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Short communication

Schistosoma mansoni albumin, a major defense against oxidative damage, was acquired by lateral gene transfer from a mammalian host

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Schistosoma mansoni parasites reside in the circulatory system of their human host where they can survive for up to 30 years. In this aerobic environment, worms must have effective mechanisms to maintain cellular redox balance, including immune-generated oxygen radicals as well as those generated in the parasite during respiration and the breakdown and consumption of host hemoglobin. Addition of one electron to O_2 produces superoxide, which is rapidly dismutated to O_2 and H_2O_2 by superoxide dismutase. The H_2O_2 formed is itself able to diffuse and cause cellular damage and must be neutralized to prevent the formation of the more damaging hydroxyl radical. In many organisms, intracellular H_2O_2 is eliminated by catalase, glutathione peroxidase (GPx), and/or peroxiredoxin (Prx). Schistosomes have abundant superoxide dismutase but completely lack catalase and have relatively low levels of GPx, whose role may be to protect bio-membranes from oxidative damage [1–4]. Peroxiredoxins provide significant, perhaps the vast majority, of H_2O_2-reducing activity in schistosomes [4]. Silencing of Prx expression in larval parasites by RNA interference is not matched by an increase in GPx expression; instead, expression of a parasite albumin is induced [4]. The *S. mansoni* albumin protein was identified by mass spectrometry of proteins in Prx-silenced larval parasites that were oxidatively damaged and subsequently labeled by 2,4-dinitrophenol hydrazine and purified by affinity chromatography. The albumin protein was present in axenically cultured parasites only after Prx silencing. The peptides identified had exact matches to a putative *S. mansoni* albumin (AF418550), and were similar, but not identical to mammalian albumins. Albumin and Prx1 appear to function as the main mechanism for hydrogen peroxide defense in the parasite. Although albumin may function as a sacrificial extracellular antioxidant protein [5] and as an enzymatic antioxidant [6], the presence of albumin in an invertebrate is highly unusual. In this study, we addressed the phylogenetic relatedness of schistosome albumin to vertebrate albumins and proposed that *S. mansoni* acquired its albumin gene from a rodent host *via* lateral gene transfer.

Extensive BLAST searches did not find any invertebrate sequences with homology to the *S. mansoni* albumin protein. As such, it represented the sole invertebrate sequence in diverse sampling of vertebrate serum albumins. Overall resolution of albumin (and alpha-fetoprotein) phylogeny was high, as indicated by posterior probabilities (Fig. 1). The majority of nodes received high support except for regions of poor taxon sampling (*e.g.*, few relatives of the horse or marmot are included in the analysis). Mammalian alpha-fetoprotein and serum albumins formed separate clades, indicative of a gene duplication event prior to mammalian diversification. The few available non-mammalian albumin sequences make interpretation of deeper relationships difficult. Support was very high for monophyly of the rodent serum albumins. Included in the rodent albumin clade was the *S. mansoni* albumin, with closest common ancestry predicted to be with the red vole *Microtus fortis*; 87.14% amino acid sequence similarity exists between these two sequences for the aligned regions. While a complete sampling of rodent diversity is needed to accurately determine the exact origins of the *S. mansoni* albumin, our phylogenetic analysis very strongly supports its origin *via* lateral gene transfer from a rodent host.

Codon usage is characteristic for an organism and is biased depending on GC content of coding sequence. Coding sequence in *S. mansoni* is 37.33% GC (1st letter GC 47.53%, 2nd letter GC 38.49%, and 3rd letter GC 25.99%) while in mouse

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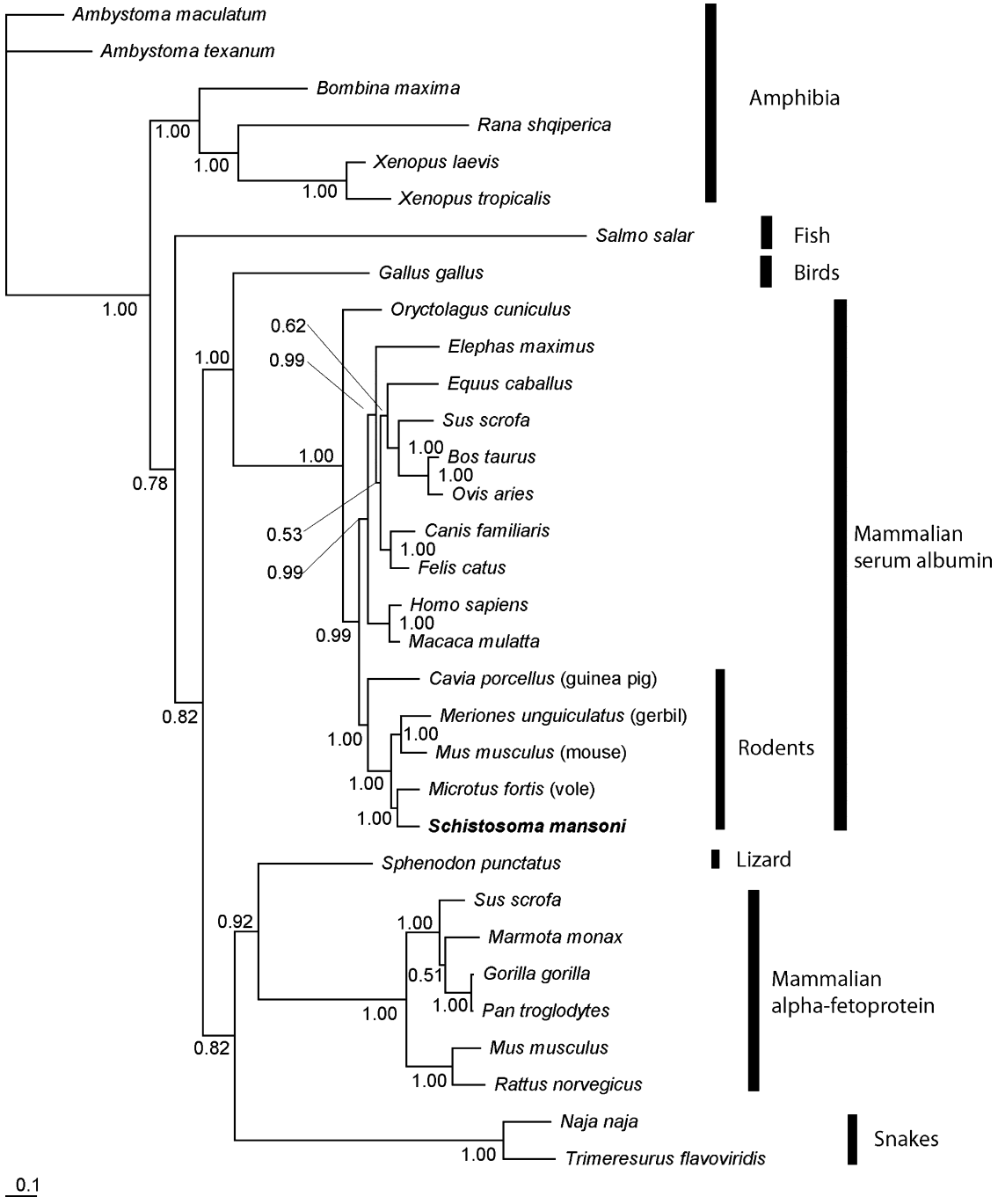

Fig. 1. The *Schistosoma mansoni* albumin gene sequence was obtained from GenBank (accession AF418550) and homologs were identified by BLAST searching NCBI's non-redundant protein database and other genome databases. An amino acid alignment was produced using MUSCLE [7], with manual curation. Gaps and highly divergent or ambiguous regions of the alignments were excluded from phylogenetic analysis, resulting in a final alignment of 568 amino acid positions. The alignment is available upon request. Phylogenetic relationship of the albumin sequences was assessed using a Bayesian statistical procedure, as implemented by the computer program MrBayes [8]. MrBayes performs a Metropolis-coupled Markov chain Monte Carlo (MC^3) estimation of posterior probabilities [9–11]. We performed MC^3 estimation of posterior probabilities using non-informative prior probabilities, the JTT + I + Γ [12] substitution model with inclusion of unequal amino acid frequencies, and four incrementally heated Markov chains with different random starting trees. The Metropolis-coupled Markov chains were run to 6,946,800 generations with sampling every 100 generations. The length of the MC^3 burn-in was 2000 of 6,946,800 generations, resulting in a sample of 69,448 trees for estimation of posterior probabilities. The 50% majority rule consensus phylogeny of serum albumins and alpha-fetoproteins, with Bayesian posterior probabilities superimposed upon the tree. The tree is rooted using amphibian albumin sequences. Horizontal branch lengths are representative of evolutionary change. The phylogeny strongly supports origins of the *S. mansoni* albumin *via* lateral gene transfer from a rodent host.