

# PIK3CA-RELATED OVERGROWTH SPECTRUM (PROS)

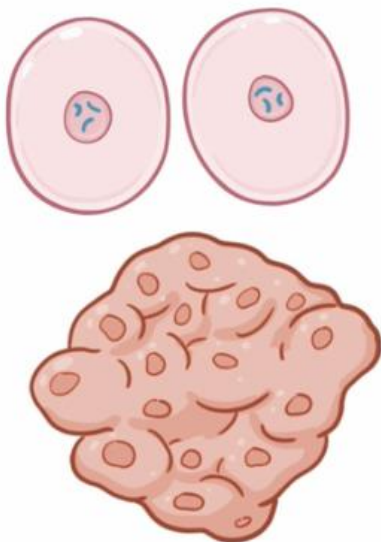
\* GROUP of DISORDERS



\* CAUSED by MUTATIONS in the PIK3CA GENE

↳ plays role in regulating cell growth and division

\* MUTATIONS can RESULT in UNCONTROLLED GROWTH of AFFECTED TISSUES



## CLOVES SYNDROME

**C**ONGENITAL

**L**IPOMATOUS

**O**VERGROWTH

**V**ASCULAR MALFORMATIONS

\* CAPILLARY, VENOUS, and/or LYMPHATIC MALFORMATIONS and/or COMBINATIONS of ALL of THOSE

**E**PIDERMAL NEVI

\* BROWN BUMPY BIRTHMARKS

**S**COLIOSIS, **S**KELETAL or **S**PINAL ABNORMALITIES

\* FATTY SWELLINGS on TRUNK  
\* OVERGROWTH of ARMS, LEGS  
\* ASYMMETRIC ENLARGEMENT



# SIGNS & SYMPTOMS

\* MANY SUBTYPES of PROS BASED on AREAS and TISSUES AFFECTED

## CLAPO SYNDROME

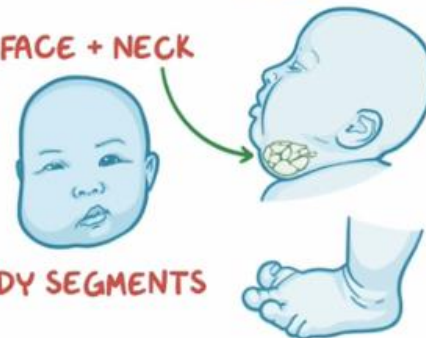
**C**APILLARY MALFORMATION in LOWER LIP

**L**YMPHATIC MALFORMATION in FACE + NECK

**A**SYMMETRY of FACE + LIMBS

**P**ARTIAL or GENERALIZED

**O**VERGROWTH of 1 or MORE BODY SEGMENTS



## KLIPPEL-TRENAUNAY SYNDROME (KTS)

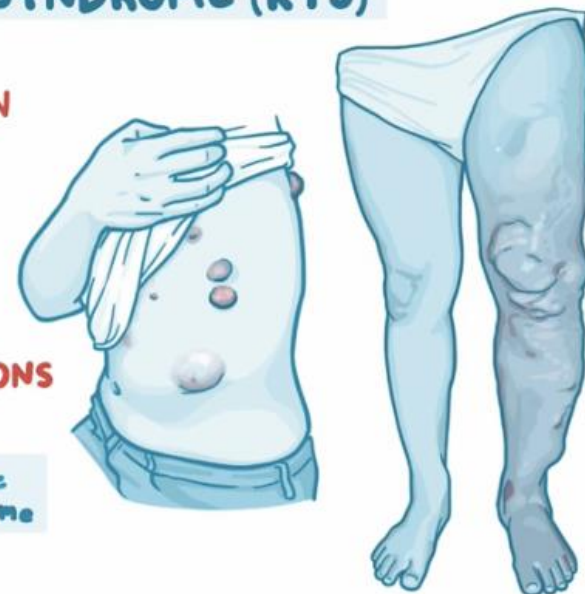
✓ CAPILLARY MALFORMATION

✓ ABNORMAL VEINS

✓ LIMB OVERGROWTH

+ LYMPHATIC MALFORMATIONS

\* depending on distribution, some overlap with CLOVES Syndrome



## DIFFUSE CAPILLARY MALFORMATION with OVERGROWTH (DCMO)

- ✓ **CAPILLARY MALFORMATION** over a **LARGE AREA** with **ACCOMPANYING OVERGROWTH**

\* **OFTEN INCREASED SIZE** of **INVOLVED LIMB** due to **INCREASED MUSCLE** and **BONE**

- ✗ **DOES NOT INCLUDE** **VENOUS** or **LYMPHATIC MALFORMATION**



## FIBRO-ADIPOSE VASCULAR ANOMALY (FAVA)

- ✓ **DEVELOPMENT** of a **MASS** of **BLOOD VESSELS** and **FATTY TISSUE** **WITHIN MUSCLES**

\* **PAINFUL**

\* **REDUCED MOBILITY**



## FIBROADIPOSE HYPERPLASIA (FAH)

- ✓ **OVERGROWTH** of **CONNECTIVE TISSUES**

## HEMIHYPERPLASIA MULTIPLE LIPOMATOSIS SYNDROME (HHML)

- ✓ **MULTIPLE FATTY GROWTHS**

+ **HEMIHYPERPLASIA**

↳ **ABNORMAL ENLARGEMENT** of **ONE LIMB** or **SIDE** of the **BODY**

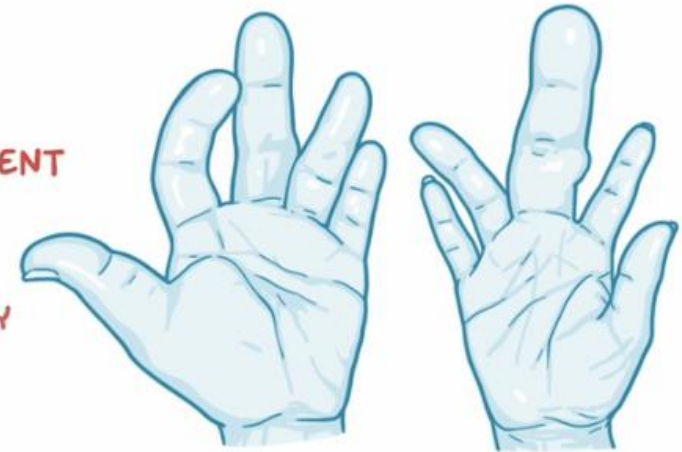


## MACRODACTYLY

- ✓ **ISOLATED ENLARGEMENT** of a **DIGIT** or **DIGITS**

\* **PAINFUL**

\* **REDUCED MOBILITY** or **DEXTERITY**



## MUSCULAR HEMIHYPERTROPHY (MH)

- ✓ **OVERGROWTH** of **MUSCLES** on **ONE SIDE** of the **BODY**

\* may overlap with **HHML**, **FAH**, or **MACRODACTYLY**

- ✓ **USUALLY PRESENT** at **BIRTH**



## LIPOMATOSIS of NERVE (LON)

- ✓ **OVERGROWTH** of **FATTY TISSUE** around **NERVE BUNDLES**  
↳ **PAIN** or **NUMBNESS** (**NEUROPATHY**)

- ✓ **MOST COMMONLY AFFECTS** the **MEDIAN NERVE**  
↳ **COMPLICATIONS** like **CARPAL TUNNEL SYNDROME**



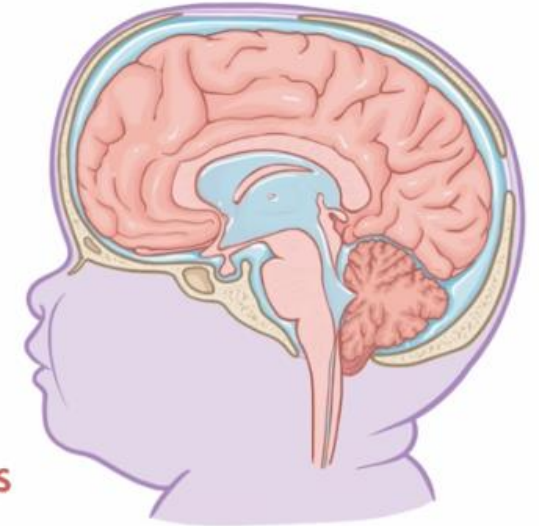
## FACIAL INFILTRATING LIPOMATOSIS (FIL)

- ✓ **OVERGROWTH** of **BONE** and **FATTY TISSUE** in the **FACE**
- ✓ **ASYMMETRICAL FACIAL ENLARGEMENT**
- ✓ **TONGUE** and **TEETH ENLARGEMENT**
- + **RARELY: NERVE TUMORS**



## SUBTYPES that AFFECT the BRAIN

- ✓ **OVERGROWTH** of **BRAIN** can **COMPRESS DRAINAGE** of **CEREBROSPINAL FLUID**  
↓  
**HERNIATION** or **HYDROCEPHALUS**  
↳ **SEIZURES**  
↳ **ABNORMAL MUSCLE TONE**  
↳ **VARIOUS COGNITIVE** and **BEHAVIORAL DISABILITIES**



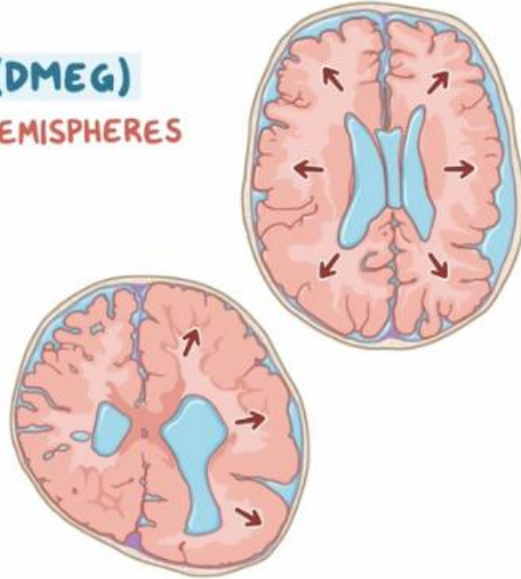
## SUBTYPES that AFFECT the BRAIN

### DYSPLASTIC MEGALENCEPHALY (DMEG)

- \* ENLARGEMENT of BOTH CEREBRAL HEMISPHERES

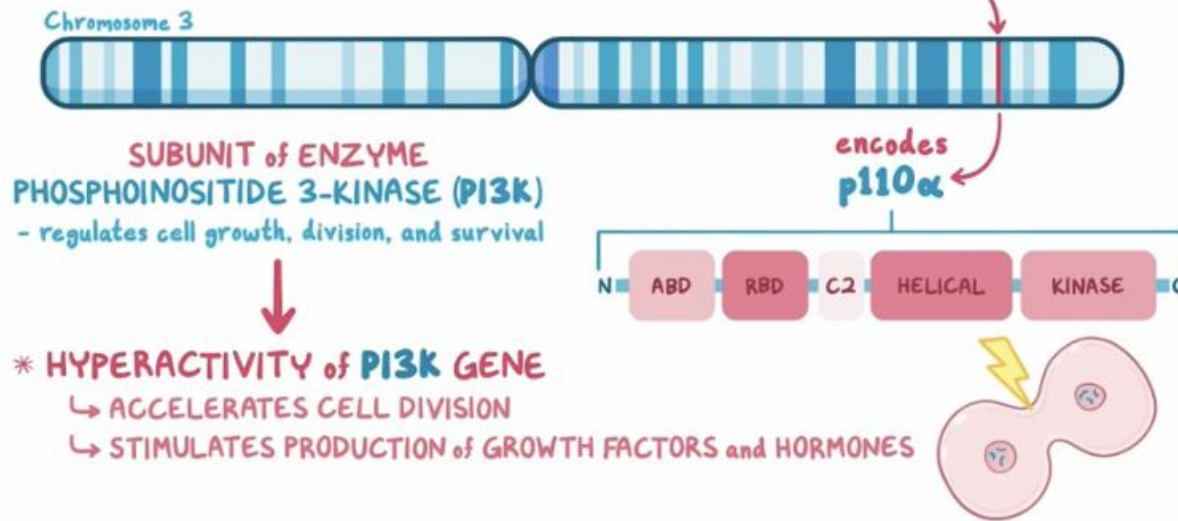
### HEMIMEGALENCEPHALY (HME)

- \* ENLARGEMENT of ONE SIDE of BRAIN
  - ↳ ASYMMETRICAL ENLARGEMENT
  - ↳ SEVERE SEIZURES



## PATHOLOGY

- \* due to SOMATIC (NON-INHERITED) MUTATIONS in PIK3CA GENE



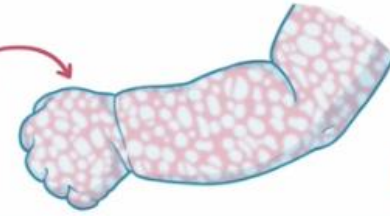
## SUBTYPES that AFFECT the BRAIN

### MEGALENCEPHALY-CAPILLARY MALFORMATION (MCAP) SYNDROME

- \* BRAIN ENLARGEMENT
- \* SKIN VASCULAR CHANGES (capillary malformations)

lacy, net-like pattern

CUTIS MARMORATA TELANGIECTATICA CONGENITA (CMTC)



- \* ABNORMAL BRAIN DEVELOPMENT → GROWTH HORMONE DEFICIENCY
  - ↳ may cause low blood sugar levels

## DIAGNOSIS

- \* CAREFUL EXAM OFTEN SUFFICIENT

### DEFINITIVE DIAGNOSIS of PROS:

- \* BIOPSY of AFFECTED TISSUE
- \* TESTING for PIK3CA GENE MUTATIONS

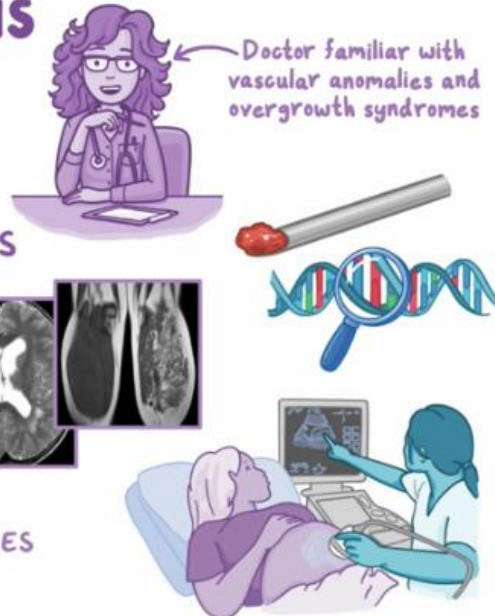
### \* IMAGING STUDIES

- BONY OVERGROWTH
- BRAIN ABNORMALITIES
- OTHER INTERNAL LESIONS



### \* PRENATAL ULTRASOUND

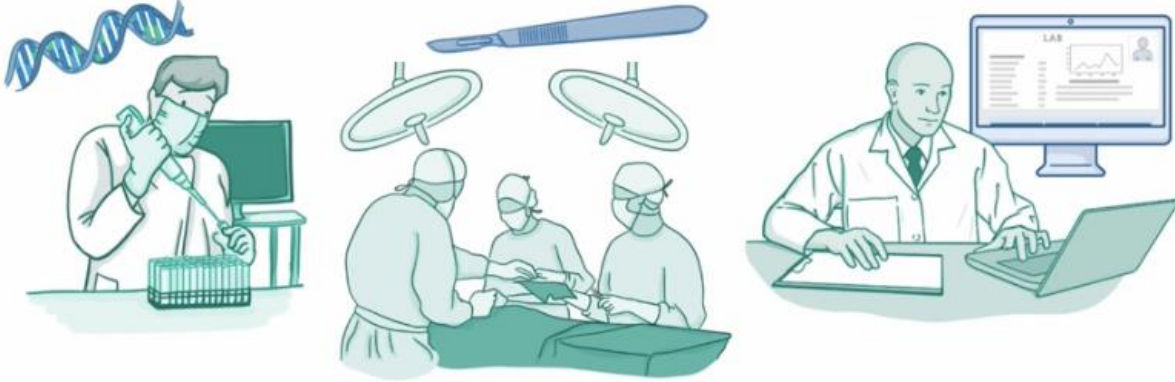
- SOMETIMES DETECT GROWTH ABNORMALITIES



# TREATMENT

\* MAJORITY would BENEFIT from INTERDISCIPLINARY EVALUATION by MEDICAL PROVIDERS FAMILIAR with these DIAGNOSES

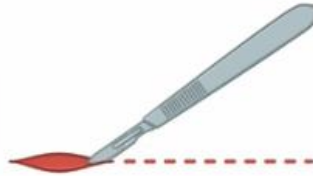
\* DEPENDS on SUBTYPE and SYMPTOM SEVERITY



SIMPLE LOCALIZED LESIONS



SURGICAL EXCISION



LARGER LESIONS



DEBULKING



IF/WHEN TISSUE REGROWS

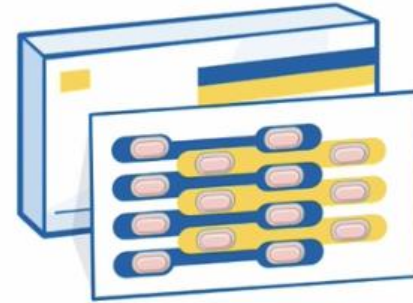


REPEAT SURGERIES



# EXTENSIVE or INVOLVED LESIONS:

\* USUALLY TREATED with MEDICINES DESIGNED to SLOW DOWN or TURN OFF the HYPERACTIVITY of the PI3K and DOWNSTREAM PATHWAY

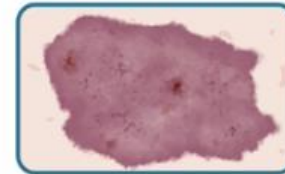


**ALPELISIB**

APPROVED in 2022 by the FDA for SEVERE CASES in ADULTS and CHILDREN 2+



SUPERFICIAL VASCULAR MALFORMATIONS



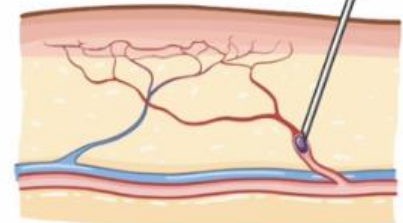
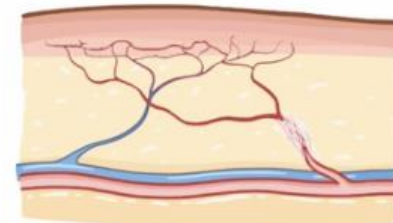
LASER ABLATION

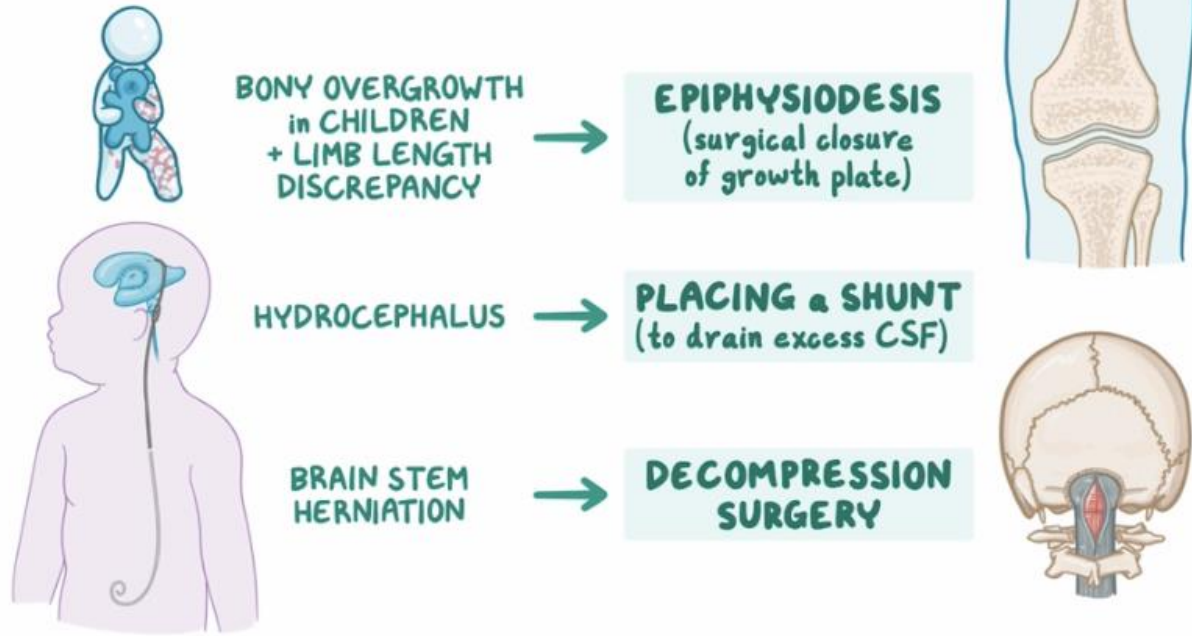
- LIGHTEN COLOR
- STOP LEAKING or BLEEDING



SCLEROTHERAPY

EMBOLIZATION





For INDIVIDUALS with  
MOTOR and/or INTELLECTUAL  
DISABILITIES related to PROS

**PHYSICAL,  
OCCUPATIONAL, and  
SPEECH THERAPIES**



## PIK3CA-RELATED OVERGROWTH SPECTRUM (PROS)

\* GROUP of RARE GENETIC DISORDERS  
CAUSED by MUTATIONS in the  
**PIK3CA GENE**



**SYMPTOMS**  
UNCONTROLLED  
GROWTH of  
AFFECTED TISSUES

- MUSCLE
- BONE
- NERVE
- BRAIN
- BLOOD and  
LYMPHATIC  
VESSELS



### DIAGNOSIS

- TISSUE BIOPSY
- GENETIC TESTING



### TREATMENT

- OFTEN REQUIRES a  
MULTIDISCIPLINARY  
APPROACH

