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Utility of expanded molecular testing for primary immunodeficiencies: disease-specific panels may miss diagnoses

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Abstract

Purpose: Primary immunodeficiency disorders (PIDs) exhibit "phenotype expansion" in which genes previously thought to be associated with specific phenotypes have an increasing circle of clinical presentations. Traditionally, genetic testing for PIDs is phenotype-specific, guided by genes associated with a given clinical presentation. However, the performance of disease specific panels versus broad panel testing has not been performed.

Methods: This study compared the diagnostic value of a 207 gene PID panel to smaller, diseasefocused panels. Based on patient phenotypic information provided, each requisition was assigned a virtual disease-focused panel. Positive diagnoses on the expanded panel and the virtual focused panel were compared for each requisition to determine the frequency of missed diagnoses if only the focused panel had been ordered.

Results: Our laboratory performed 6,257 expanded PID panels between April 2017 and October 2019. A virtual focused panel could be assigned based on clinical indication for 3,384 unique orders, 105 of which had positive results. Positive results would have been missed in 24.8% (26/105) of cases had the expanded panel not been ordered. The Antibody Deficiencies panel had the highest rate of missed diagnoses (42.5%).

Conclusion: These results indicate the importance of ordering an expanded panel or having the option to re-requisition to the expanded panel for conditions with overlapping symptoms.