

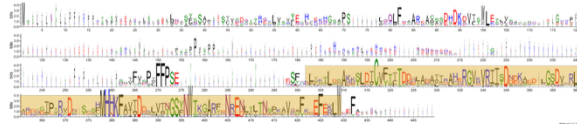
## **Supplementary Materials**

Conservation of antiviral systems across domains of life identifies immune genes in humans

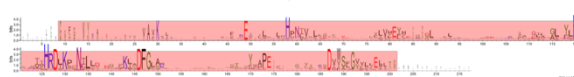
MkoA - This study



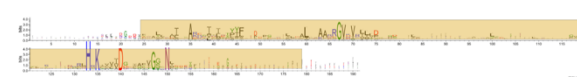
MkoB - This study



MkoA - Jackhmmer

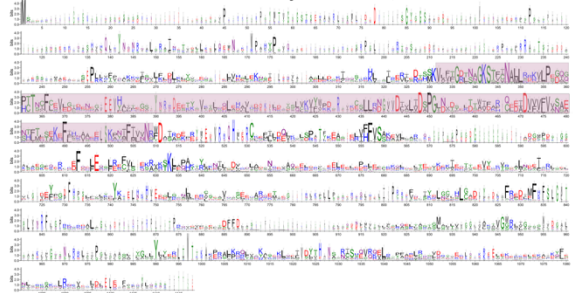


MkoB - Jackhmmer

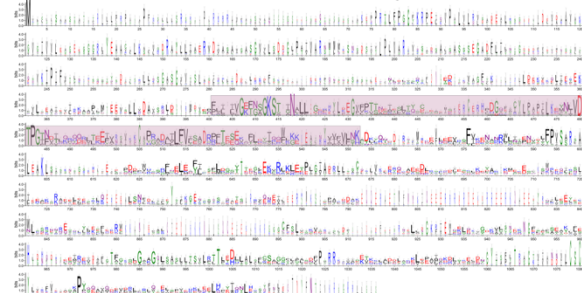


- DEXXQ-box helicase domain of Mov10L1 (cd18078)
- C-terminal helicase domain of Upf1-like family helicases (cd18808)
- PLD like domain (PF13091)
- Protein kinase domain (PF00069)

LeoA - This study



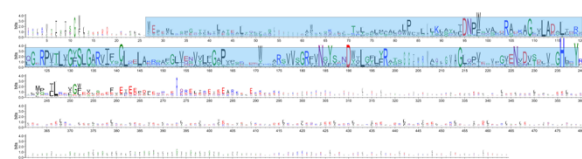
LeoBC - This study



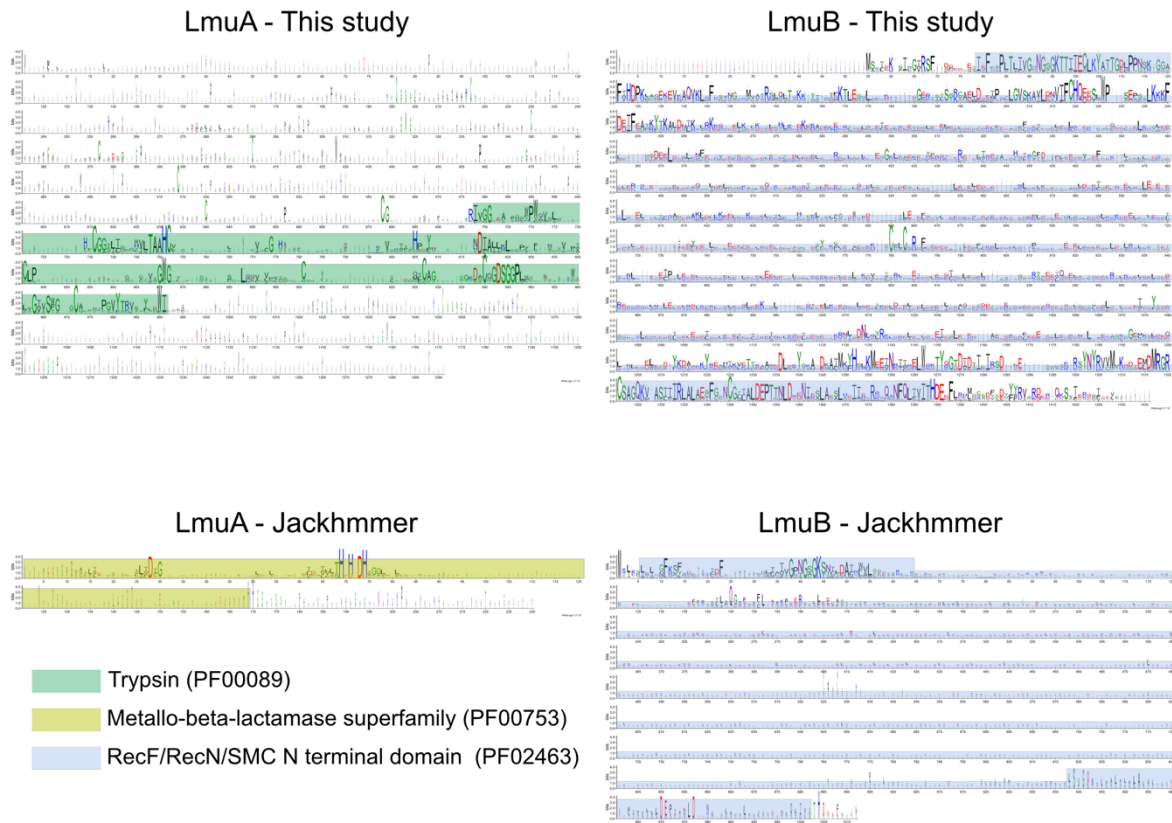
LeoA - Jackhmmer



LeoBC - Jackhmmer

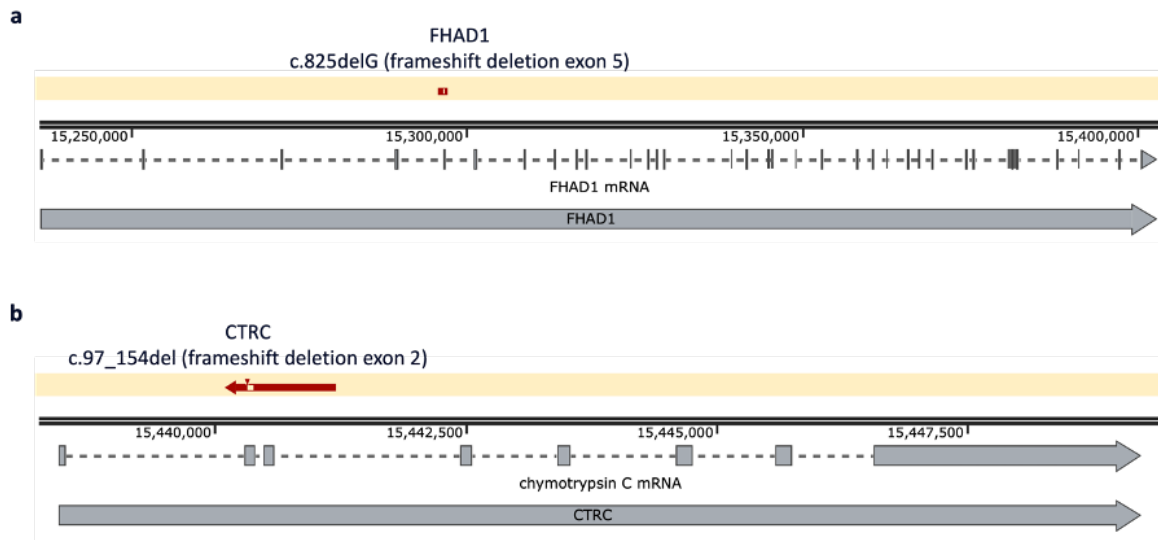


- 50S ribosome-binding GTPase PF01926
- Protein of unknown function (DUF726) PF05277



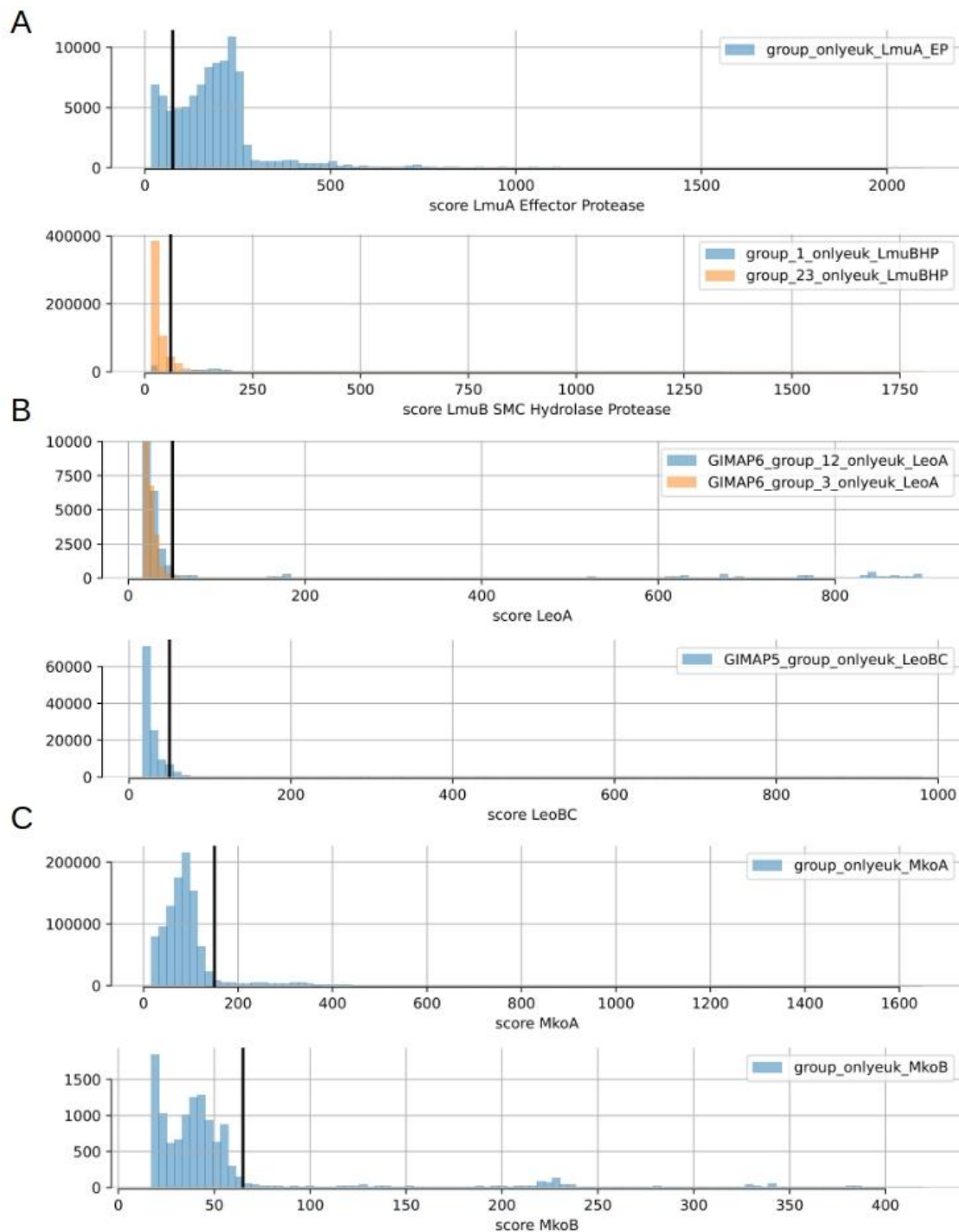
### Weblogos of the alignment used to build HMM profiles with our method and jackhmmer.

The main domains are highlighted. Jackhmmer weblogo are obtained after 3 iterations, except for MkoA and LmuB for which 2 iterations are performed, to avoid a too important number of hits leading to the algorithm's divergence. Weblogo of MkoA-in-house pipeline is truncated in the interest of space and displays a full length of 4529 amino acids.



### Verification of single-cell cloned knock-out THP-1 cells

THP-1 clones were verified by nanopore sequencing of PCR products. The consensus sequences obtained from nanopore sequencing were mapped to the reference genes FHAD1 (A) and CTRC (B), with mutations indicated by markers. Homozygosity was confirmed by mapping all individual reads onto the reference genome.



### Score distribution used to select hits based on eukaryotic HMM profiles.

Positive hits obtained from the analysis using new eukaryotic profiles are selected with the indicated threshold (vertical bar), determined by the distribution of scores. When two different clades are selected, two profiles are used (represented in blue and orange, see Figure S1B). Labels in the top right corner correspond to the name of the eukaryotic HMM profiles.