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### Investigating the genetic underpinning and associated audiological features of childhood hearing loss in Puerto Rico

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**OBJECTIVES/GOALS:** Hearing loss (HL) can result from environmental and genetic factors. Some genetic variants may be more prevalent in populations living in geographic or cultural isolation. This study explores the genetic variants associated with HL in Puerto Rico and correlates these with auditory and balance disorders to uncover novel variants. **METHODS/STUDY POPULATION:** After obtaining individual informed consent and assent for a minor when applicable, we will collect clinical audiological data and biological samples (n = 600) from families across Puerto Rico with a history of severe to profound HL. Genomic DNA will be extracted, and exome and mitochondrial genome sequencing will be conducted to identify causal variants in genes associated with HL. The study will assess the prevalence of both novel and reported variants in genes associated with HL and investigate founder variants in the Puerto Rican population. Involvement of genes so far not associated with HL will also be considered when a genetic diagnosis cannot be established. Auditory phenotypes will be correlated with genetic findings, allowing for a comprehensive analysis of genetic contributions to HL in this population. **RESULTS/ANTICIPATED RESULTS:** This research will advance understanding of the genetic causes of HL in Puerto Rico, leading to more accurate diagnoses, personalized treatment options, and the discovery of novel genes associated with HL. It will also serve as an evidence-based reference to analyze the adequacy of current neonatal hearing screening protocols in PR. Recruitment and sample collection have begun, and we expect our findings to uncover population-specific variants. These results will provide a foundation for further genetic studies aiming at identifying the causes of HL in Puerto Ricans regardless of age of onset. **DISCUSSION/SIGNIFICANCE OF IMPACT:** This study will enhance our understanding of hereditary HL and serve as a basis for developing population-specific diagnostic tools and interventions, particularly in the Puerto Rican population. The research will support future genetic studies and address health disparities in HL in the island.

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### Association of microbiome dysregulation with differential gene expression in a spontaneous equine model of osteoarthritis\*

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**OBJECTIVES/GOALS:** Osteoarthritis (OA) is a multifactorial disease where sustained gut inflammation is a continued source of inflammatory mediators driving degenerative processes in joints. The goal was to use spontaneous equine model to compare fecal and leukocyte microbiome and correlation to transcriptome in OA. **METHODS/STUDY POPULATION:** Seventy-six horses (31 OA, 45 controls) were enrolled by population-based sampling. Feces and peripheral blood mononuclear cells (PBMC) were collected. Horses were determined to have OA by clinical and radiographic evidence. Horses were excluded if they received medications or joint injections within two months. Fecal and circulating leukocyte bacterial microbial 16s-seq was performed. Bulk RNAseq of PBMC was performed by the Illumina platform. Gene expression data were mapped to the equine genome, and differential expression analysis was performed with DESeq2. Qiime2 was used for microbial analysis. Enrichment analysis was performed with a cluster profiler. Correlation analyses were performed between the datasets. **RESULTS/ANTICIPATED RESULTS:** Beta and alpha microbial diversity differed in feces and PBMC of OA vs. healthy horses. Horses with OA had an increased Firmicutes to Bacteroidetes ratio compared with controls. The fecal microbiome of OA horses had significantly higher amounts of Firmicutes *Oribacterium* (q DISCUSSION/SIGNIFICANCE OF IMPACT: These data suggest that altered microbiome and PBMC gene expression are associated with naturally occurring OA in the translational equine model. While *Oribacterium* has been detected in humans with rheumatoid arthritis, its role in OA warrants further proteomic and metabolomic profiling.

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### The role of peroxisome proliferator-activated receptor-alpha on blood pressure, glomerular filtration rate, and renal inflammation during high-salt hypertension\*

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**OBJECTIVES/GOALS:** The study's goal is to investigate the role of PPAR-α on regulating blood pressure, glomerular filtration rate (GFR), renal inflammation, and renal sodium reabsorption in mice on a 4% high-salt diet. **METHODS/STUDY POPULATION:** GFR, systolic blood pressure (SBP), inflammatory biomarkers (KIM-1, TIMP2, NGAL, MCP-1, TNF-α, IL-6, IL-10, and IL-17), and renal sodium transporter expression (NKA, NHE3, NKCC2, NCC, ENaC, Aqp-2, and NHERF1) were measured in PPAR-α KO mice