Identification of Trichomonas vaginalis 5-nitroimidazole resistance targets to inform future drug development

Keonte Graves1, Jyoti Sharma2, Colin Reilly2,3, Hemant Tiwari3, Vinodh Srinivasasainagendra4, W. Evan Secor5, Jan Novak5 and Christina A. Muzny2
1CCTS, 2Department of Medicine, The University of Alabama at Birmingham, 3Department of Microbiology, The University of Alabama at Birmingham, 4Department of Biostatistics, The University of Alabama at Birmingham and 5Division of Parasitic Diseases and Malaria, Center for Global Health, Centers for Disease Control and Prevention

OBJECTIVES/GOALS: 5-nitroimidazoles are the only FDA-approved medications for T. vaginalis treatment. Resistance has been observed in 5-10% of cases, but may be rising. We aimed to delineate mechanisms of resistance in isolates of T. vaginalis using transcriptome profiling of resistant and sensitive T. vaginalis isolates. METHODS/STUDY POPULATION: T. vaginalis isolates (4 nitroimidazole (MTZ)-resistant were grown in triplicate in Diamond’s Trypticase-Yeast-Maltose medium. MTZ susceptibility testing con- firm MTZ MLCs of T. vaginalis isolates. Total RNA extraction was done using Trizol reagent (Invitrogen; Carlsbad; CA); according to the manufacturer’s instructions. RNA sequencing (RNAseq) and bioinformatics analyses were performed to identify significantly differentially expressed genes (DEGs) in MTZ-resistant vs. sensitive isolates. Subsequent qPCR was performed to confirm and extend RNAseq data and gene targets related to 5-nitroimidazole resistance. RESULTS/ANTICIPATED RESULTS: RNAseq identified key DEGs in MTZ-resistant vs. sensitive isolates. DEGs from MTZ-resistant isolates included those encoding transcription factors (MYB DNA-binding protein), ribosomal proteins (30S, 40S, 50S, 60S), protein kinases (CAMK, ser/thr, CMGC), Ankyrin repeat proteins, surface proteins (Surface antigen BspA-like) and various uncharacterized hypotheti- cal proteins. RT-qPCR experiments confirmed reduced expression of genes encoding ferredoxin (drug activation) and flavin reductase 1 (oxygen scavenging) in MTZ-resistant T. vaginalis isolates as com- pared to MTZ-sensitive isolates. DISCUSSION/SIGNIFICANCE: In this study, we identified several DEGs in resistant T. vaginalis isolates. Further studies with large number of isolates representing a broad range of MTZ-susceptibility patterns are needed to identify genes that may represent new targets for future drug development.

Antibody function, antigenic target and glycans determine the transfer of herpes simplex virus (HSV) antibodies (Abs) from mothers to newborns and transfer is altered by SARS-CoV-2

Aakash Mahant Mahant1, Fatima A. Estrada Trejo1, Jennifer T Aguinal1, Simone Sidoli1 and Betsy C. Herold1
1MSc

OBJECTIVES/GOALS: Murine and clinical data suggest that anti- body-dependent cellular cytotoxicity (ADCC) is associated with greater protection against disseminated neonatal HSV disease. To quantify the relative transfer of Abs with different functions and targets, we conducted a prospective study of mother-infant term and postmenopausal women. A total of 78 subjects completed the study, with 12 subjects dropping out due to non-compliance and medical reasons. Supplementation with fish oil attenuated the thrombin receptor PAR4-induced platelet aggregation, whereas primrose oil supple- mentation attenuated aggregation mediated by PAR4 or collagen. Supplementation with â-3 or â-6 fatty acids decreased platelet dense granule secretion and attenuated basal levels of integrin âIIbβ3 activation. Post-washout following supplementation with primrose oil, the thrombin receptor PAR1-induced platelet aggregation was similarly attenuated. For either treatment, the observed effects post supple- mentation on dense granule secretion and basal integrin activation were sustained after the washout. DISCUSSION/SIGNIFICANCE: Postmenopausal women are at increased risk for a cardiovascular event due to platelet hyperactivity. This study indicates that supple- mentation with â-3 and â-6 fatty acids may offer significant protec- tion for postmenopausal women against cardiovascular diseases and occlusive thrombotic events by reducing platelet reactivity.