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SPEAKING THE SAME LANGUAGE: INTERNATIONAL CROSS-VALIDATION OF EMERGING BIOMARKERS FOR JUVENILE IDIOPATHIC ARTHRITIS

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Introduction: To date, several studies have validated the use of key biomarkers such as IL-18, CXCL9 and S100 proteins in diagnosis and monitoring of treatment response of systemic juvenile idiopathic arthritis (sJIA). Despite the promise of these biomarkers, their clinical utility is still limited by their overall lack of standardization.

Objectives: In this project we set out to cross-validate emerging systemic JIA biomarkers across different measurement platforms and different international centers to facilitate their wider introduction into routine clinical care.

Methods: In a first step healthy donor serum samples spiked with defined concentrations of recombinant S100 proteins, CXCL9, CXCL10, IL-18 and sCD25 were distributed in blinded manner among all participating centers (CARRA member sites: Cincinnati, Philadelphia, Toronto, Vancouver; PReS centers: Leuven, Muenster, Rome, Utrecht). Individual spiked protein levels were determined using locally established platforms including commercial ELISA, commercial/custom luminex, Ella and Mesoscale. In a second step patients' samples enrolled in the FROST study will be distributed for respective biomarker analyses. All data will be analyzed for variances across different platforms and agreement across identical platforms in different labs.

Results: We observe extremely tight correlation of spiked IL-18 and CXCL9 levels with the amounts quantified by the employed measurement platforms (IL-18 R^2=0.744-0.999, P<0.0001; CXCL9 R^2=0.924-0.999, P<0.0001). However, the actual spike recovery of the individual assays varied substantially. While some assays met 90-100% spike recovery over almost the entire tested concentration range (1pg-500ng/mL), others consistently yielded high (approx. 500%) or low (approx. 60-70%) spike recovery. Further, our data determined the lower level of detection for each assay to provide consistent performance. At present, this analysis is extended to other spiked parameters and measurements in patients' samples are in preparation.

Conclusion: Our spike recovery approach demonstrates - as expected - high correlation of individual assay results but widely divergent absolute concentrations measured. From our data we can now clearly identify assays with almost perfect spike recovery and calculate conversion factors for those that over- or underperform in their concentration output. This may allow for correction factors for IL-18 and CXCL9 levels (and others) quantified in future studies using the tested assay systems. We will further expand to utilize patient samples from the FROST study to validate the utility of correction factors. Altogether, the results from our study will enable wide interpretation and translation of respective biomarker data and pave the way towards their wider use in routine clinical practice and international collaborative studies.

Patient Consent: Not applicable (there are no patient data)

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