Papillon-Lefevre syndrome

GENERAL INFORMATION

Description:

Defects in CTSC are a cause of Papillon-Lefevre syndrome. Cathepsin C (CTSC) is a lysosomal protease known to activate enzymes that are vital to the body's defenses. Onset of disease occurs between the first and fifth years of life. PLS is mainly detected by dentists because of the severe periodontitis that affects patients. Both the deciduous and permanent dentitions are affected, resulting in premature tooth loss. Palmoplantar keratosis, varying from mild psoriasiform scaly skin to overt hyperkeratosis, typically develops within the first three years of life. Keratosis also affects other sites such as elbows and knees. A variant, Haim-Munk syndrome, features, in addition to PPK and periodontitis, arachnodactyly, acroosteolysis, and onychogryphosis.

Alternative names:

- PLS, PALS, PPP, HMS
- Keratosis palmoplantaris with periodontopathia, Palmoplantar keratoderma (PPK) with periodontitis, CTSC deficiency

Classification:

- Defects of phagocyte function

Inheritance:

Autosomal recessive

OMIM:

- *602365 Cathepsin c; CTSC
- #245000 Papillon-Lefevre syndrome; PALS

Incidence:

4/1,000,000

CLINICAL INFORMATION

Description:

Patients have psoriasiform hyperkeratosis of the palms, soles and the dorsal surfaces of the hands and feet. Scaly, psoriasiform lesions over the knees, elbows, and interphalangeal joints Psoriasiform lesions can also be seen on the limbs. Diffuse transgredient palmoplantar keratoderma, typically developing within the first 3 years of life. Punctiform accentuation, particularly along the palmoplantar creases. This keratoderma associates, as early as infancy, intense gingivitis with alveolar bone lysis and early loss of baby teeth. During childhood, this phenomenon of periodontal disease recurs with rapid loss of adult teeth. Unless treated, periodontosis results in severe gingivitis and loss of teeth by age 5 years. Patients exhibit increased susceptibility to cutaneous (furunculosis, skin abscesses, hidradenitis suppurativa) and systemic infections. Anomalies of chemotaxis and phagocytosis by polymorphonuclear leukocytes have been observed. Patients may have malodorous hyperhidrosis.

Diagnosis:

Diagnostic laboratories:

Clinical:

- Papillon Lefevre Syndrome, ORPHANET

Genetic:

- IDdiagnostics

Therapeutic options:

- Treatment includes oral retinoids for the PPK. Retinoids slow the alveolar bone lysis and attenuate the palmoplantar keratoderma. Elective extraction of involved teeth may prevent excess bone resorption. Appropriate antibiotic therapy may be required for periodontitis and recurrent cutaneous and systemic infections. Treatment with acitretin starting at an early age shows promise towards allowing patients to have normal adult dentition.
- Keratosis palmaris et plantaris, eMedicine

Research programs, clinical trials:

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GENE INFORMATION

Names:

HUGO name: CTSC
Alias(es): CTSC, CPPI, PALS, PLS, HMS, JPD

Localization:

Reference sequences:

DNA: D0022 (IDRefSeq) , **cDNA:** X87212 (EMBL) , **Protein:** P53634 (SWISSPROT) Other Sequences

Chromosomal Location:

11q14.1-q14.3

Maps:

CTSC (Map View)

Variations / Mutations:

- CTSCbase; Mutation registry for Papillon - Lefevre syndrome

Other gene-based resources:

Ensembl: ENSG00000109861, GENATLAS: CTSC, GeneCard: CTSC, UniGene: 128065, Entrez Gene: 1075, euGenes: 1075, GDB: 642234, HomoloGene: 1373

PROTEIN INFORMATION

Description:

Protein function:

Thiol protease. Has dipeptidylpeptidase activity. Can act as both an exopeptidase and endopeptidase. Activates serine proteases such as elastase, cathepsin g and granzymes a and b. Can also activate neuraminidase and Factor XIII.

Catalytic activity:

Release of an N-terminal dipeptide, xaa-yaa-|-zaa-, except when xaa is arg or lys, or yaa or zaa is pro.

Subunit:

Tetramer of heterotrimers consisting of exclusion domain, heavy- and light chains.

Subcellular location:

Lysosome

Post-translational modification:

N-glycosylated

Cofactor:

Binds 1 chloride ion per heavy chain.

Induction:

Up-regulated in lymphocytes by Il2.

Tissue specificity:

Ubiquitous. Highly expressed in lung, kidney and placenta. Detected at intermediate levels in colon, small intestine, spleen and pancreas.

Similarity:

Belongs to the peptidase C1 family.

Structures (PDB):

1K3B .

Other features:

Signal peptide: 1-24

Dipeptidyl-peptidase 1 exclusion domain chain: 25-134

Propeptide: 135-230

Dipeptidyl-peptidase 1 heavy chain: 231-394

Dipeptidyl-peptidase 1 light chain: 395-463

Chloride binding site: 302

Chloride; via amide nitrogen binding site: 304

Chloride binding site: 347

N-linked (glcnac...) glycosylation sites: 29,53,119,276

Disulfide bonds: 30-118, 54-136, 255-298, 291-331, 321-337

Other related resourses:

PIR: S66504, InterPro: IPR000169; Pept_cys_AS, InterPro: IPR013128; Peptidase_C1A, InterPro: IPR000668; Peptidase_C1A_C, Pfam: PF00112; Peptidase_C1, PRINTS: PR00705; PAPAIN, ProDom: PD000158; Peptidase_C1, SMART: SM00645; Pept_C1, PROSITE: PS00640; THIOL_PROTEASE_ASN, PROSITE: PS00139; THIOL_PROTEASE_CYS, PROSITE: PS00639; THIOL_PROTEASE_HIS

Expression pattern for human:

Tissue	Exp. (%)	Clones
mouth_lining	16.54	3:1861
blood	6.68	40:61437
salivary_gland	5.80	11:19467
stomach	3.91	28:73494
esophagus	3.84	7:18719
placenta	3.66	68:190488
lung	3.56	100:288686
connective_tissue	2.78	26:96057
kidney	2.77	52:192551
mammary_gland	2.45	19:79431

Animal models:

Mouse:

MGD: ; Ctsc

OTHER RESOURCES

Societies:

General:

- European Society for Immunodeficiencies
- International Patient Organization for Primary Immunodeficiencies
- Immune Deficiency Foundation
- March of Dimes Birth Defects Foundation
- NIH/National Institute of Allergy and Infectious Diseases

Disease specific:

- National Foundation for Ectodermal Dysplasias

Other information sources:

- Therapeutique dermatologique