FOR AJC USE ONLY
Patient Code: _____
Lab Order No.: _____

Molecular Genetics Laboratory
Comprehensive Whole Exome Sequencing (WES) DUO/TRIO
Service Request

Index Patient

Name: Gender: ☐Male ☐Female
Date of Birth: / / CPR/ID No: Nationality: Clinically Affected: ☐Yes ☐No
Parental Consanguinity: ☐ Yes ☐ No

Individual 1

Name: Gender: ☐Male ☐Female
Date of Birth: / / CPR/ID No: Nationality: Clinically Affected: ☐Yes ☐No
Parental Consanguinity: ☐Yes ☐No
Relationship to Index Patient (if applicable): ☐Proband ☐Mother ☐Father ☐Sibling ☐Other:

Individual 2

Name: Gender: ☐Male ☐Female
Date of Birth: / / CPR/ID No: Nationality: Clinically Affected: ☐Yes ☐No
Parental Consanguinity: ☐Yes ☐No
Relationship to Index Patient (if applicable): ☐ Proband ☐ Mother ☐ Father ☐ Sibling ☐ Other:

Referring Physician/Institution Details

Referring Clinic/hospital: Ordering Physician:	Dr. Signature & Stamp:
Physician Phone: Email:	Date:

Type of Specimen

Index Patient	Individual 1	Individual 2
☐EDTA Blood ☐DNA	☐EDTA Blood ☐DNA	☐EDTA Blood ☐DNA
Collection date: / /	Collection date: / /	Collection date: / /
Patient has had blood transfusion: ☐Yes ☐No Date: _____	Patient has had blood transfusion: ☐Yes ☐No Date: _____	Patient has had blood transfusion: ☐Yes ☐No Date: _____
Patient has had bone marrow/organ transplant: ☐Yes ☐No Date:_____	Patient has had bone marrow/organ transplant: ☐Yes ☐No Date: _____	Patient has had bone marrow/organ transplant: ☐Yes ☐No Date: _____

Test Requested

Please select the appropriate test and indication:

DSMG016	☐Comprehensive Whole Exome Sequencing Duo (*bsCNV + **mtDNA)
DSMG017	☐Comprehensive Whole Exome Sequencing Trio (*bsCNV + **mtDNA)

*bsCNV: Backbone-supported Copy number variation (intronic/intergenic/large deletion/duplication)
**mtDNA: Mitochondrial DNA

Indication:

☐Diagnostic (symptomatic) ☐Secondary Findings (optional – ACMG SF v3.1) ☐Reanalysis
*ACMG: American College of Medical Genetics and Genomics — sets standards for genetic testing and variant interpretation.

Clinical Information of Index Patient
Clinical Diagnosis/Indication:
Clinical Summary/Symptoms:
Relevant Findings (imaging, metabolic, etc.):
Previous Genetic Testing (if any):
Onset Age:
Phenotypic Information: Please provide any additional information. Please avoid abbreviations and include any reference ranges for lab results.
Further clinical information attached (if applicable): ☐ Previous Genetic Testing reports ☐ Laboratory/Radiology Reports ☐ Clinical Summary
Family History: • Is there a family history of a similar condition? ☐ Yes ☐ No ☐ Unknown • Are there affected siblings? ☐ Yes ☐ No ☐ No siblings • Is the patient in/from a consanguineous marriage? ☐ Yes ☐ No ☐ Unknown
Pedigree: Please provide any relevant family history in pedigree and/or written form. Please provide details of Individual 1 and Individual 2, if affected.

Clinical Symptoms Information: ☐ Affected ☐ Unaffected (Please tick the appropriate boxes)

BLOOD
- Abn. [1] of coagulation
- Abn. [1] bleeding
- Anemia
- Hemolytic anemia
- Leukocytosis
- Leukopenia
- Neutropenia
- Pancytopenia
- Thrombocytopenia
- Thrombocytosis

CARDIOVASCULAR
- Abn.[1] blood vessel morphology
- Abn.[1] heart valve morphology
- Arrhythmia
- Atrial septal defect
- Bradycardia
- Cardiomyopathy
- Congestive heart failure
- Dilated cardiomyopathy
- Hypertension
- Hypertrophic cardiomyopathy
- Left ventricular hypertrophy
- Myocardial infarction
- Patent ductus arteriosus
- Patent foramen ovale
- Pulmonary arterial
- Tachycardia
- Ventricular septal defect

CNS MORPHOLOGY
- Abn.[1] CNS myelination
- Abn.[1] of cerebral white matter
- Agenesis of corpus callosum
- Brain atrophy
- Cerebellar atrophy
- Cerebellar hypoplasia
- Cerebral ischemia
- Encephalopathy
- Hypoplasia of corpus callosum
- Leukodystrophy
- Macrocephaly
- Microcephaly
- Stroke
- Ventriculomegaly

CNS PHYSIOLOGY
- Aggressive behavior
- Attention deficit hyperactivity disorder
- Autistic behavior
- Behavioral abnormality
- Bilateral tonic-clonic seizure
- Cognitive impairment
- Delayed speech/language
- Dementia
- Developmental regression
- Dysarthria
- Dysphagia
- EEG abnormality
- Focal-onset seizure
- Generalized-onset seizure
- Global developmental delay
- Hyperactivity
- Intellectual disability
- Lethargy
- Mental deterioration
- Migraine
- Motor delay
- Neurodegeneration
- Neurological speech impairment
- Obsessive-compulsive behavior
- Parkinsonism
- Seizure
- Sleep disturbance
- Stereotypy

DIGESTIVE SYSTEM
- Ascites
- Cholestasis
- Cirrhosis
- Constipation
- Diarrhea
- Gastroesophageal reflux
- Hepatic failure
- Hepatic steatosis
- Hepatitis
- Hepatomegaly
- Hernia of the abdominal wall
- Jaundice
- Nausea
- Pancreatitis
- Splenomegaly
- Vomiting

GROWTH
- Decreased body weight
- Failure to thrive
- Growth delay
- Intrauterine growth
- Obesity
- Overgrowth
- Premature birth
- Short stature
- Tall stature

HEAD AND FACE
- Abn.[1] facial shape
- Abn.[1] of the dentition
- Brachycephaly
- Cleft lip
- Cleft palate
- Coarse facial features
- Craniosynostosis
- Depressed nasal bridge
- Dolichocephaly
- Epicanthus
- Frontal bossing
- High palate
- Hypertelorism
- Long philtrum
- Low-set ears
- Macroglossia
- Micrognathia
- Microphthalmia
- Midface retrusion
- Ptosis
- Retrognathia
- Short neck

HEARING
- Hearing impair.[3]
- Sensorineural hearing impair.[3]
- Conductive hearing impair.[3]

KIDNEY
- Chronic kidney disease
- Focal segmental glomerulosclerosis
- Hydronephrosis
- Hyperechogenic kidneys
- Nephrolithiasis
- Nephrotic syndrome
- Polycystic kidney dysplasia
- Renal cyst
- Renal hypoplasia/aplasia
- Renal insufficiency
- Renal tubular dysfunction

METABOLISM
- Albuminuria
- Aminoaciduria
- Elev.[2] hepatic transaminases
- Elev.[2] serum creatine kinase
- Elev.[2] serum creatinine
- Elev.[2] alkaline phosphatase
- Hyperammonemia
- Hyperbilirubinemia
- Hypercholesterolemia
- Hyperglycemia
- Hypertriglyceridemia
- Hypocalcemia
- Hypoglycemia
- Hypokalemia
- Hyponatremia
- Hypophosphatemia
- Lactic acidosis
- Metabolic acidosis
- Proteinuria
- Respiratory alkalosis

MOVEMENT/MOTOR FUNCTION
- Areflexia
- Ataxia
- Bradykinesia
- Chorea
- Dyskinesia
- Dystonia
- Frequent falls
- Gait disturbance
- Hyperreflexia
- Hyporeflexia
- Involuntary movements
- Peripheral neuropathy
- Polyneuropathy
- Positive Romberg sign
- Spastic paraparesis
- Spastic paraplegia
- Spasticity
- Tremor

MUSCLE/JOINT
- Calf m. pseudohypertrophy
- Flexion contracture
- Gowers's sign
- Hip dysplasia
- Hypertonia
- Hypotonia
- Joint hypermobility
- Joint laxity
- Lower limb muscle weakness
- Multiple joint contractures
- Muscle weakness
- Muscular dystrophy
- Myopathy
- Myotonia
- Progressive muscle weakness
- Proximal muscle weakness
- Rigidity
- Skeletal muscle atrophy
- Talipes equinovarus

RESPIRATORY
- Apnea
- Asthma
- Dyspnea
- Pulmonary hemorrhage
- Pulmonary hypoplasia
- Recurrent respiratory infections
- Respiratory insufficiency

SKELETAL 1/2
- Abn.[1] vertebral morphology
- Abn.[1] of limb bone morphology
- Abn.[1] of the ribs
- Arachnodactyly
- Brachydactyly
- Clinodactyly
- Dysostosis multiplex
- Increased bone mineral density
- Kyphosis
- Limb undergrowth
- Pectus carinatum
- Polydactyly
- Recurrent fractures
- Reduced bone mineral density
- Scoliosis
- Skeletal dysplasia
- Spondylolysis

SKELETAL 2/2
- Increased bone mineral density
- Kyphosis
- Limb undergrowth
- Pectus carinatum
- Polydactyly
- Recurrent fractures
- Reduced bone mineral density
- Scoliosis
- Skeletal dysplasia
- Spondylolysis

SKIN / NAILS / HAIR
- Abn.[1] hair morphology
- Abn.[1] of skin morphology
- Angiokeratoma
- Anhidrosis
- Cafe-au-lait spot
- Hirsutism
- Hyperextensible skin
- Hyperpigmentation of the skin
- Hypertrichosis
- Hypohidrosis
- Hypopigmentation of the skin
- Ichthyosis

VARIOUS
- Abn.[1] external genitalia
- Ambiguous genitalia
- Cryptorchidism
- Diabetes mellitus
- Hypospadias
- Hypothyroidism
- Immunodeficiency
- Paresthesia
- Recurrent fever
- Recurrent infections
- Sensory impairment

VISION
- Abn.[1] of eye movement
- Abn.[1] cornea morphology
- Cataract
- Corneal opacity
- Glaucoma
- Nystagmus
- Ophthalmoplegia
- Optic atrophy
- Reduced visual acuity
- Rod-cone dystrophy
- Strabismus
- Visual impairment
- Visual loss

[1] Abn. = Abnormal / Abnormality
[2] Elev. = Elevated
[3] Impair. = Impairment

Important Notice: Submission of a completed and signed Consent Form is mandatory. Samples will not be processed or tested without an accompanying consent form. Please ensure the consent is attached to this request form.

Molecular Genetics Laboratory
Comprehensive Whole Exome Sequencing (WES) DUO/TRIO
Consent Form

Index Patient information	
Name:	Gender: ☐ Male ☐ Female
Date of Birth: / / CPR/ID No:	
Contact Number:	E-mail:

Individual 1 information	
Name:	Gender: ☐ Male ☐ Female
Date of Birth: / / CPR/ID No:	
Contact Number:	E-mail:

Individual 2 information	
Name:	Gender: ☐ Male ☐ Female
Date of Birth: / / CPR/ID No:	
Contact Number:	E-mail:

1. Purpose of the Test

Whole Exome Sequencing (WES) is a genetic test that examines the exome — the portion of the genome that codes for proteins. Variants (changes) in these regions may cause or influence disease. This test may be done on you or your child (or unborn child, where applicable). WES can identify genetic changes related to your current symptoms. In some cases, it may also uncover findings unrelated to your symptoms but with medical significance.

In addition to analyzing individual gene changes, this test also includes backbone-supported copy number variation (bsCNV) analysis. bsCNV helps detect larger genetic changes, such as missing or extra pieces of DNA (deletions or duplications), including regions outside of genes that may not be captured by standard exome testing alone. This analysis improves the ability of the test to identify certain genetic conditions caused by large DNA changes.

It is important to understand that:

- A positive finding (pathogenic/likely pathogenic variant) does not always predict disease severity or guarantee a change in clinical management.
- A negative result does not rule out all possible genetic causes.
- Variants of uncertain significance (VUS) may be found, requiring further analysis or follow-up.

2. Types of Test Results

There are several possible types of genetic test results that may be reported:

- Positive:
  A positive or "abnormal" result means that a DNA variant has been detected, which is related to your or your child's medical condition, or that indicates an increased risk of developing a certain disease in the future. It is possible to test positive for more than one variant. Positive results may include pathogenic variants (known to be associated with disease) and likely pathogenic variants (variants that are likely to be associated with disease).
- Negative:
  A negative or "normal" result means that no relevant variants were found that are associated with your or your child's current medical condition or that would increase the risk of developing a disease in the future. This may

Types of Results (Continued)

suggest that no disease-related variants are present in the genes tested. However, genetic testing, while highly accurate, may not detect all existing variants. This can occur due to limitations in current scientific knowledge about certain genes or the technical boundaries of the testing method used.

- Variant of Uncertain Significance (VUS):
  Sometimes, testing identifies a DNA variant whose clinical impact is not yet fully understood. These are referred to as **variants of uncertain significance (VUS).** If a VUS is identified in a gene that could be related to your or your child's medical condition, additional testing or family studies may be recommended to help clarify its significance.
- Secondary and Carriership Findings
  Secondary and/or Carriership Findings will be reported only if You have provided Your explicit consent by selecting **"Yes."** During the course of genetic analysis, it is possible to identify a pathogenic variant that is not related to the primary reason for testing but is nonetheless clinically significant for Your health or that of Your family members. Such findings are considered medically relevant due to their clear and immediate implications. The following types of findings may be reported:

1. Secondary Findings:
   The American College of Medical Genetics and Genomics (ACMG) has issued guidelines for reporting certain findings, referred to as Secondary Findings, which are available at www.acmg.net. These recommendations form the basis for Princess Al Jawhara Al Ibrahim Center for Molecular Medicine and Genetics ("Al Jawhara Center") when reporting Secondary Findings.
2. Carriership Findings:
   Upon request, and if available, Al Jawhara Center will report Carriership Findings, which mainly include:
   - Variants indicating carrier status for recessive disorders

These findings will be reported only for variants that have undergone prior evaluation by Al Jawhara Center. Interpretation is based on medical and scientific information available at the time of analysis and may evolve as knowledge advances.

3. Limitations & Additional Considerations

- Not all disease-causing variants may be detected because of technical or knowledge limitations.
- Some variants may remain ambiguous (VUS) despite additional analyses.
- CNVs are reported at screening level and require orthogonal confirmation by MLPA or microarray.
- Samples from family members (parents, siblings) may help interpretation; your provider may request this.
- Whole Exome Sequencing (WES) may occasionally reveal unexpected familial relationships, such as non-paternity or other undisclosed biological connections.
- Interpretation of variants and carrier status is based on the medical and scientific information available at the time of analysis and may change as knowledge advances.
- Al Jawhara Center cannot guarantee detection of every medical condition associated with pathogenic or likely pathogenic variants. In some cases, the test may not yield valid results if the sample quality or quantity is insufficient, in which case an alternative sample may be requested.
- Samples and data may be stored (de-identified or coded) for quality control, development, or internal research purposes.
- You and/or your physician may be recontacted in the future if new information emerges about variants discovered.

Disclaimer: Please note that genetic analyses are not always conclusive. Due to technological limitations and/or the current state of medical knowledge, certain disease-causing variants may remain undetected. As a result, it is not possible to fully eliminate all risks associated with potential genetic conditions.
In some instances, the analysis may suggest the presence of a genetic abnormality when none exists (false positive) or fail to detect one when it is present (false negative). If the underlying cause of a false-positive or false-negative result cannot be identified by Al Jawhara Center, Al Jawhara Center shall not be held liable for any incomplete, potentially misleading, or inaccurate outcome of the analysis.

4. Reporting Preferences & Updates

You may choose whether or not to have certain categories of additional findings reported:

	Index Patient	Individual 1	Individual 2
Option	Yes / No	Yes / No	Yes / No
Report the ACMG recommended Secondary Findings	☐Yes ☐ No	☐Yes ☐ No	☐Yes ☐ No
Report Carriership Findings	☐Yes ☐ No	☐Yes ☐ No	☐Yes ☐ No

If you do not make a selection, the default is **No** for both options.

Reanalysis/Updates: As diseases, genes, and variants continue to be subjects of ongoing scientific research, it may be beneficial to re-evaluate Your Sample **("Reanalysis")** when new discoveries emerge. If relevant to Your health status, Al Jawhara Center may re-examine Your Sample for clinically significant variants, with only the raw DNA sequencing data being used for the Reanalysis. Should new ("novel") findings differ from those in the original report, Al Jawhara Center will issue an updated report to You and/or Your Physician. You may also request a Reanalysis of Your Sample even without new clinical information; however, it is recommended to wait at least **one year** after the original Analysis or to request it when there are changes in the clinical presentation (phenotype).

5. Confidentiality, Data Use, Data Protection & Specimen Retention

- Your results and specimen will be treated confidentially and shared only with those you authorize, your physician, or as required by law.
- Unless otherwise authorized, no additional genetic tests will be performed beyond those you consent to.
- The biological specimen may be stored (in a coded or de-identified fashion) in accordance with institutional policy for quality, validation, or development purposes.
- Your personal and genomic data will be stored on secure institutional servers with restricted, role-based access and regular secure backups. Data are used solely for your clinical care and handled under applicable privacy policies.
- De-identified data may be submitted to public databases (e.g., ClinVar) to contribute to medical knowledge, with minimal information to help interpretation.

6. Optional Research Consent for Future Use of Sample and Personal Data

I understand that my biological sample **("Sample")** and related personal data may help Al Jawhara Center to develop and improve diagnostic methods and potential treatments for genetic diseases in general. I acknowledge that neither I nor the person for whom I am the legal guardian or representative will receive any financial benefit or compensation from such use.

If I do **not** check a box, it will be considered as "**No**" for that item.

a. Consent for Internal Research Index Patient ☐ Yes ☐ No
Individual 1 ☐ Yes ☐ No
Individual 2 ☐ Yes ☐ No

I consent to the use of my Sample and personal data by Al Jawhara Center for scientific or medical research focused on understanding, early detection, and/or treatment of rare or inherited diseases. Because scientific knowledge advances over time, it is not possible to specify all future research purposes in detail. The Sample and data may therefore be used in medical research projects that cannot be foreseen today, provided such use complies with ethical and legal requirements.

b. Consent for Long-Term Storage and Ownership Index Patient ☐Yes ☐No
Individual 1 ☐Yes ☐No
Individual 2 ☐Yes ☐No

I consent to the secure storage of my Sample and related personal data for up to **10 years** after the final test report has been issued. I hereby donate and transfer ownership of the Sample to Al Jawhara Center, for continued use in

Optional Research Consent for Future Use of Sample and Personal Data (Continued)

authorized scientific or medical research aimed at improving prevention, detection, or treatment of rare and genetic

diseases. After 10 years, identifying information will be deleted, and the Sample will be kept only in a fully anonymized form, meaning that I can no longer be personally identified from it. Anonymized Samples may be used indefinitely for research purposes, provided they comply with ethical and legal standards.

Signing this section is entirely optional and does not affect your clinical testing or diagnosis.

7. Authorization & Consent

By signing below, I confirm that:

- I have read this consent document, or it has been explained to me in a language I understand.
- I have had the opportunity to ask questions, and my questions have been answered to my satisfaction.
- I understand the benefits, limitations, and risks of WES.
- I authorize the performance of WES as ordered by my physician.
- I understand I may withdraw consent before testing begins.
- I authorize the release of my results to my physician, authorized individuals, and myself (or my legal representative).

Index Patient / Legal Representative		
Patient Name:	Patient Signature:	Date: / /
If signed by a representative, relationship to patient:		
Individual 1		
Name:	Signature:	Date: / /
Individual 2		
Name:	Signature:	Date: / /
Ordering Physician:		
Physician Name:	Physician Signature:	Date: / /

Specimen Requirements

Type of Analysis	Type of Specimen	Specimen Volume/Concentration		Transport Temperature
		Minimum	Ideal	
WES	Peripheral blood (EDTA tube)	5 ml	10 mL	+2°C to + 8°C
WES	DNA	50ng/µl (10µl -100µl)	70 ng/µl (10µl -100µl)	-20°C to + 8°C

Note:

- Assure sample sterility.
- Close tubes properly.
- Label all samples.
- Send the sample on the day of collection if possible or store it at 4°C for up to 72 hours as maximum. "Older Samples May Be Rejected, if not stored properly".
- Close shipping box tightly and enclose requisition and consent form.