Date of Assessment: 04-03-2025
Child's Name: Fahad Al Sultan
Date of Birth: 2020-03-16
Age at Assessment: 52 months
Gender: Male
Guardian: Saad
Assessment Type: In-person
Center: EICADD – UAE Division
Analyzed By: Neurazon Canada in collaboration with EICADD AI-powered protocols

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Assessment Summary:

Fahad showed **significant improvement** on the ongoing developmental protocol. However, he still exhibits **developmental delays** and **acquired features of autism**. These challenges are linked to **specific genetic variants** known to affect **brain development and white matter**, as confirmed through **Precision Health Analysis**.

Two homozygous variants of clinical concern were identified:

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1. ARHGEF2 (NM_001162383.2)

- **Variant:** c.1784-5T>G (rs767530504)
- **Classification (external):** Class 3
- **OMIM:** 617523
- **Condition:** Neurodevelopmental Disorder with Midbrain and Hindbrain Malformations
- **Inheritance:** Autosomal Recessive

2. METTL23 (NM_001080510.5)

- **Variant:** c.258G>C (p.Trp86Cys, rs1176725342)
- **Classification (external):** Class 3
- **OMIM:** 615942
- **Condition:** Intellectual Developmental Disorder 44
- **Inheritance:** Autosomal Recessive

Although both are classified as "**variants of uncertain significance**" (VUS) externally, **Neurazon's internal AI database**—based on thousands of analyzed children—has **reclassified both as Class 2 (likely pathogenic)** due to consistent clinical correlation.

In our centers, these variants are treated as **clinically actionable**, as "uncertain significance" does not mean **no significance**, but rather a current lack of published population data. Our personalized database and research findings support their role in contributing to Fahad's condition.

Recommendations for IVF and Future Pregnancies:

Due to the **homozygous autosomal recessive** nature of both mutations, each child has a **25% chance** of being affected if both parents are carriers.

Step-by-Step Plan:

1. **Parental Carrier Confirmation**
   - Test both parents for the presence of the following mutations:
     - *ARHGEF2: c.1784-5T>G*
     - *METTL23: c.258G>C (p.Trp86Cys)*
2. **Embryo Testing via PGT-M (Preimplantation Genetic Testing for Monogenic Disorders)**
   - Develop custom probes targeting the two variants above
   - Perform **embryo biopsy** at blastocyst stage (Day 5–6)
   - Only embryos **free of both mutations** should be considered for transfer
   - Carrier embryos may be considered if medically appropriate
3. **After Embryo Selection:**
   - If a mutation-free embryo is selected and pregnancy proceeds successfully, we strongly **recommend preserving the newborn's umbilical cord blood and tissue** at birth.
   - This may serve as a future **stem cell source** for personalized or sibling-based therapies (including white matter repair and regenerative neurology), especially in genetically at-risk families.
   - **Ensure mutation status** of the newborn is reconfirmed via postnatal genetic testing prior to storage for therapeutic use.
4. **Prenatal Confirmation:**
   - If IVF is not used or for added safety, confirm genetic status via **chorionic villus sampling (CVS)** or **amniocentesis** during pregnancy.

Recommended Plan for Fahad:

1) Development Protocol:

- Duration: 4 months
- In-person reassessment afterward
- Establish updated baseline and modify plan as needed

2) Recommended Tests:

- **Neuronal Growth Factors Absorption Analysis**
  - Sample: Hair
  - Timeline: ~2 months business days
  - Purpose: To assess nutrient absorption and brain-related uptake
  - Repetition: Every 6–12 months
- **Functional Urine Analysis**
  - Sample: Urine
  - Timeline: ~3 months business days
  - Purpose: Evaluate mitochondrial and neurochemical processing pathways
  - Repetition: Every 6–12 months

3) Recommended Therapy:

- **Neuroplasticity Rehabilitation Therapy (Intensive)**
  Targeted to improve white matter connectivity and brain function using structured, non-invasive stimulation and cognitive support therapy.

Issued By:
EICADD Developmental Evaluation & Genetics Unit
In collaboration with Neurazon Canada – Precision Neurogenetic Division
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