope, as they are the only representatives of the superfamily drawn from the higher eukaryotes and because, while current work suggests that p68 is a DNA binding protein and may well be a cellular DNA helicase active in replication, eIF-4A does not have such a function. Instead, it is a polynucleotide stimulated ATPase, which exerts a helicase activity on double-stranded RNA and acts as an initiation factor for eukaryotic translation, probably by rendering the end of the mRNA single stranded to permit

ment along the polynucleotide backbone, but whether that is so awaits the determination of the polarity of more helicases.

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## Schistosomiasis vaccine

SIR—We read with great interest the letter entitled "Paramyosin and actin in schistosomal teguments" by Matsumoto *et al.*<sup>1</sup> In addition to corroborating published data on the presence of actin in tegumental spines<sup>2</sup>, this report confirms our own observation using monoclonal anti-schistosome antibodies which suggested that paramyosin may be localized in "subtegumental cells or . . . tegument itself"<sup>3</sup>.

We would like to correct a possible source of misinterpretation, however. While paramyosin is indeed located in the tegument, as Matsumoto and his colleagues describe, it is most definitely *not* exposed on the parasite surface in a manner accessible for antibody binding. We have made this observation repeatedly on intact worms<sup>4</sup> as well as worms damaged by brief exposure to praziquantel (P. J. Brindley, manuscript in preparation).

We have hypothesized that paramyosin functions as a vaccine antigen by being released from the parasite and eliciting a T-lymphocyte-dependent cell-mediated response rather than by serving as a surface-exposed target for protective antibodies<sup>5,6</sup>. In this context, the results presented by Matsumoto *et al.* are intriguing as they suggest a possible route (transport to the exterior via inclusion in membrane-bound elongate bodies) by which paramyosin may be liberated from the schistosome.

Regardless, it is clear from a recently completed vaccine trial that immunization with paramyosin can induce consistent protection against murine-schistosomiasis<sup>6</sup>.

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## Two chimps, too few

SIR—In their zeal to minimize the numbers of chimpanzees needed for AIDS vaccine tests (*Nature* 333, 513; 1988), Prince *et al.* disregard the biostatistical principles which form the basis of drug and vaccine testing. Acknowledging that it is "necessary to determine whether immunization is protective", they state that "This is most rapidly and economically done by immunizing two chimpanzees and then challenging them with a small dose of live virus to see if infection is prevented. If it is, clinical trials would ensue". I assume that they use the conventional definition of clinical trials, meaning tests in humans.

It is unfortunate for all who love animals that this sample size of two is not adequate for statistical inference. According to the elementary laws of probability, if a vaccine fails to confer protection in 10% of cases, we would need a study with 29 animals before we could be 95% certain of detecting at least a single such failure in our experiment. Indeed, if the vaccine fails 50% of the time, there is a 25% chance that both chimps in an experimental pair of animals would be successfully protected, as well as a 25% chance that both would fail to be protected. (I have assumed for simplicity an all-or-nothing response.) Thus if we make a decision based on two animals we may either move too confidently to clinical trials, or else erroneously judge a vaccine to be utterly worthless, and discard it. It seems to me terribly premature to move drug or vaccine testing from the preclinical to the clinical stage based on the slender evidence provided by small numbers of experimental animals, for to do so is to shift an unknown burden of risk from animals to human subjects.

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