Tinea Manuum (a fungal skin infection) on hand or foot: very common, and treatable with topical medication (ointment/cream). If vigorous, treat with infusion (IV) drugs.

Tinea manuum

Tinea manuum

Acral Peeling Skin Syndrome is a genetic defective disease — very rare, still does not have a cure yet. Keep comfort with some topical meds.

Acral Peeling Skin Syndrome

Acral Peeling Skin Syndrome

To: Ms. Suong July 12, 2025

Nashville, Tennessee a professor of medicine

Cc: Dermatologist Physician: Dr. Nhu-Linh Tran (Formerly Emory University)

I have investigated the inflammation in your hand and found two matching disease names. Neither is contagious to other people; however, they can gradually spread to other areas of the same body part- specifically, the fingers in the hands and feet. You may experience soreness and discomfort.

Let's start with the rare one- Acral Peeling Skin Syndrome (fewer than 1,000 cases). It shares many symptoms with other conditions but is caused by a genetic defect, making it extremely rare. Currently, there's no cure. Treatment focuses on reducing pain using medications or ointments. Wearing special gloves can help prevent contact and exposure, especially during physical tasks. There are fewer than 1,000 known cases. I hope it's not what you're dealing with!

Caused by two defective genes: TGM5 & CSTA. See notes for a full list of temporary drugs and a direction for new treatment drug discovery.

The second one is very common: Tinea Manuum, or Ringworm of the hand, is a fungal infection treated with antifungal medications. Other notes: Treat it similarly to an allergy- maintain consistent use of medication and ointment. Symptoms may improve depending on environmental factors such as weather (heat or cold) and working conditions. Use special gloves to avoid contact and exposure, especially during manual work.

See a full list of the treatment drugs suggested by Yale Medical School. Also, a guide to choose an infusion (IV) drug based on our CYP2C19 metabolism enzyme gene.

Acral peeling skin syndrome

- Type: a genetic skin disorder
- Cause: changed in TGM5 gene or CSTA gene by inheritance (Autosomal Recessive)

Other Names: acral deciduous skin; acral PSS; localised deciduous skin; localised PSS; localized deciduous skin; localized PSS; peeling skin syndrome type 2

Navigate to sub-section

Disease Information

Summary

Acral peeling skin syndrome is a genetic skin disorder characterized by painless peeling of the top layer of skin. Acral refers to the fact that the peeling is most apparent on the hands and feet, although peeling may also occur on the arms and legs. The peeling is usually present from birth, but can appear later in childhood or early adulthood. Acral peeling skin syndrome can be caused by genetic changes in the TGM5 gene. Genetic changes in the CSTA gene have also been linked to this condition. It is inherited in an autosomal recessive pattern.

Read More

Resource(s) for Medical Professionals and Scientists on This Disease:

- RARe-SOURCE™ offers rare disease gene variant annotations and links to rare disease gene literature.

About Acral peeling skin syndrome

Many rare diseases have limited information. Currently, GARD aims to provide the following information for this disease:

- **Population Estimate:** Fewer than 1,000 people in the U.S. have this disease. ⓘ
- **Symptoms:** May start to appear as a Newborn and as an Infant.
- **Cause:** This disease is caused by a change in the genetic material (DNA).
- **Organizations:** Patient organizations dedicated to this rare disease are available on GARD, or you may contact a GARD Information Specialist for additional information.
- **Categories:** Genetic diseases ⓘ Skin diseases ⓘ

Causes

What Causes This Disease?

an inheritance

Genetic Mutations

Known Genetic Mutations

Can This Disease Be Passed Down From Parent to Child?

Yes. It is possible for a biological parent to pass down genetic mutations that cause or increase the chances of getting this disease to their child. This is known as inheritance. Knowing whether other family members have previously had this disease, also known as family health history, can be very important information for your medical team. This tool from the Surgeon General can help you collect your family health history.

TGM5 Gene - Transglutaminase 5

Protein Coding **(Updated: Mar 30, 2025 ; GC15M048143 ; GIFtS: 52)**

This gene encodes a member of the transglutaminase family. The encoded protein catalyzes formation of protein cross-links between glutamine and lysine residues, often resulting in stabilization of protein assemblies. This reaction is calcium dependent. Mutations in this gene have been associated with acral peeling skin syndrome. [provided by RefSeq, Oct 2009] See more...

Aliases for TGM5 Gene

Aliases for TGM5 Gene

GeneCards Symbol: *TGM5* [2]

Transglutaminase 5 [2 3 5]

TGMX [2 3 4 5]

TGX [2 3 4 5]

Protein-Glutamine Gamma-Glutamyltransferase 5 [2 3 4]

Transglutaminase X [3 4]

EC 2.3.2.13 [4 47]

TGase X [3 4]

TGase-5 [3 4]

TG(X) [3 4]

Transglutaminase V [3]

Transglutaminase-5 [4]

TGASE5 [3]

TGASEX [3]

PSS2 [3]

TGM6 [3]

External Ids for TGM5 Gene

HGNC: 11781 NCBI Gene: 9333 Ensembl: ENSG00000104055 OMIM®: 603805 UniProtKB/Swiss-Prot: O43548

Previous GeneCards Identifiers for TGM5 Gene

GC15M038893, GC15M036421, GC15M041104, GC15M041241, GC15M041312, GC15M043527, GC15M020373, GC15M043234, GC15M043236, GC15M043254, GC15M043273, GC15M043296, GC15M043313, GC15M043346, GC15M043388, GC15M043538, GC15M043609, GC15M043751, GC15M043836, GC15M043953, GC15M044043, GC15M044138, GC15M044225, GC15M044365, GC15M044456, GC15M044555, GC15M044680, GC15M044786, GC15M044896, GC15M045021, GC15M047033

Search aliases for TGM5 gene in PubMed and other databases

Summaries for TGM5 Gene

NCBI Gene Summary for TGM5 Gene

This gene encodes a member of the transglutaminase family. The encoded protein catalyzes formation of protein cross-links between glutamine and lysine residues, often resulting in stabilization of protein assemblies. This reaction is calcium dependent. Mutations in this gene have been associated with acral peeling skin syndrome. [provided by RefSeq, Oct 2009]

GeneCards Summary for TGM5 Gene

TGM5 (Transglutaminase 5) is a Protein Coding gene. Diseases associated with TGM5 include Peeling Skin Syndrome 2 and Peeling Skin Syndrome 1. Among its related pathways are Keratinization and Nervous system development. Gene Ontology (GO) annotations related to this gene include *protein-glutamine gamma-glutamyltransferase activity*. An important paralog of this gene is TGM7.

UniProtKB/Swiss-Prot Summary for TGM5 Gene

Catalyzes the cross-linking of proteins and the conjugation of polyamines to proteins. Contributes to the formation of the cornified cell envelope of keratinocytes. (TGM5_HUMAN,O43548)

Additional gene information for TGM5 Gene

HGNC (11781) NCBI Gene (9333) Ensembl (ENSG00000104055) OMIM® (603805) UniProtKB/Swiss-Prot (O43548)
Open Targets Platform(ENSG00000104055)

Monarch Initiative
Alliance of Genome Resources

Search for TGM5 at DataMed
Search for TGM5 at HumanCyc

No data available for CIViC Summary , Tocris Summary , Gene Wiki entry , PharmGKB Summary , Rfam classification and piRNA Summary for TGM5 Gene

Genomics for TGM5 Gene

Subsections: **Promoters/Enhancers** / **Location**

GeneHancer (GH) Regulatory Elements (see citations)

Download GeneHancer 2017 data
Request up-to-date GeneHancer data Download GeneHancer data sheet

Promoters and enhancers for TGM5 Gene

CSTA Gene - Cystatin A

Protein Coding **(Updated: Mar 28, 2025 ; GC03P122325 ; GIFtS: 57)**

Search in Gene | Follow Gene

The cystatin superfamily encompasses proteins that contain multiple cystatin-like sequences. Some of the members are active cysteine protease inhibitors, while others have lost or perhaps never acquired this inhibitory activity. There are three inhibitory families in the superfamily, including the type 1 cystatins (stefins), type 2 cystatins, and kininogens. This gene encodes a... See more...

Aliases for CSTA Gene

Aliases for CSTA Gene

GeneCards Symbol: *CSTA* [2]
Cystatin A [2 3 5]
STF1 [3 4 5]
STFA [3 4 5]
Cystatin A (Stefin A) [2 3]
Cystatin-A [3 4]
Cystatin AS [3]
Cystatin-AS [4]
Stefin A [2]
Stefin-A [4]
AREI [3]
PSS4 [3]

External Ids for CSTA Gene

HGNC: 2481 NCBI Gene: 1475 Ensembl: ENSG00000121552 OMIM®: 184600 UniProtKB/Swiss-Prot: P01040

Previous HGNC Symbols for CSTA Gene

STF1, STFA

Previous GeneCards Identifiers for CSTA Gene

GC03P118765, GC03P121992, GC03P123325, GC03P123364, GC03P123526, GC03P122044, GC03P119417

Search aliases for CSTA gene in PubMed and other databases

Summaries for CSTA Gene

NCBI Gene Summary for CSTA Gene

The cystatin superfamily encompasses proteins that contain multiple cystatin-like sequences. Some of the members are active cysteine protease inhibitors, while others have lost or perhaps never acquired this inhibitory activity. There are three inhibitory families in the superfamily, including the type 1 cystatins (stefins), type 2 cystatins, and kininogens. This gene encodes a stefin that functions as a cysteine protease inhibitor, forming tight complexes with papain and the cathepsins B, H, and L. The protein is one of the precursor proteins of cornified cell envelope in keratinocytes and plays a role in epidermal development and maintenance. Stefins have been proposed as prognostic and diagnostic tools for cancer. [provided by RefSeq, Jul 2008]

GeneCards Summary for CSTA Gene

CSTA (Cystatin A) is a Protein Coding gene. Diseases associated with CSTA include Peeling Skin Syndrome 4 and Peeling Skin Syndrome 2. Among its related pathways are Keratinization and Nervous system development. Gene Ontology (GO) annotations related to this gene include *structural molecule activity* and *protein-macromolecule adaptor activity*. An important paralog of this gene is CSTB.

UniProtKB/Swiss-Prot Summary for CSTA Gene

This is an intracellular thiol proteinase inhibitor. Has an important role in desmosome-mediated cell-cell adhesion in the lower levels of the epidermis. (CYTA_HUMAN,P01040)

Gene Wiki entry for CSTA Gene

Additional gene information for CSTA Gene

HGNC (2481) NCBI Gene (1475) Ensembl (ENSG00000121552) OMIM® (184600) UniProtKB/Swiss-Prot (P01040) Open Targets Platform(ENSG00000121552)

Monarch Initiative
Alliance of Genome Resources

Search for CSTA at DataMed
Search for CSTA at HumanCyc

No data available for CIViC Summary , Tocris Summary , PharmGKB Summary , Rfam classification and piRNA Summary for CSTA Gene

Genomics for CSTA Gene

Subsections: Promoters/Enhancers / Location

GeneHancer (GH) Regulatory Elements (see citations)

Download GeneHancer 2017 data
Request up-to-date GeneHancer data Download GeneHancer data sheet

Promoters and enhancers for CSTA Gene

Publication | Article | May 24, 2023
Dermatology Times
Dermatology Times, May 2023 (Vol. 44. No. 05) | Volume **44** | Issue **05**

An Overview of Acral Peeling Skin Syndrome

Excellent Article- matched with National Institue of Health (NIH) - Genetics & Rare Diseases Info. Center- Winston Vo (Oct 3, 2025)

Author(s): Fazila Rajab

The autosomal recessive disorder is primarily caused by mutations in the TGM5 gene and less frequently in the CSTA gene.

Acral peeling skin syndrome (APSS) is a rare condition that affects fewer than 1000 individuals in the United States.[1] Only a few dozen cases are documented in medical literature. The hereditary skin condition is characterized by painless shedding of the epidermis.[2] The condition primarily involves extremities such as hands and feet (hence acral), but sometimes it can also affect the arms and legs. The peeling manifests mostly at birth but can emerge later in early adulthood.[3] Overall, the condition is mild and does not significantly affect patients' quality of life.

Clinical Presentation

o1559kip/Envato Elements

The disease appears shortly after birth or in early infancy as superficial painless peeling on the palmar, plantar, and dorsal surfaces of the hands and feet, leaving persistent erythema. APSS may cause superficial blisters. Moreover, the palmoplantar skin can also be hyperkeratotic.[4] Skin exfoliation can be induced by heat, humidity, occlusion, exposure to water, friction, or slight trauma. The lesions are usually painless and heal without leaving scars; however, a burning sensation may be felt before or after peeling.

Causes

It is an autosomal recessive disorder that is primarily caused by mutations in the TGM5 gene and less frequently in the CSTA gene.[2,5,6] The TGM5 gene produces the TGM5 enzyme in the epidermis that helps create a cornified cell envelope, forming a protective barrier between the skin and the environment,[7] whereas the CSTA gene encodes for CSTA enzyme that plays a role in cell-to-cell adhesion.[8]

There are 2 genetic mutations that, when homozygous, mainly cause APSS. The first is mutation G113C, which results in the complete loss of TG5 function.[6] The second mutation is T109M, which is not harmful on its own but is a polymorphism that affects the same allele and is usually coupled with the G113C mutation.[9]

Diagnosis

The diagnosis is mainly based on personal history and clinical presentation of superficial skin peeling and blisters, often exacerbated by maceration, trauma, or heat. Histopathologic examination shows mild hyperkeratosis and superficial separation between stratum granulosum and corneum or intracorneal split.[10]

Because the condition is uncommon and has little to no serious consequences, it is frequently misdiagnosed as epidermolysis bullosa simplex, with which its symptoms resemble.[11,12] However, after ruling out epidermolysis bullosa simplex, it is recommended to screen for TGM5 or CSTA mutations. Other diseases considered in the differential diagnosis of APSS may include keratolytic winter erythema, tinea manuum, keratolysis exfoliativa, allergic contact dermatitis, and dyshidrotic eczema. Molecular genetics may help with diagnosing complicated cases.[10]

Management

There is currently no cure for APSS.[1] However, management is mainly symptomatic and preventive, which includes protection from heat, humidity, and trauma, predominantly caused by pressure and friction.[13] Skin-softening ointments such as petroleum jelly may help some patients improve their symptoms. This works best if the ointment is applied immediately after a bath, when the skin is still moist. The topical emollients might aim at reducing maceration and trauma caused by APSS. Moreover, keratolytic agents may also improve symptoms associated with the condition.[14] Various treatment modalities including methotrexate, isotretinoin, topical keratolytic agents, topical corticosteroids, and

phototherapy, have been used but were found to be ineffective in treating APSS.[14]

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