Validation of a Novel Autism Spectrum Disorder Assay Using Whole-Genome Sequencing

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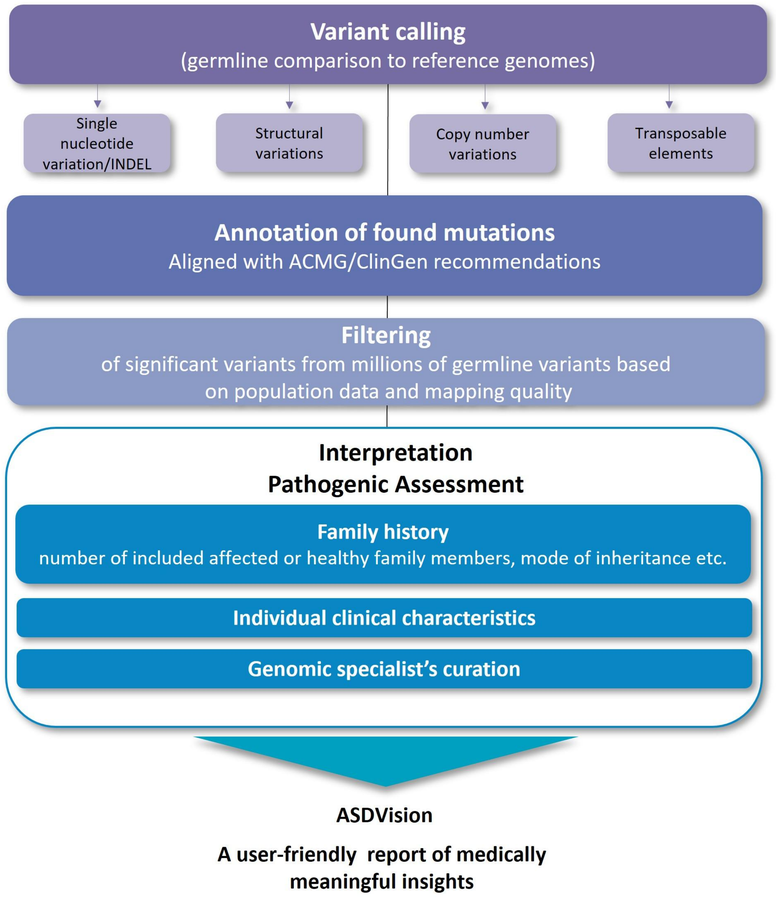
Introduction

Autism Spectrum Disorder (ASD) presents significant challenges in diagnosis and treatment due to its complex genetic underpinnings. The ASD Assay, developed by Inocras Inc., aims to detect pathogenic and likely pathogenic variants associated with ASD. The assay provides clinicians with valuable insights for early intervention and personalized treatment strategies. Additionally, the assay includes a polygenic score (PGS) for assessing the risk of ASD and other neurological disorders. This study documents the analytical validation of this novel assay.

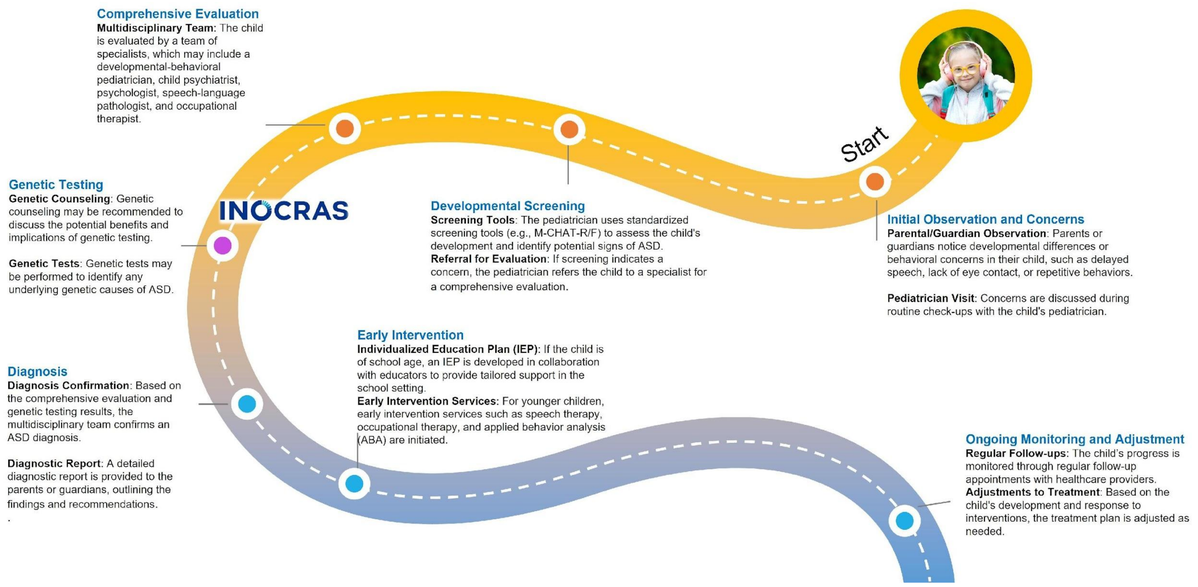
Methods

The ASD Assay was validated using well-characterized cell lines and patient samples. The assay was performed on genomic DNA extracted from buccal swabs, saliva, buffy coat, or peripheral blood samples. The DNA was processed using the Watchmaker DNA Library Preparation Kit, sequenced on the Illumina NovaSeq X+ platform, and analyzed through the proprietary Inocras ASD pipeline. Analytical validation was conducted using six cell lines with known variants, including single nucleotide variants (SNVs) and insertions/deletions (indels). Clinical validation involved a cohort of previously diagnosed ASD patients (n=25), as well as a control group of negative germline samples. Variants detected by the assay were compared to the known clinical outcomes.

End-to-end WGS pipeline



ASD Patient Journey



Integrating Whole-Genome Sequencing (WGS) into the ASD Patient Journey
This diagram illustrates the stepwise approach to evaluating and managing autism spectrum disorder (ASD), from initial observation to ongoing intervention. WGS potentially enhances this pathway by providing a comprehensive genetic assessment, enabling early identification of underlying variants associated with ASD. By uncovering genetic contributors, WGS may support more precise diagnoses, informs tailored intervention strategies, and guides personalized treatment plans.

Results

Sensitivity	**SNVs: 99.64% (with a 95% CI of 99.61% - 99.68%)**
	InDels: 96.46% (with a 95% CI of 96.34% to 96.58%)
Positive Predictive Value (PPV)	**SNVs: 97.84% (with a 95% CI of 97.68% to 98.01%)**
	InDels: 92.60% (with a 95% CI of 92.39% to 92.81%)

Conclusion: ASDVision is designed to transform high-performance testing into clinically meaningful insights, driving precision in ASD diagnosis and management.