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Abstract

An Endogenous Retrovirus from Human Hookworm Encodes an Ancient Phlebovirus-Like Class II Envelope Fusion Protein †

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Abstract: Within the parasitic nematode *Ancylostoma ceylanicum*, a ~20 million-year-old Bel/Pao LTR retrotransposon encodes an ancient viral class II envelope fusion protein termed Atlas Gc. Typically, retroviruses and related degenerate retrotransposons encode a hemagglutinin-like class I envelope fusion protein. A subset of Bel/Pao LTR retrotransposons within the phylum *Nematoda* have acquired a phlebovirus-like envelope gene and utilized the encoded fusion machinery to escape the genome as intact exogenous retroviruses. This includes *C. elegans* retroelement 7 virus which was recently reclassified as a member of the genus *Semotivirus*. A 3.76 Å cryoEM reconstruction confirms Atlas Gc as a closely related phleboviral homologue and class II fusion protein in a novel case of gene exaptation. Preliminary biophysical and biochemical characterization indicate Atlas Gc functions under specific physiological conditions targeting late-endosomal membranes, much like modern viral class II envelope fusion proteins. Phylogenetic analyses support the reclassification of the Atlas endogenous retrovirus and five other *A. ceylanicum* ERVs as novel semotiviruses of *Belpaoviridae* of the new viral order of reverse-transcribing viruses *Ortervirales*.

Keywords: transposable element; retrotransposon; endogenous retrovirus (ERV); envelope protein; membrane fusion; horizontal gene transfer (HGT); virus evolution; gene exaptation; nematode