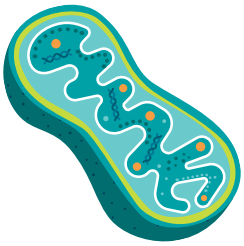
Understanding TK2d

A Rare, Under-Recognized Genetic Mitochondrial Disorder

THYMIDINE KINASE 2 DEFICIENCY

Thymidine kinase 2 deficiency (TK2d) is a debilitating and life-threatening genetic disorder 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?

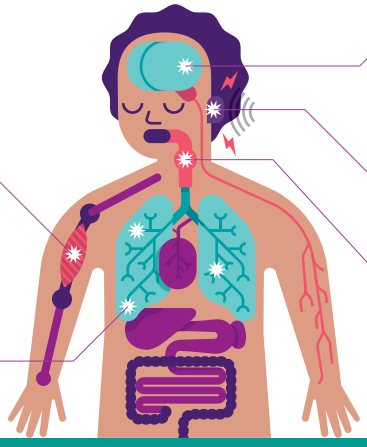
TK2d is caused by a genetic mutation in the TK2 gene.[1,4] This mutation leads to a decrease in mitochondrial DNA production.[1,4] Mitochondria generate most of the energy that powers our cells. Errors in mitochondrial DNA can lead to insufficient energy, and as a result, muscles and organs can't function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

Ears
Progressive hearing loss

Gastrointestinal
Difficulty swallowing

Muscles
Muscle weakness
Low muscle tone
Difficulty walking, talking
Droopy eyelids (ie, ptosis)

Lungs
Difficulty breathing

IMPACTS ALL AGES: Age of onset predicts disease severity[1,2]

EARLY ONSET: MORE SEVERE — LATER ONSET: LESS SEVERE

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

TK2D TREATMENT TODAY: No FDA-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 many specialists[7]

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

Genetic Testing Is Necessary

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 (muscular dystrophy, Pompe, SMA, mtDNA depletion syndrome, and others), genetic testing is needed to confirm a diagnosis.[1]

If you or your family member has TK2d:

Learn more at www.tk2d.com

Our Commitment

At Zogenix, 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. Accessed April 27, 2021. **5** United Mitochondrial Disease Foundation. Understanding & Navigating Mitochondrial Disease. https://www.umdf.org/what-is-mitochondrial-disease-2/. Accessed April 27, 2021. **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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Rare Disease Therapies