Les duplications du pouce sont des fentes radiales

Thumb duplications are radial clefts

- S. GUERO
- Institut de la Main
- Hôpital Necker Enfants Malades
- PARIS
Handplate formation

- The thumb is the last to form
- 4-2-5-3-1
The thumb: molecular development

- The thumb is the last to form: 4, 2, 5, 3 and 1
  - higher risk of developmental disruption
  - OMIM: >229 entries or syndromes with thumb anomalies

Review of the Molecular Development of the Thumb: Digit Primera

Kerby C. Oberg MD, PhD
Thumb duplication (radial polydactyly)

- Unilateral, sporadic, isolated
Wassel’s classification(s) for thumb duplications

- Radiologic study
- Seven types
- Simple but...
- ...Inexact

Figure 4: The Wassel classification for radial polydactyly.
Thumb duplication

- Triphalangeal thumb
Unusual thumb duplication: triphalangism

Thumb duplication or preaxial polydactyly?
Preaxial polydactyly

• Five-fingered hand: non opposable thumb, distal epiphysis
Radio-ulnar differentiation

- Signaling center: ZPA
  - On the posterior (ulnar) part of the limb bud
- Morphogene: Sonic hedgehog
  - SHH loss of function: ulnar club hand
- Gli3 is the transcription factor of the Shh pathway
- Gradient of Gli3 activated (GLI3A) from ulnar to radial
- Gli3R/Gli3A ratio determines digit number and identity
  - Gli3 mutations cause pre and post axial polydactyly, Pallister-Hall syndrome and Greig cephalopolysyndactyly
Misexpression of the Shh gene
Disorders in the ZRS

Chromosome 7: hedgehog gene on 7q36

Mutations in:
- Human
- Mouse
- Cat
- Chicken

Isolated triphalangeal thumb
Preaxial polydactyly type 2
Postaxial polydactyly type A
Triphalangeal thumb polysyndactyly

Polysyndactyly HAAS type
Duplication of the ZRS
Two distinct entities

• **Thumb duplication**
  • Frequent
  • Unilateral
  • No family history
  • No mutation identified
  • Triphalangism

• **Preaxial polydactyly**
  • Rare
  • Bilateral
  • Family history
  • Mutations identified on ZRS
  • Cardiac anomalies
  • Triphalangism
  • Delta phalanx
  • Great toe duplication
Rotterdam classification(s) for preaxial polydactyly

• More ambitious
• Complex
• Forgot five-fingered hands
Preaxial polydactyly

• Geneticists: four types of preaxial polydactyly:
  
  I. Thumb polydactyly (6 types for Flatt)
  II. Triphalangeal thumb
      • Opposable
      • Normal proximal epiphysis
  III. Five-fingered hand
      • Non opposable
      • Epiphysis is at the metacarpal head
  IV. Polysyndactyly

• Sporadic thumb duplication = 90%
• Familial preaxial polydactyly = 10 %
Median cleft Hypothesis:

- Critical zone
  - Disruption of the central AER?
    - *DLX5* and *DLX6* products are critical for maintenance of the proliferation of the central AER (Robledo, 2002)

Thumb duplication: hypothesis

- Radial cleft
  - Radial AER disruption
  - The thumb is the last to form
AER disruption

- Central = cleft or central polydactyly
- Radial = thumb duplication
- Global = transverse arrest...
  - ...+ thumb duplication
Conclusions

• True duplications are similar to central polydactylies
  • Radial AER failure?

• Classifications on radial polydactyly are uncomplete
  • Triphangeal thumb are frequent
  • Bilateral, syndromic form are rare and are radio-ulnar axis failures

• Helpful for parental information
  • It’s a split thumb
  • None of the thumbs is normal