Isolated Lymphatic Malformation

Klippel-Trenaunay Syndrome

Epidermal nevus, benign lichenoid keratosis, or seborrheic keratosis

Understanding **P**IK3CA-**R**elated **O**vergrowth **S**pectrum, or **PROS**, conditions

A guide for patients and caregivers

Megalencephaly-Capillary Malformation

HemiMegalEncephaly/ Dysplastic MEGalencephaly/ Focal cortical dysplasia type II

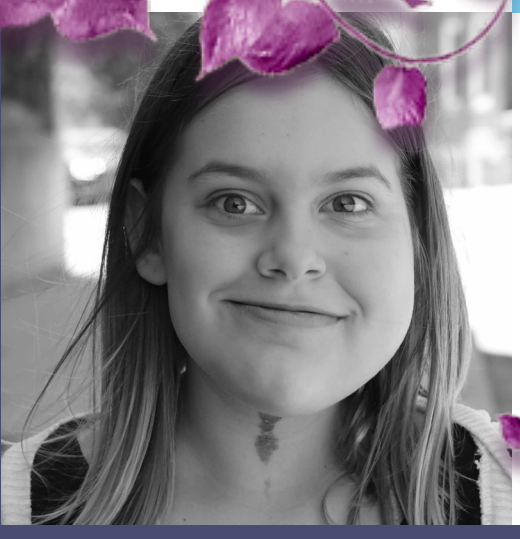
FibroAdipose Vascular Anomaly

CLOVES syndrome

Muscular HH

CLAPO syndrome

Facial Infiltrating Lipomatosis



Macrodactyly

FibroAdipose hyperplasia or Overgrowth

HemiHyperplasia-Multiple Lipomatosis

Visit **understandingpros.com** to learn more.

Patient images from top to bottom: MCAP/M-CM; CLOVES syndrome; MCAP/M-CM; CLOVES syndrome; CLOVES syndrome.

UnderstandingPROS

Different conditions, **one root cause**

Many abnormal growth and vascular malformations, including lymphatic conditions, are caused by PIK3CA mutations, meaning that part of the DNA known as the "PIK3CA gene" is abnormal and isn't working correctly. Because these disorders share this common gene mutation, they were grouped together under the name PIK3CA-Related Overgrowth Spectrum, **or "PROS" for short.**

You or someone you care for may have been diagnosed recently with one of the following conditions, which may be associated with PIK3CA mutations:

KTS	(**K**lippel-**T**renaunay **S**yndrome)
CLOVES syndrome	(**C**ongenital **L**ipomatous **O**vergrowth, **V**ascular malformations, **E**pidermal nevi, **S**coliosis/skeletal and spinal)
ILM	(**I**solated **L**ymphatic **M**alformation)
MCAP or **M–CM**	(**M**egalencephaly-**C**apillary **M**alformation)
HME	(**H**emi**M**egal**E**ncephaly)/**DMEG** (**D**ysplastic **MEG**alencephaly)/**Focal cortical dysplasia type II**
HHML	(**H**emi**H**yperplasia-**M**ultiple **L**ipomatosis)
FIL	(**F**acial **I**nfiltrating **L**ipomatosis)
FAVA	(**F**ibro**A**dipose **V**ascular **A**nomaly)
Macrodactyly	
Muscular HH	(**H**emi**H**yperplasia)
FAO	(**F**ibro**A**dipose hyperplasia or **O**vergrowth)
CLAPO syndrome	(**C**apillary malformation of the lower lip, **L**ymphatic malformation of the face and neck, **A**symmetry of the face and limbs, and **P**artial or generalized **O**vergrowth)
Epidermal nevus, benign lichenoid keratosis, or **seborrheic keratosis**	

Other conditions may be identified and characterized as PROS.
Talk to your doctor to find out if your condition is a PROS condition

Due to the nature of PIK3CA mutations in PROS, a positive mutation status may be difficult to detect. This is because the PIK3CA mutation may not affect all cells in your body. Your doctor may call this mosaicism.

Common features of **PROS conditions**

- PROS conditions can look very different from each other in **size, shape, and type of growth or malformation**
- They also may occur in different parts of the body and **cause a wide variety of signs and symptoms that can worsen over time**
- No matter what the symptom, it's important to **keep your health care team updated** on the status of your condition

These conditions can include diverse features and can affect each person differently.

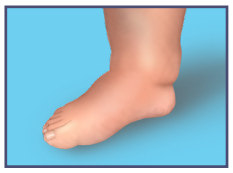
Some common features driven by the PIK3CA mutation include:

Enlarged digits:

the appearance of one or more unusually large fingers or toes

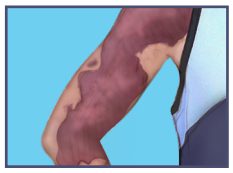
Scoliosis:

a sideways curvature of the spine, which in a PROS condition is caused by an abnormal growth



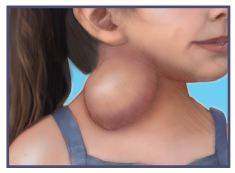
Abnormal growth:

when certain parts of the body grow too much or too little. This may occur in muscles, fatty tissue (like a lipoma), organs, and the spine or skeleton. It may also affect the surface of the skin



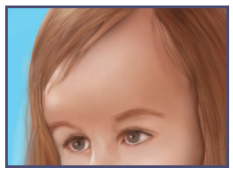
Vascular malformations:

when vessels like veins, arteries, and capillaries grow in abnormal ways



Lymphatic malformations:

when vessels that contain clear fluid, called lymph, grow abnormally



Enlarged head:

when brain complications, such as hydrocephalus (fluid in the brain) or seizures, cause overgrowth in the brain that may also result in neurological issues. These conditions are particularly seen in MCAP/M-CM and HME/DMEG/focal cortical dysplasia type II

Here's how PIK3CA mutations can cause PROS conditions

- **The PIK3CA gene gives instructions to the cells in your body** to make phosphoinositide 3-kinase, or "PI3K" for short. This PI3K protein is involved in the life cycle of the cell and making sure cells grow, develop, live, and die in the right way
- **When the PIK3CA gene is mutated, the instructions that the gene gives for making the PI3K protein are damaged**
- The PI3K protein does not work the way it should, causing cells to grow and divide abnormally, **which results in the features of these PROS conditions**
- The mutation first occurs during embryo development, or the early stages of pregnancy. **This means that it is not passed down from parents to children**

Diagnosing PROS

It is important to know if a PIK3CA mutation is the cause of your abnormal growth, vascular condition, or lymphatic condition. Knowing its cause can give doctors a more complete picture of the condition and help them make decisions about tests, follow-up procedures, and management that may be part of your care plan.

Watch this **interactive video** to learn about the connection between the PIK3CA mutation and your specific PROS condition.

Several steps may be needed to diagnose PROS. These could include:

Need help finding a diagnosis? These **resources** could help.

Management of PROS is limited and may be based on symptoms rather than its root cause—PIK3CA mutations

The way your doctor manages your PROS symptoms can vary depending on which PROS condition you have been diagnosed with and how it presents (appears) in your body. You will work with your health care team to determine which approach makes sense to you based on your symptoms and goals. You may need the care of a multidisciplinary team to manage all symptoms and potential complications.

Connect with one of these **support groups** to help you navigate your PROS condition

K-T Support Group www.k-t.org

Find resources and support for people with Klippel-Trenaunay Syndrome and related conditions.

CLOVES Syndrome Community www.clovessyndrome.org

Find resources, educational materials, a patient-led research network, and support for people with CLOVES syndrome and their families.

Lymphangiomatosis & Gorham's Disease Alliance www.lgdalliance.org

The mission of the LGDA is to bring hope to and improve the quality of life of patients with generalized lymphatic anomaly (GLA) (previously known as lymphangiomatosis), kaposiform lymphangiomatosis (KLA), Gorham-Stout disease (GSD), and central conducting lymphatic anomaly (CCLA) (previously known as lymphangiectasia), by providing support to members of the patient community and their families; education for the community, professionals, and the general public; and supporting research that will improve understanding of these diseases and establish best practices for their diagnosis and management.

M-CM Network www.m-cm.net

Find information, resources, and patient-centered research for people with M-CM and their families.

WonderFIL smiles www.wonderfilsmiles.com

WonderFIL smiles is a global community for those affected by Facial Infiltrating Lipomatosis (FIL). Our goal is to support people with FIL and their families, and to empower them with information, knowledge, and connectivity.

Project FAVA www.projectfava.org

Project FAVA is a 501(c)(3) nonprofit patient advocacy group that promotes awareness of fibroadipose vascular anomalies; educates patients, their families, and the global community; and provides helpful resources to those with FAVA.

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Let's get to the **root of PROS**

Many **conditions caused by PIK3CA mutations** were grouped together under the name PIK3CA-Related Overgrowth Spectrum, or **"PROS" for short**

Even people with the **same PROS condition** may experience **differences in manifestations, symptoms, and severity**

Management of PROS is limited and may be **based on symptoms rather than its root cause—PIK3CA mutations**

It is important to know if a **PIK3CA mutation is the cause** of your abnormal growth, vascular condition, or lymphatic condition

Understanding your PROS diagnosis and its cause can help you and your doctor **create a care plan**

To learn more about PROS, talk to your doctor and visit **understandingpros.com**.

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