

POSTER 43**THE ARTIODACTYL *APOBEC3* INNATE IMMUNE REPERTOIRE SHOWS EVIDENCE FOR A MULTI-FUNCTIONAL DOMAIN ORGANIZATION THAT EXISTED IN THE ANCESTOR OF PLACENTALS AND ENABLED PRIMATIFICATION**

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APOBEC3 (*A3*) proteins deaminate DNA cytosines and block the replication of retroviruses and retrotransposons. Each *A3* gene encodes a protein with one or two conserved zinc-coordinating motifs (*Z1a*, *Z1b* or *Z2*). The presence of one *A3* gene (*Z1a-Z2*) in mice and seven in humans (*Z1b*, *Z1a-Z1b*, *Z1a*, *Z1a-Z1a*, *Z1a-Z1a*, *Z1a-Z1b*, *Z2*) suggests extraordinary evolutionary flexibility. To gain insights into the mechanism and timing of *A3* gene expansion and into the functional modularity of these genes, we analyzed the genomic sequences, expressed cDNAs and activities of the full *A3* repertoire of three artiodactyl lineages: cattle, pigs and sheep. Sheep and cattle have two *A3* genes, *A3A* and *A3F* (*Z1b* and *Z1a-Z2*, respectively), whereas pigs only have *A3F*. A comparison between domestic and wild pigs indicated that *A3A* was deleted in the pig lineage. In all three species, premature transcription termination and internal initiation also produced additional catalytically active single domain *A3F* variants (either *Z1a* or *Z2*) with distinct subcellular localizations. Thus, the two *A3* genes of sheep and cattle encode four conserved and active proteins. These data, together with phylogenetic analyses, indicated that a similar, functionally modular *A3* repertoire existed in the common ancestor of artiodactyls and primates (*i.e.*, the ancestor of placental mammals). This mammalian ancestor therefore possessed the minimal *A3* gene set, *Z1b-Z1a-Z2*, required to evolve through a remarkable series of eight recombination events into the present day eleven *Z* domain human repertoire. This dynamic recombination-filled history is consistent with a model in which most of these events were selected by ancient pathogenic retrovirus infections during primatification.