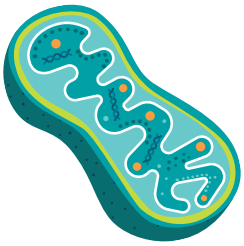
Understanding TK2d

THYMIDINE KINASE 2 DEFICIENCY

A Rare, Autosomal Recessive Mitochondrial Disease That Manifests Predominantly as Progressive Myopathy[2]

Thymidine kinase 2 deficiency (TK2d) is a debilitating and life-threatening genetic disease that causes progressive and severe muscle weakness.[1,2,3,4] Many patients lose the ability to walk, eat, and breathe independently.[1,2,3,4]



What causes TK2d?

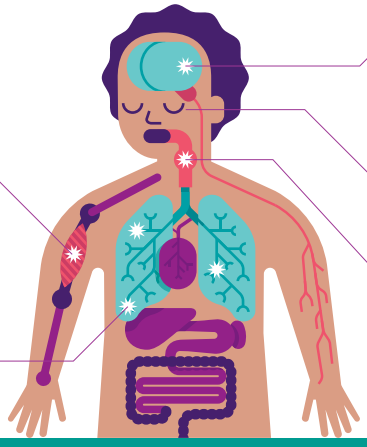
TK2d is caused by a genetic mutation in the TK2 gene.[1,4] This mutation leads to a decrease in mitochondrial DNA production.[1,4] Mitochondria generate most of the energy that powers our cells. Errors in mitochondrial DNA can lead to insufficient energy, and as a result, muscles and organs can't function properly.[4,5,6]

How many people have TK2d?

1 in 5,000 people have some form of genetic mitochondrial disease.[7] Prevalence of TK2d itself is still being researched.

PROGRESSIVELY WORSENING SYMPTOMS

TK2d can manifest in different ways and affect different parts of the body[1,2,3]



Nervous System
Fatigue
Developmental delays/ missed milestones (younger patients)

Eyes
Droopy eyelids (ie, ptosis)

Gastrointestinal
Difficulty swallowing

Muscles
Muscle weakness
Low muscle tone
Difficulty walking, talking

Lungs
Difficulty breathing

IMPACTS ALL AGES: Symptoms can progress slowly or rapidly[1,2]

EARLY ONSET: OFTEN MORE SEVERE — LATER ONSET: OFTEN LESS SEVERE

Normal Development | **Infant/Child Onset** | **Adolescent Onset** | **Adult Onset**

TK2D MANAGEMENT TODAY: No health-authority-approved therapies currently available[8]

Patients require medical equipment and therapies[1,3,8]

- Respiratory support
- Feeding tubes
- Wheelchairs
- Respiratory physiotherapy
- Physical therapy

Patients may take nutraceuticals (“mito-cocktail”) to manage disease symptoms[8]

Patients rely on supportive care provided by multi-disciplinary team[7]

- Neurologists
- Pulmonologists
- Metabolic specialists
- Gastroenterologists
- Physical therapists
- Speech therapists
- Clinical geneticists
- Genetic counselors

Genetic testing is the most direct path to confirm diagnosis of TK2d

Earlier accurate diagnosis helps to identify patients sooner and get them on supportive care and into clinical trials faster.[1,2,3]

Because TK2d can present like other diseases (e.g. muscular dystrophy, Pompe, SMA, mtDNA depletion syndrome, and others), genetic testing is needed to confirm a diagnosis.[1]

Our Commitment

At UCB, we are proud to partner with physicians and patient communities in our work.

Together we can bring hope and support to patients and families impacted by rare diseases.

1 Garone C, Taylor RW, Nascimento A, et al. Retrospective natural history of thymidine kinase 2 deficiency. J Med Genet. 2018;55(8):515-21. **2** Wang J, Kim E, Dai H, et al. Clinical and molecular spectrum of thymidine kinase 2-related mtDNA maintenance defect. Mol Genet Metab. 2018;124:124-30. **3** Domínguez-González C, Hernández-Laín A, Rivas E, et al. Late-onset thymidine kinase 2 deficiency: a review of 18 cases. Orphanet J Rare Dis. 2019;14(1):100. **4** National Institute of Health. TK2-related mitochondrial DNA depletion syndrome, myopathic form. https://medlineplus.gov/genetics/condition/tk2-related-mitochondrial-dna-depletion-syndrome-myopathic-form/#genes. Last Access on January 2023. **5** United Mitochondrial Disease Foundation. Understanding & Navigating Mitochondrial Disease. https://www.umdf.org/what-is-mitochondrial-disease-2/. Last Access on January 2023. **6** Hirano M, Marti R, Ferreiro-Barros C, et al. Defects of intergenomic communication: autosomal disorders that cause multiple deletions and depletion of mitochondrial DNA. Semin Cell Dev Biol. 2001;12:417-27. **7** Parikh S, Goldstein A, Karaa A, et al. Patient care standards for primary mitochondrial disease: a consensus statement from the Mitochondrial Medicine Society. Genet Med. 2017;19(12):10.1038/gim.2017.107. **8** El-Hattab AW and Scaglia F. Mitochondrial DNA depletion syndromes: review and updates of genetic basis, manifestations, and therapeutic options. Neurotherapeutics. 2013;10:186-98.

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