**Supplementary figure S1**: Correlation across species between fold-change (log2 scale) responses among genes that are either significant in LPS treatment at 4 and 24h (A and B respectively) or GARD treatment at 4 and 24h (C and D respectively) at FDR < 0.05 in at least one of the species studied. Spearman and Pearson correlation coefficients are indicated on each plot.
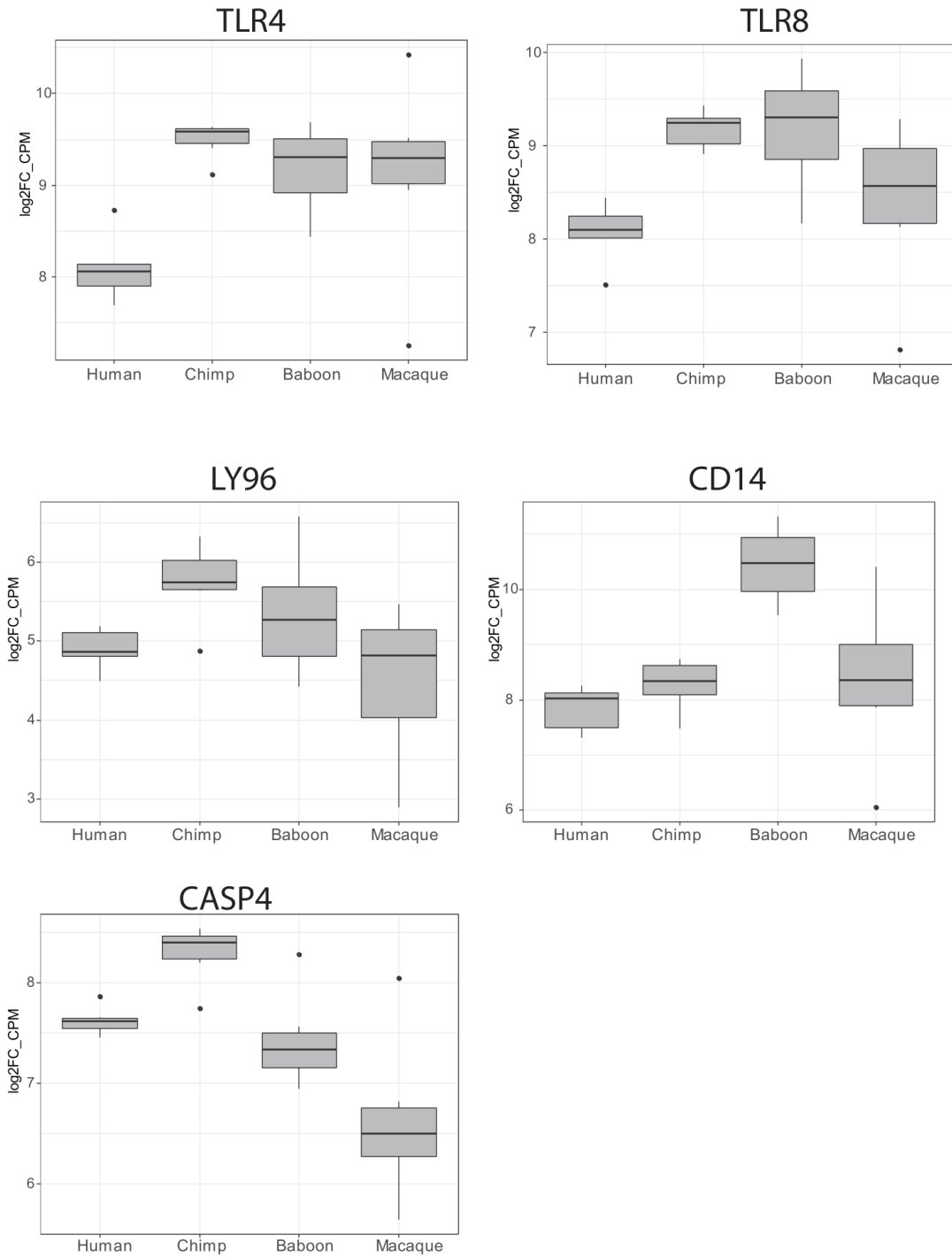
Supplementary figure S2: Boxplots representing expression values across species (log2 count per million; log2CPM) of key sensors involved in the recognition of the ligands used in this study, LPS and GARD.
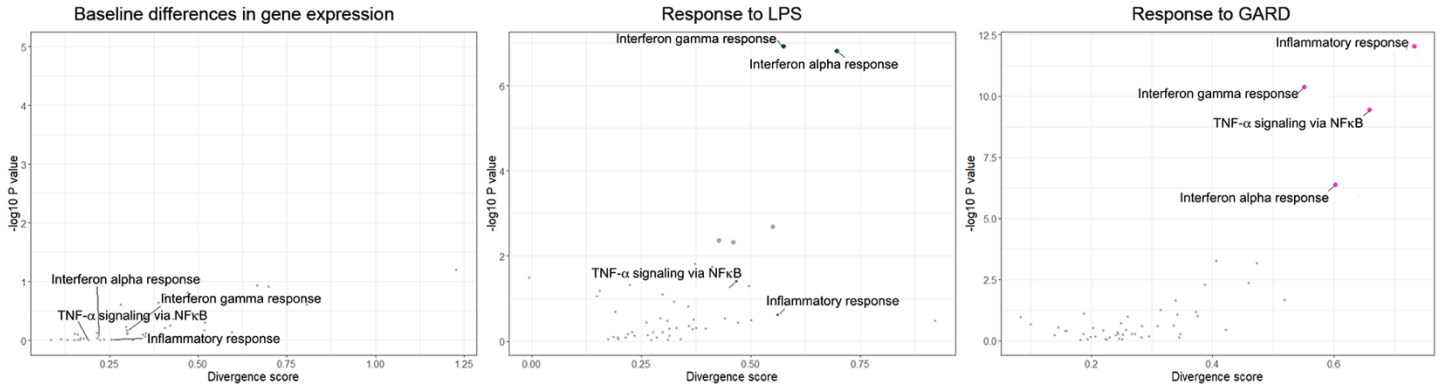
Supplementary figure S3: Scatter plot displaying total divergence scores (x-axis) of hallmark pathways when comparing baseline gene expression levels, the response to LPS (4 hours stimulation), and the response to Gard (4 hours stimulation) between apes and AAMs. We highlight the pathways showing the most significant divergence scores (y-axis) for both the response to LPS and GARD. We note that inflammatory and interferon-associated pathways show very low divergence scores at baseline conditions.
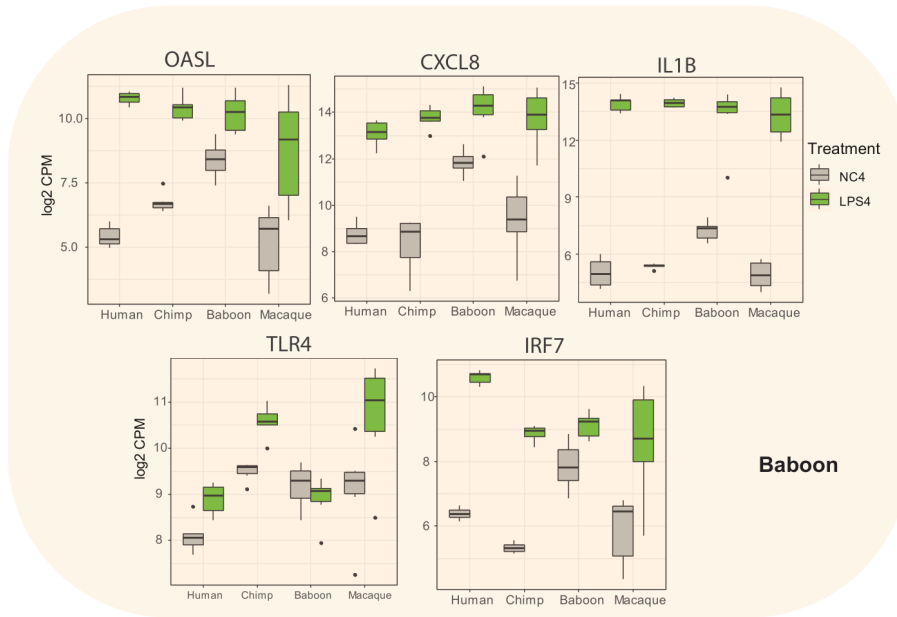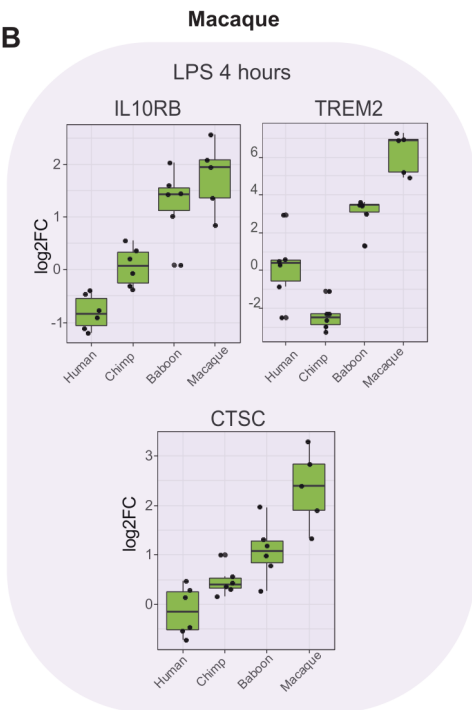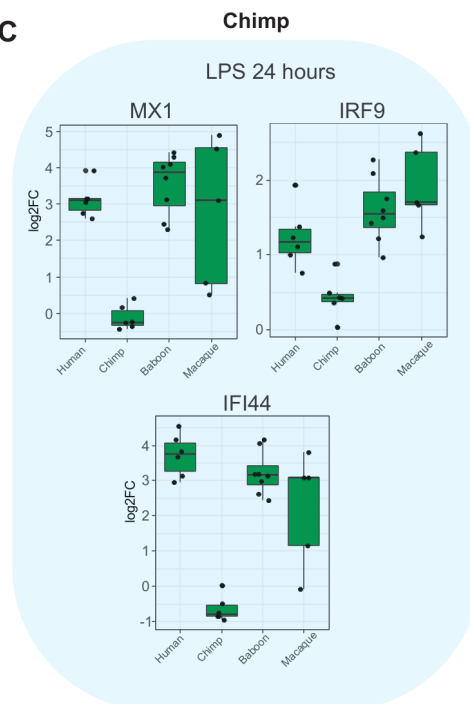
Supplementary figure S4: **(A)** Example of baboon-specific genes. The boxplots represent the expression values across species in non-stimulated cells (gray) and cells stimulated with LPS for 4 hours (green). In all cases showed herein baboons show a weaker response to LPS compared to all other species, which is primarily due to an increased baseline expression of these genes. **(B)** Example of rhesus-specific genes at 4 hours post LPS stimulation. **(C)** Example of chimpanzee-specific genes at 24 hours post LPS stimulation.
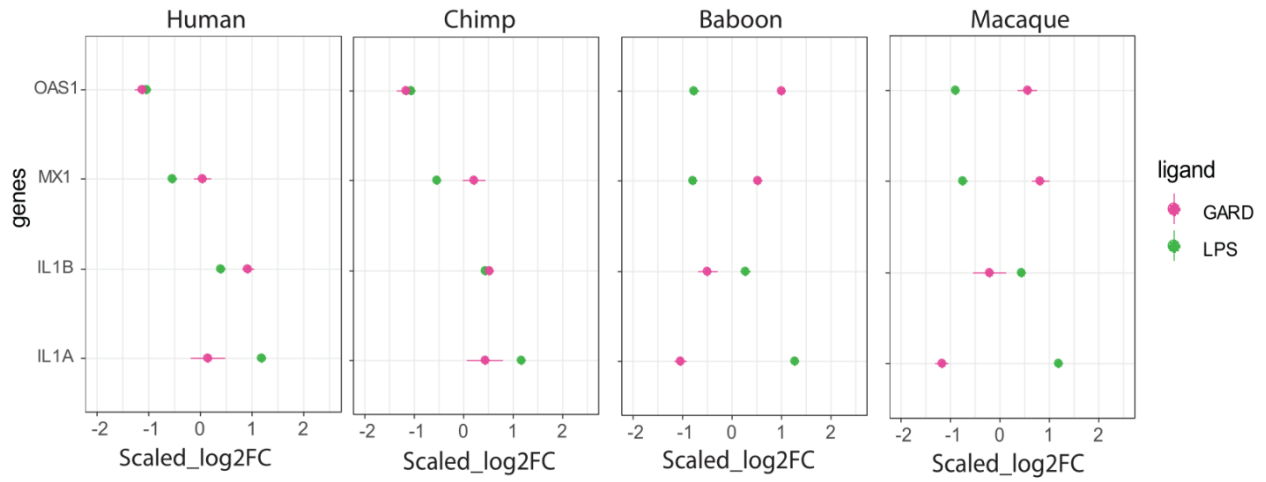
Supplementary figure S5: Scaled log2FC of number of key innate immune genes that showed distinct response to bacterial or viral ligands in monkeys vs apes at 4h time point.

Supplementary Datasets

SI Appendix, Dataset S1: Summary of all samples included in this study and associated metadata.

SI Appendix, Dataset S2: Pairwise comparisons of cell population proportions between primate species.

SI Appendix, Dataset S3: Summary of log2FC and FDR for all orthologs for all species across all treatments.

SI Appendix, Dataset S4: Conserved genes that are responding in all species in LPS and GARD 4h treatments.

SI Appendix, Dataset S5: Clade differentially responsive genes across all treatments.

SI Appendix, Dataset S6: Divergence scores and p values for all hallmark pathways in all treatments.

SI Appendix, Dataset S7: Clade differentially responsive genes at baseline (i.e, no treatment).

SI Appendix, Dataset S8: Gene ontology enrichment analysis of differentially expressed genes between apes and AAMs at baseline.

SI Appendix, Dataset S9: Species-specific differentially responsive genes. Two sets are provided for every species, genes with higher response in this species vs. all other species (species.DRSG.higherRes) and genes with lowest response compared to all other species (species.DRSG.lowerRes).

SI Appendix, Dataset S10: Gene ontology enrichment analysis of all clade and species specific differentially responsive genes.

SI Appendix, Dataset S11: List of genes underwent temporal reduction or increase in response at later time point in each species and treatment (LPS and GARD).

SI Appendix, Dataset S12: List of antibodies used to characterize primate's leukocytes composition.