INVITAE

Discover Dysplasias™

No-Charge Genetic Test for Skeletal Dysplasias

ORDER ID
For Invitae internal use only

Requisition Form

Discover Dysplasias TRF965-1

This requisition form can be used to submit a specimen for the Discover Dysplasias™ program, a no-charge U.S. testing program brought to you by BioMarin Pharmaceutical Inc. and Invitae. Please confirm that the patient meets the eligibility requirements for the program. To submit orders for genetic testing outside of this program, please order through Invitae's online portal or use a standard requisition form, accessible at www.invitae.com/order-forms.

REQUIRED PROGRAM ELIGIBILITY

This program is available to patients in the US with one or more of the following signs and symptoms suggestive of or consistent with a diagnosis of skeletal dysplasia. Please select all patient criteria that apply:

- ☐ **Skeletal abnormalities suggestive of skeletal dysplasia**
- ☐ **Short stature**
- ☐ **Disproportionate growth**
- ☐ **Dysmorphic facial features**
- ☐ **Other signs or symptoms suggestive of skeletal dysplasia**

PATIENT INFORMATION

First name	MI	Last name
Date of birth (MM/DD/YYYY)	Biological sex ◯ M ◯ F	MRN (medical record number)

Ancestry ◯ Asian ◯ Black/African American ◯ White/Caucasian ◯ Ashkenazi Jewish ◯ Hispanic ◯ Native American ◯ Pacific Islander ◯ French Canadian ◯ Sephardic Jewish ◯ Mediterranean ◯ Other: _____

Phone	Email address
Address	City
State	Zip code / Country

SPECIMEN INFORMATION

Label each tube with the patient's full name, date of birth, and specimen collection date.
A requisition form MUST accompany each specimen. www.invitae.com/specimen-requirements

Specimen type : ◯ Blood ◯ Saliva ◯ Assisted saliva ◉ DNA - source:

DNA must be extracted in a CLIA or other suitably certified laboratory

We are unable to accept blood/saliva from patients with:

- *Allogeneic bone marrow transplants*
- *Blood transfusion <2 weeks prior to specimen collection*

Collection date (MM/DD/YYYY) *If not provided, date will be 1 day prior to our receipt of specimen. For DNA, provide date retrieved from archive.*

Special cases : ◯ History of/current hematologic malignancy

REASON FOR TESTING

Previous results *(if applicable and not included in clinical criteria, enclose copy of report)*

ORGANIZATION INFORMATION

Organization name and address

Organization name	
Phone	Fax
Address	City
State / Zip code	Country

Primary clinical contact

Name	NPI
Specialty	
Email address (for report access)	

Ordering provider

◯ **Same as primary clinical contact**

Name	NPI
Specialty	
Email address (for report access)	

Additional clinical or laboratory contact (optional)

Name	Email address (for report access)

INVITAE PARTNER CODE SKEL

CLINICAL INFORMATION

When was the first sign or symptom of skeletal dysplasia noted?

- ☐ **Prenatally**
- ☐ **At Birth**
- ☐ **Age in Years** _____

FAMILY VARIANT TESTING

Invitae's family variant testing involves analysis of the gene(s) in which the original family member's pathogenic or likely pathogenic variant was identified. Learn more at www.invitae.com/family.

Please attach the proband's clinical report or provide Invitae RQ#

INVITAE PROBAND RQ#	RELATIONSHIP TO PROBAND	GENE(S)	VARIANT(S)

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MEDICAL HISTORY AND PHYSICAL EXAMINATION (Please check all that apply.)

Growth
- ☐ Short stature
- ☐ Tall stature
- ☐ Intrauterine growth retardation
- ☐ Postnatal growth retardation
- ☐ Asymmetric bone growth
- ☐ Normal stature and/or growth

Development
- ☐ Developmental delay
- ☐ Developmental regression
- ☐ Intellectual disability
- ☐ Progressive cognitive impairment
- ☐ Normal intellect
- ☐ Normal development

Head and neck
- ☐ Macrocephaly
- ☐ Microcephaly
- ☐ Craniosynostosis
- ☐ Cloverleaf skull
- ☐ Wormian bones
- ☐ Large fontanelles
- ☐ Wide cranial sutures
- ☐ Hydrocephalus
- ☐ Frontal bossing
- ☐ Decreased calvarial ossification
- ☐ Short neck
- ☐ Normal head size/shape

Facial features
- ☐ Coarse facial features
- ☐ Midface hypoplasia
- ☐ Depressed nasal bridge
- ☐ Prominent nasal bridge
- ☐ Anteverted nares
- ☐ Hypertelorism
- ☐ Downslanted palpebral fissures
- ☐ Long philtrum
- ☐ Micrognathia
- ☐ Proptosis
- ☐ Other dysmorphic facial features
- ☐ No noted facial dysmorphism

Oral/dental
- ☐ Cleft lip
- ☐ Cleft palate
- ☐ High arched palate
- ☐ Bifid uvula
- ☐ Multiple oral frenula
- ☐ Natal teeth
- ☐ Supernumerary teeth
- ☐ Dentinogenesis imperfecta
- ☐ Hypoplasia of dental cementum

Eyes and ears
- ☐ Congenital cataract
- ☐ Corneal clouding
- ☐ Severe myopia
- ☐ Microspherophakia
- ☐ Ectopia lentis
- ☐ Retinal degeneration or detachment
- ☐ Low-set ears
- ☐ Posteriorly rotated ears
- ☐ Microtia
- ☐ Cystic swelling of the pinnae
- ☐ Sensorineural hearing loss
- ☐ Conductive hearing loss

Limbs
- ☐ Rhizomelia
- ☐ Mesomelia
- ☐ Acromelia
- ☐ Acromesomelia
- ☐ Micromelia
- ☐ Disproportionately long limbs
- ☐ Bowing of the long bones
- ☐ Coxa vara
- ☐ Genu varum
- ☐ Genu valgum
- ☐ Talipes equinovarus
- ☐ Radial ray defects
- ☐ Absence of a limb
- ☐ Patellar hypoplasia or aplasia

Hands and feet
- ☐ Brachydactyly
- ☐ Arachnodactyly
- ☐ Preaxial polydactyly
- ☐ Postaxial polydactyly
- ☐ Syndactyly
- ☐ Clinodactyly
- ☐ Camptodactyly
- ☐ Ectrodactyly
- ☐ Hitchhiker thumb
- ☐ Trident hand
- ☐ Broad or spatulate fingers/toes
- ☐ Pes planus
- ☐ Nail hypoplasia or dysplasia

Thorax
- ☐ Thoracic hypoplasia
- ☐ Short thorax
- ☐ Long thorax
- ☐ Narrow chest
- ☐ Bell-shaped chest
- ☐ Barrel-shaped chest
- ☐ Pectus carinatum
- ☐ Pectus excavatum
- ☐ Abnormal ribs
- ☐ Hypoplastic clavicles
- ☐ Hypoplastic scapulae

Spine
- ☐ Scoliosis
- ☐ Kyphosis
- ☐ Kyphoscoliosis
- ☐ Lumbar lordosis
- ☐ Platyspondyly
- ☐ Other abnormal form of the vertebral bodies
- ☐ Atlanto-axial instability
- ☐ Cervical spine instability
- ☐ Cervical medullary compression
- ☐ Craniovertebral junction stenosis
- ☐ Spinal stenosis

Joints
- ☐ Joint laxity
- ☐ Joint hypermobility
- ☐ Congenital joint contractures
- ☐ Progressive joint contractures
- ☐ Limb joint contracture
- ☐ Multiple joint dislocations
- ☐ Joint stiffness
- ☐ Joint pain
- ☐ Osteoarthritis
- ☐ Carpal tunnel syndrome in a child

Bone structure
- ☐ Fracture of the long bones
- ☐ Recurrent fractures
- ☐ Thickened long bones
- ☐ Thin long bones
- ☐ Delayed bone age
- ☐ Advanced bone age
- ☐ Decreased bone mineralization

Skin and hair
- ☐ Redundant skin folds
- ☐ Ichthyosiform erythroderma
- ☐ Acanthosis nigricans
- ☐ Aberrant mongolian spots
- ☐ Thickened skin
- ☐ Soft and/or thin skin
- ☐ Skin hyperextensibility
- ☐ Thickened coarse hair
- ☐ Brittle hair
- ☐ Hirsutism
- ☐ Sparse or absent hair

Heart and lungs
- ☐ Cardiomegaly
- ☐ Atrial septal defect or single atrium
- ☐ Patent ductus arteriosus
- ☐ Transposition of the great vessels
- ☐ Cardiac valve prolapse
- ☐ Valvular stenosis
- ☐ Aortic root dilation
- ☐ Heart conduction abnormalities
- ☐ Lung hypoplasia
- ☐ Spontaneous pneumothorax

Neuromuscular
- ☐ Abnormal gait
- ☐ Frequent falls
- ☐ Hypotonia
- ☐ Hypertonia
- ☐ Muscle weakness and/or atrophy
- ☐ Spasticity
- ☐ Neuropathy or impaired sensation
- ☐ Reduced or absent deep tendon reflexes
- ☐ Increased deep tendon reflexes

Other Systems
- ☐ Hepatomegaly
- ☐ Splenomegaly
- ☐ Genital abnormalities
- ☐ Renal abnormalities
- ☐ Inguinal or umbilical hernia
- ☐ Autoimmune disease

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Does this patient have a clinical or suspected diagnosis of a specific skeletal dysplasia? If so, please provide diagnosis.

◯ Clinical Diagnosis ◯ Suspected Diagnosis

RADIOGRAPHIC FINDINGS

Please provide information about relevant radiographic findings not addressed in the checklist above.

LABORATORY FINDINGS

Please provide information about relevant laboratory findings, including biochemical testing results.

ASSAY

Invitae is a CAP-accredited and CLIA-certified clinical diagnostic laboratory performing full-gene sequencing and deletion/duplication analysis using next-generation sequencing technology (NGS). Search for details on the analysis of any gene in our test catalog at www.invitae.com/physician/search.

To request a complimentary specimen collection kit, visit www.discoverdysplasias.com.

SHIPPING INSTRUCTIONS

Please ship specimen to Invitae:

Attn: Invitae Client Services
1400 16th Street
San Francisco, CA 94103 USA

TEST OPTIONS

Invitae continually updates its panels based on the most recent evidence. Please note that if an order is placed using an older version of this form, Invitae reserves the right to upgrade any ordered panel(s) to the current version(s).

TESTS INCLUDED IN THE PROGRAM

Test code	Test name	# of gene(s)	Gene list
◯ 89100	Invitae Expanded Skeletal Dysplasia Panel	109	*ACP5, ADAMTS10, AGPS, ALPL, ANKH, ARSB, ARSE, B3GALT6, B3GAT3, BGN, BMP2, BMPR1B, CFAP410, CANT1, CDC45, CDC6, CDT1, CHST14, CHST3, COL10A1, COL11A1*, COL2A1, COL9A1, COL9A2, COL9A3, COMP, CUL7, DDR2, DLL3, DVL1, DVL3, DYM, EBP, EIF2AK3, EVC, EVC2, FBN1, FGFR1, FGFR2, FGFR3, FLNA, FLNB, FN1*, GALNS, GDF5, GLB1, GMNN, GNPAT, GNPTAB, GNPTG, GNS, GORAB, GPC6, GUSB, HES7, HGSNAT, HSPG2, HYAL1, ICK, IDS*, IDUA, IFT172, IHH, IMPAD1, INPPL1, KAT6B, KIF22, LBR, LEMD3, LFNG, LIFR, LMX1B, MAP3K7, MATN3, MESP2, MGP, MMP13, MMP2, MMP9, NAGLU, NKX3-2, NPR2, OBSL1, ORC1, ORC4, ORC6, PAPSS2, PEX5, PEX7, PTH1R, RIPPLY2, RMRP, ROR2, RSPRY1, RUNX2, SGSH, SH3PXD2B, SLC26A2, SLC39A13, SMAD4, SMARCAL1, SOX9, TBCE, TBX6, TRPV4, WDR35, WISP3, WNT5A, XYLT1*

**Denotes gene offered with limitation.*

By signing this form, the medical professional acknowledges that the individual/family member authorized to make decisions for the individual (collectively, the "Patient") has been supplied information regarding and consented to undergo genetic testing, substantially as set forth in Invitae's Informed Consent for Genetic Testing (www.invitae.com/patient-consent), and in connection with the Discover Dysplasias™ Program, has been informed that Invitae may notify them of clinical updates related to genetic test results (in consultation with the ordering medical professional as indicated), has been informed that de-identified Patient data may be used and shared for research purposes and shared with third parties, including BioMarin Pharmaceutical, Inc. The medical professional warrants that he/she will not seek reimbursement for this sponsored test from any third party, including but not limited to federal healthcare programs. The medical professional also hereby acknowledges that organization and clinician contact information provided in the order may be shared with third parties, including BioMarin Pharmaceutical, Inc. that may contact you directly in connection with the Discover Dysplasias™ Program. In addition to the above, I attest that I am the ordering physician, or I am authorized by the ordering physician to order this test, or I am authorized under applicable law to order this test.

Medical professional signature (required)	Date