I have a SOMATIC mutation in *PIK3CA*

Do you know what she means?

NO PROBLEM!

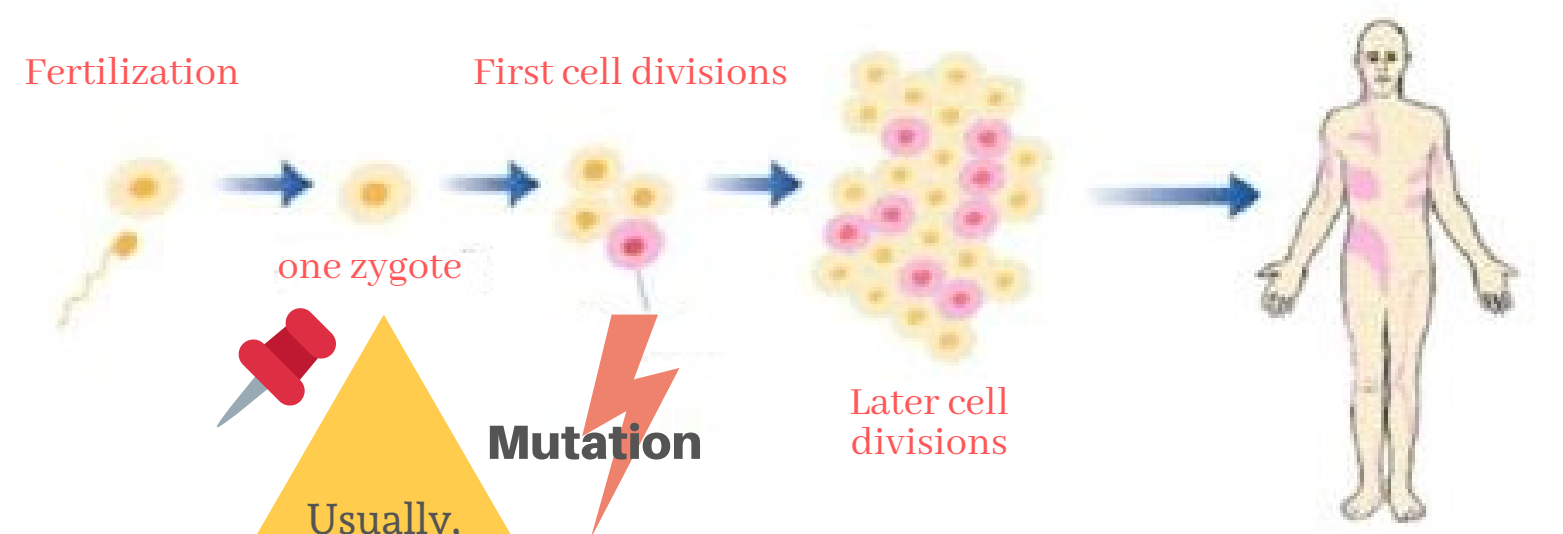
WE WILL BE YOUR TEACHERS

A somatic mutation does not involve the genetic material (DNA) of ALL the cells that make up an individual, but only those originated from the first mutated cell.

Together, normal and mutated cells form a sort of MOSAIC.

Somatic mutations occur after conception (postzygotic).

What is a SOMATIC mutation?



Usually, the mutation found in PROS **cannot** be identified in theblood but with a **biopsy** from the overgrown tissue

What is *PIK3CA*?

PIK3CA is a very important **gene**. It contains the instructions for making a piece of an enzyme (**PI3K**) which plays a fundamental role in cell growth and division (proliferation), movement (migration) of cells, production of new proteins, transport of materials within cells and cell survival.

The PROS spectrum

2012
was a very important year. Thanks to a technique called **Next Generation Sequencing (NGS)**, scientists found out that several diseases were all due to somatic mutations in the PIK3CA gene.

Klippel-Trenaunay
CLOVES
Macrodactyly
M-CM
Hemimegalencephaly
Facial Infiltrating Lipomatosis
... and others

→ **PROS**

Some individuals with PROS have localized overgrowth, while in others various body parts and organs are involved.
This depends on:

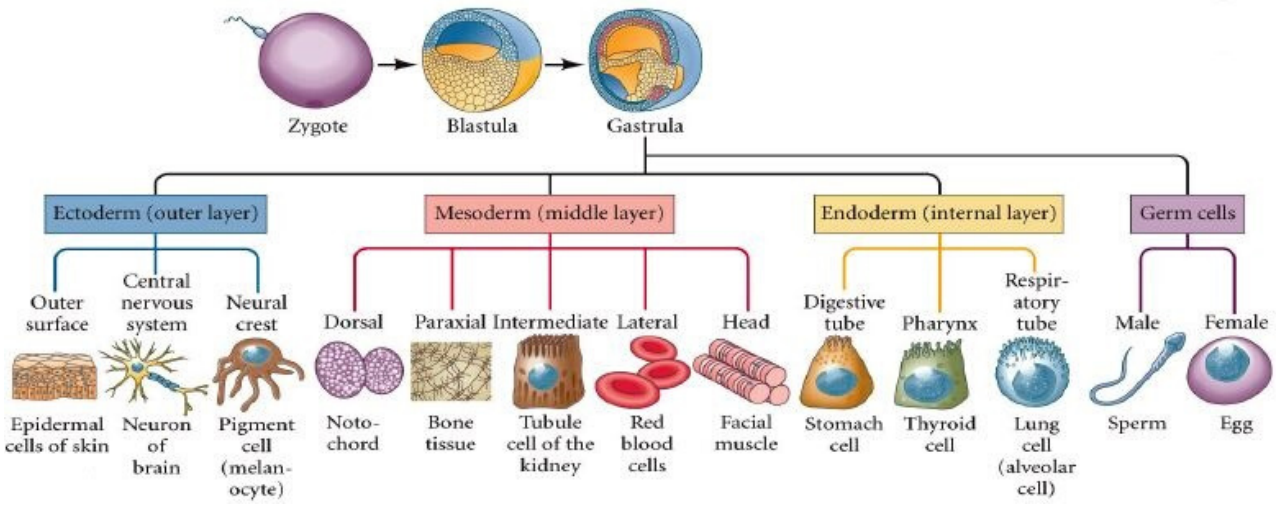
- **when** the mutation occurred in the very first cell
- **where** it occurred
- **the type of mutation**

Why are the symptoms so different?

the first stages of development

Cleavage: rapid cell divisions divide the cytoplasm of the fertilized egg into numerous cells (blastomers)

Gastrulation: cells formed during cleavage move in a coordinated fashion and rearrange themselves. Gastrulation is the process by which the three layers of the embryo are formed (ectoderm, mesoderm, and endoderm), which then give rise to every organ and tissue in the body



Possible SIGNS and SYMPTOMS

BRAIN

- Brain overgrowth (megalencephaly)
- Excessive collection of cerebrospinal fluid (hydrocephalus)
- Enlarged brain ventricles (ventriculomegaly)
- An abnormally large head size (macrocephaly), as a consequence of megalencephaly and/or hydrocephalus
- One side of the brain larger than the other (asymmetry) or one side of the brain larger than the other and malformed (hemimegalencephaly)
- Herniation of a portion of the cerebellum (cerebellar tonsillar herniation), that dips down into the upper spinal canal. This can lead to symptoms including headache, balance problems, difficulty swallowing, muscle weakness, neck pain, hearing loss, seizures, etc.

FUNCTIONAL PROBLEMS

- Psychomotor impairment
- Cognitive impairment not associated with decline
- Seizures

GROWTH

- Overgrowth of one or more limbs
- Overgrowth of other body parts
- Internal organ overgrowth
- Delayed bone age

HANDS and FEET

- Extra fingers or toes (polydactyly)
- Fusion of the skin between toes or fingers (syndactyly)
- Overgrowth of one or more toes or fingers (macrodactyly)
- Wide sandal gap

VASCULAR MALFORMATIONS

- Capillary malformations
- Combined lymphatic and vascular anomalies & arteriovenous malformations
- Abnormal lymphatic channels

CONNECTIVE TISSUE

- Abnormality in tendons, bones and cartilage
- Loose or lax joints
- Joint Instability and possible joint dislocation
- Soft and loose skin

HEART

- *In a small percentage of individuals*: increased risk of heart defects present at birth (congenital) and irregular heartbeat

LUNGS

- Respiratory issues

This list is not all inclusive and should cause no fear as some signs and symptoms are extremely rare.

What about the management of PROS?

Regardless of the location of signs and symptoms, management of PROS must be:

- ongoing
- multidisciplinary
- carried out by a clinical site with experience in this kind of rare diseases

The number and type of professionals involved in the management varies from case to case, depending on the signs and symptoms and on the parts of the body/organs involved.

This informational brochure on PROS, geared for adolescents and adults, is a joint project of **CLOVES Syndrome Community** and of the **Italian Macrodatctyly and PROS Association**

Both organizations are committed to:

- mutual aid
- support and information for families
- support for research
- collaboration with clinical centers

YOU CAN FIND OUT MORE on our websites

https://clovessyndrome.org/
http://www.associazione-nazionale-macrodattilia.org