IDENTIFICATION, QUANTIFICATION, AND CHARACTERIZATION OF HUMAN POLYCLONAL ANTIBODIES. Zoe Turner, Yasmine Rais, Weize Tang, Zhiqiang Fu, and **Andrei P. Drabovich**, Division of Analytical and Environmental Toxicology, Department of Laboratory Medicine and Pathology, University of Alberta, Edmonton, AB T6G 2R3, Canada. (drabovic@ualberta.ca)

Recent advances in proteomics facilitated the development of selective, sensitive, and reproducible assays for quantification of low-abundance proteins in biological samples [1-2]. Here, we will present the development of immunoaffinity–mass spectrometry (IA-MS) assays for quantification of the endogenous polyclonal antibodies in blood serum and characterization of antibody isotypes (IgG, IgA, IgM, IgE, IgD) and subclasses (IgG1-4, IgA1-2). IA-MS assays revealed relatively high levels (>1 μg/mL IgG1) and pathogen-specific diversity of serum polyclonal antibodies against SARS-CoV-2 [3] and Respiratory Syncytial Virus [4] antigens. Autoantibodies against prostate-specific antigens were detected at substantially lower levels (<10 ng/mL). Profiling of the repertoire diversity of variable chains revealed the use of several dozen IGHV genes in polyclonal antibody response. The presented IA-MS assays will facilitate the comprehensive characterization of the endogenous polyclonal antibodies, rational design of serological testing, and precision approaches in immunology.

[1] Zhang J et al. *Mol. Cell. Proteomics* 2023, 22, 100556
[2] Fu Z et al. *Mol. Cell. Proteomics* 2021, 20, 100075
[3] Fu Z et al. *Anal. Chem.* 2022, 94, 12990–12999
[4] Weize T et al. *bioRxiv* 2023, 10.1101/2023.10.27.564451