CANNABIS-RESPONSIVE BIOMARKERS: A NEW TECHNOLOGY TO DETERMINE THE IMPACT OF MEDICAL CANNABIS TREATMENT IN CHILDREN WITH AUTISM SPECTRUM DISORDER

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Cannabis-Responsive™ (C-Res™) Biomarkers in Autism: Impact of Medical Cannabis on Children with Autism Spectrum Disorder

Abstract

Autism spectrum disorder (ASD) is a complex neurodevelopmental condition characterized by a range of symptoms and severity levels. The increasing prevalence of ASD and the lack of effective treatment options have led to a growing interest in cannabis as a potential alternative or adjunct therapy. Importantly, physicians and families using a "low and slow" approach to MC treatment have found success. However, to consider cannabis as a therapeutic option for ASD, objective assessment methods are needed. This overview explores the innovative technology of Cannabis-Responsive™ (C-Res™) biomarkers developed by Cannformatics, Inc., a San Francisco-based biotech company. Cannformatics' mission is to deliver scientifically-validated medical cannabis (MC) treatment guidance to healthcare providers and patients to improve health and quality-of-life for individuals with ASD. This paper summarizes the findings of Cannformatics' ASD Pilot Study, which have been published in four peer-reviewed scientific papers:

1. Cannabis-Responsive Biomarkers: A Pharmacometabolomics-Based Application to Evaluate the Impact of Medical Cannabis Treatment on Children with Autism Spectrum Disorder (Cannabis & Cannabinoid Research)

2. The Potential of Salivary Lipid-Based Cannabis-Responsive Biomarkers to Evaluate Medical Cannabis Treatment in Children with Autism Spectrum Disorder (Cannabis & Cannabinoid Research)

3. A Machine Learning Approach for Understanding the Metabolomics Response of Children with Autism Spectrum Disorder to Medical Cannabis Treatment (Scientific Reports)

4. The Importance of Data Sources for Machine Learning Applications in Autism: A Mini Review (J Neurology & Neuromedicine)

The challenges of treating patients with ASD

ASD is characterized by its complexity and heterogeneity which pose difficulties in developing targeted medications. To date, there are no available medications specifically developed to treat ASD.

The lack of targeted medicines adds to a wide variety of challenges physicians face when treating ASD including:

- **Communication/Behavior**: Many ASD patients struggle with communication, and deciphering nonverbal cues, gestures, and facial expressions can be complex. Further complicating assessment and treatment, ASD patients may display a wide variety of challenging behaviors.

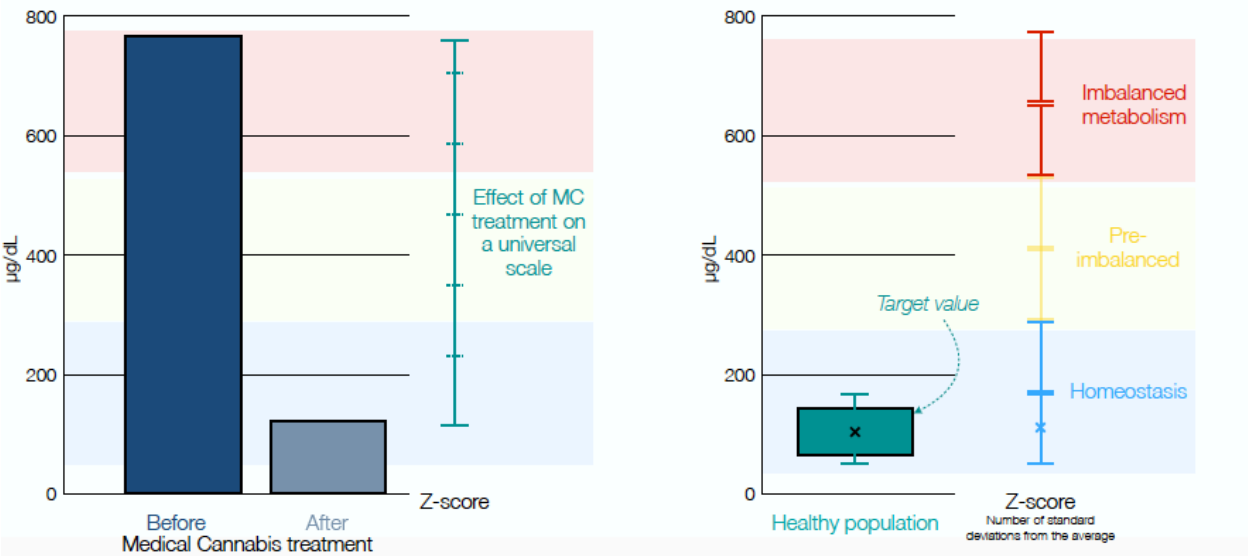
- **Comorbidities:** Many individuals with ASD have co-occurring conditions such as anxiety, ADHD, epilepsy, and gastrointestinal issues which need to be addressed simultaneously, complicating treatment plans.

- **Limited understanding of the underlying conditions:** The metabolic pathways and targets leading to ASD symptoms are not well-defined, making it challenging to use existing lab tests and medications.

- **Personalized Approach:** No two patients with ASD are the same, and each patient's condition develops differently over time. The individualized nature of ASD necessitates a personalized and dynamic treatment approach.

Introducing Cannabis-Responsive™ (C-Res™) Biomarkers

Cannabis-Responsive (C-Res) biomarkers are a new class of molecules found in saliva of individuals with medical conditions that objectively measure the response to MC treatment and indicate the impact in comparison to targeted values determined in a typically developing population.



Cannabis-Responsive (C-Res) biomarkers are an objective, universal tool for measuring the impact of cannabinoid-based treatments on any medical condition characterized by dysfunction of the endocannabinoid system (ECS), allowing physicians to:

- **Evaluate** if a patient is a good candidate for cannabis-based treatment, without the patient needing to try cannabis first.

- **Recommend** the correct product and dosage, minimizing trial and error. Currently, it can take up to 18-months for a physician to find the correct product and dosage for a person with ASD.

- **Optimize** a patient's treatment regimen over time, in response to changes in development (e.g., puberty), lifestyle or medical conditions.

- **Track** the progress of treatment by monitoring the levels of imbalanced biomarkers in comparison to the physiological range, determined by matched typically-developing cohorts.

This approach is similar to when a physician orders a lipid profile to determine if a patient's cholesterol levels indicate treatment, and then routinely monitors lipid levels.

Potential Role of Cannabis in Treating Patients with ASD

Cannformatics' research has identified, in children with ASD, that cannabis impacts biomarkers associated with anti-inflammation, redox regulation, bioenergy production, mitochondrial function and neural function. Some C-Res biomarkers were categorized as neurotransmitters, amino acids, and endocannabinoids.

Significantly, our study of children with ASD found three well-characterized biomarkers that moved into the physiological range after MC treatment:

- **N-acetylaspartic acid (NAA) -** a known ASD neuronal function and viability biomarker since 1997
- **Spermine** - a known pain biomarker
- **Dehydroepiandrosterone sulfate (DHEA-S)** - a known aggression biomarker

Cannabis-Responsive Biomarkers and Advanced Machine Learning Applications

Cannformatics' paper, published August 22, 2023 in *Nature Scientific Reports,* demonstrates that by combining C-Res biomarkers with machine learning applications we can:

- Define the mechanism of action (MOA) and therapeutic window of cannabinoids such as THC, CBD and CBG in children with ASD.
- Use C-Res biomarkers in a novel approach to categorize ASD patients into cohorts based on their specific type of metabolic imbalance and response to cannabis treatment, opening new opportunities for developing targeted therapies that go beyond the use of MC.
- Understand the synergistic role of cannabinoids and phytochemicals found in hemp and cannabis, commonly referred to as the Entourage Effect.

A New Paradigm in Cannabis-based Precision Medicine

C-Res biomarkers are opening up a new precision medicine paradigm in ASD treatment. As the Cannformatics database of C-Res biomarkers and clinical assessments grows, it will enhance the accuracy of treatment prediction and optimization. Through collaborative efforts between Cannformatics, healthcare professionals, and regulatory entities, the integration of C-Res biomarker-driven approaches into clinical practice can bring us closer to personalized, evidence-based MC treatment for individuals with ASD. In the future, we will expand the application of C-Res biomarkers

to other medical conditions characterized by ECS dysfunction including: Alzheimer's disease, PTSD, epilepsy, neuropathic pain, general anxiety disorder, amyotrophic lateral sclerosis (ALS), Parkinson's disease, and multiple sclerosis.