Treatment of 13q Retinoblastoma IA/Ivit era

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No financial declarations

Off label use of Melphalan, Carboplatin, Topotecan

Summary

- Problem:
- 13q=5-?15% of all Rb
- No survivors during my fellowship
  - Because of many comorbidities
- Tolerate systemic chemotherapy poorly

- This study:
- MSKCC patients
  - IA/Ivit (lower doses)
  - 13/14 patients survived (Sepsis w Mets)
  - KM Eye Survival 83%
  - Few side effects IA
    - 1 F/N. 1 Transfusion platelets
  - Systemic chemo: More side effects
  - Ivit: More side effects (ERG)
- Conclusion:

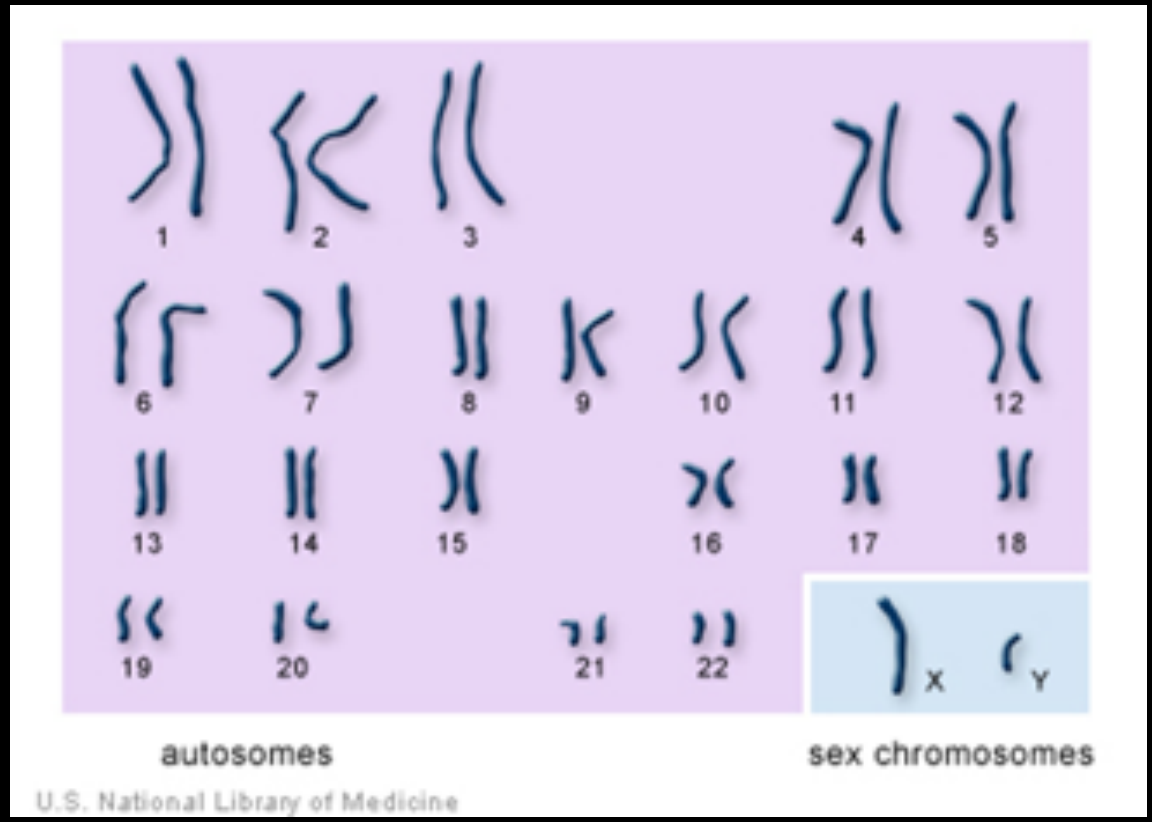
  With IA/Ivit most lives, eyes and vision saved but still more sensitive to chemotherapy

This Presentation: Rb with Deletion Syndrome

- What's Deletion Syndrome?

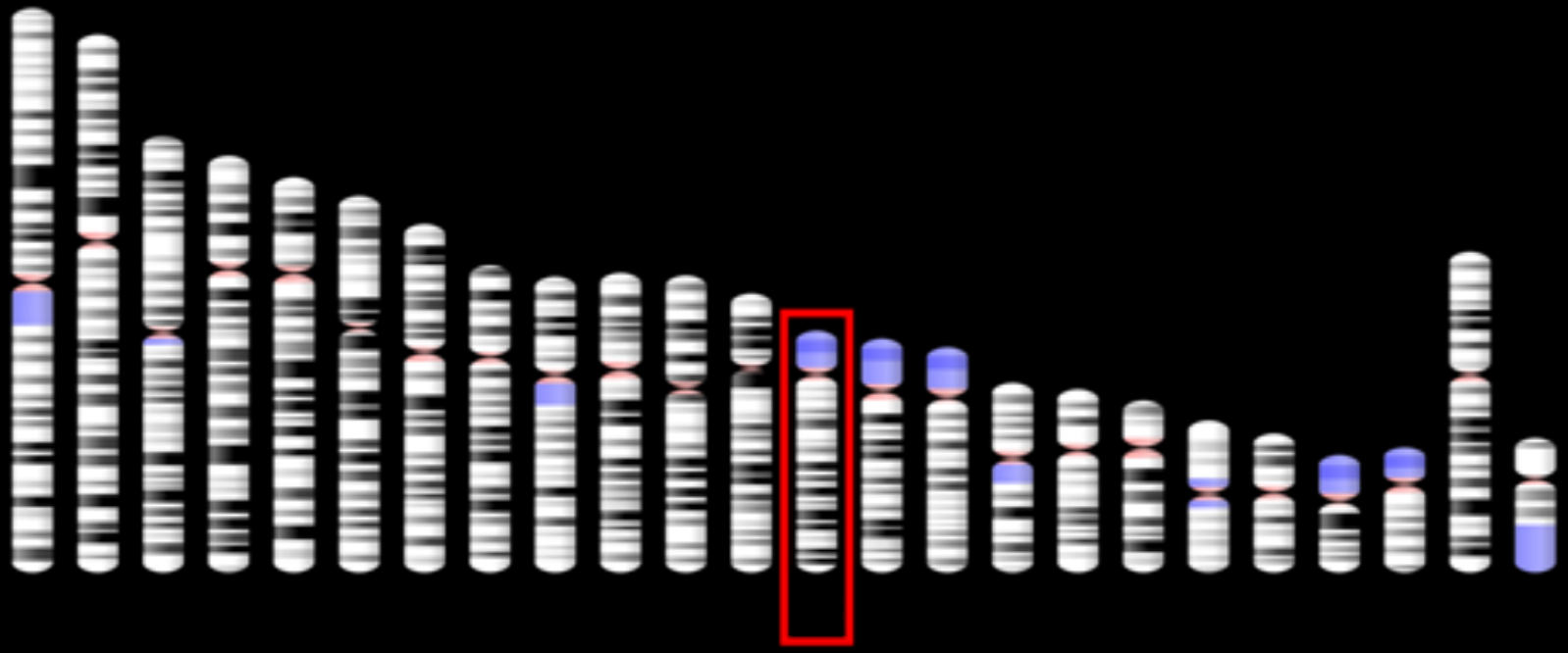
Quick Review

- Humans have 23 paired chromosomes



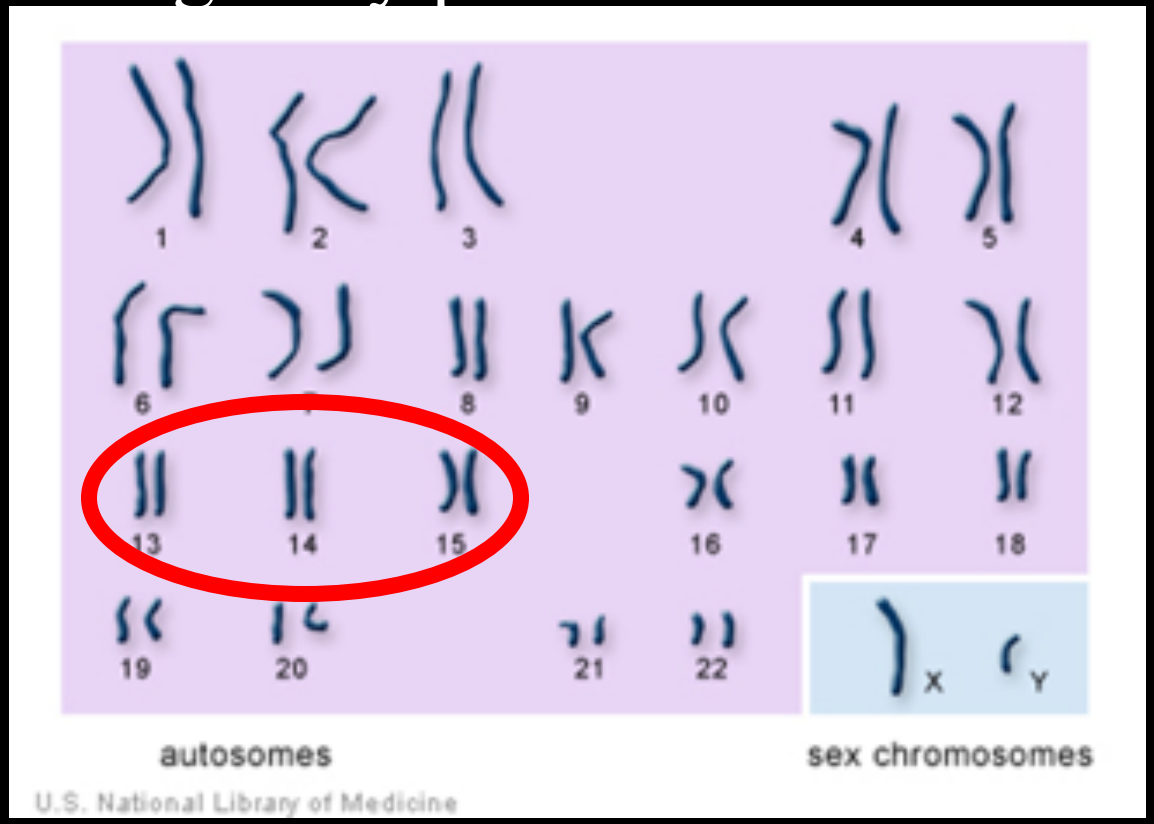
Quick Review

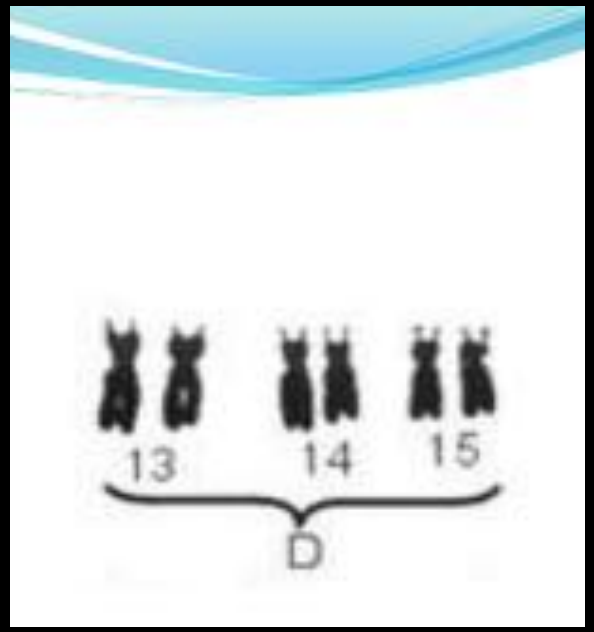
- Humans have 23 paired chromosomes
- Numbered by size



Chromosome 13

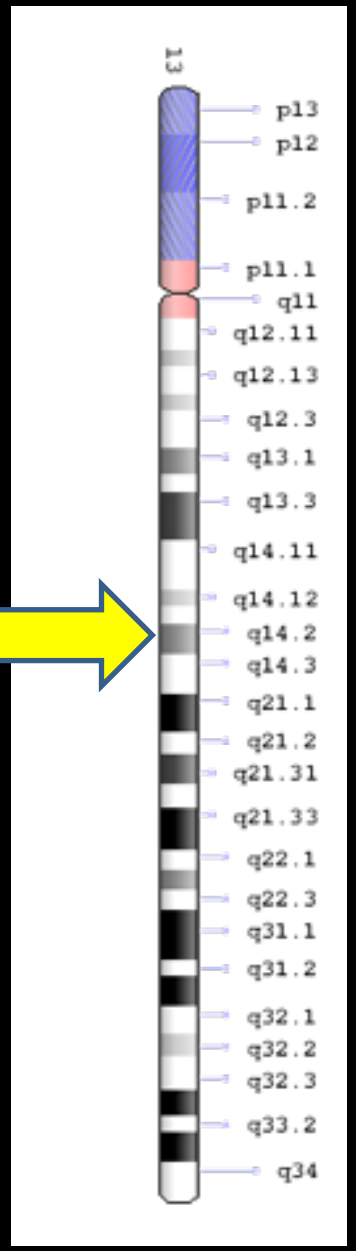
- Chromosome 13 is the largest acrocentric human chromosome
- Originally part of the “D” Chromosome group





Chromosome 13

- 929 Genes
- One of the lowest gene density of all chromosomes
- Bands identified, numbered
- Gene for Rb is on long arm (“q”) in the 1,4 band
  - Band: Stain metaphase prep with Giemsa dye=G Banding
    - Stains regions rich in Adenine (A) and Thymine (T)



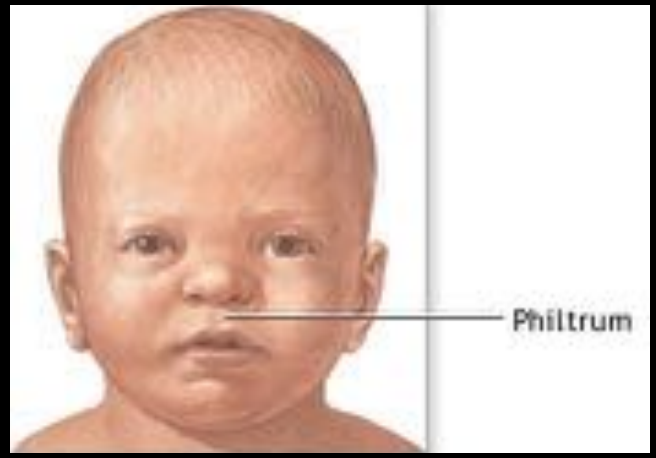
Deletion Syndrome (Dq-)

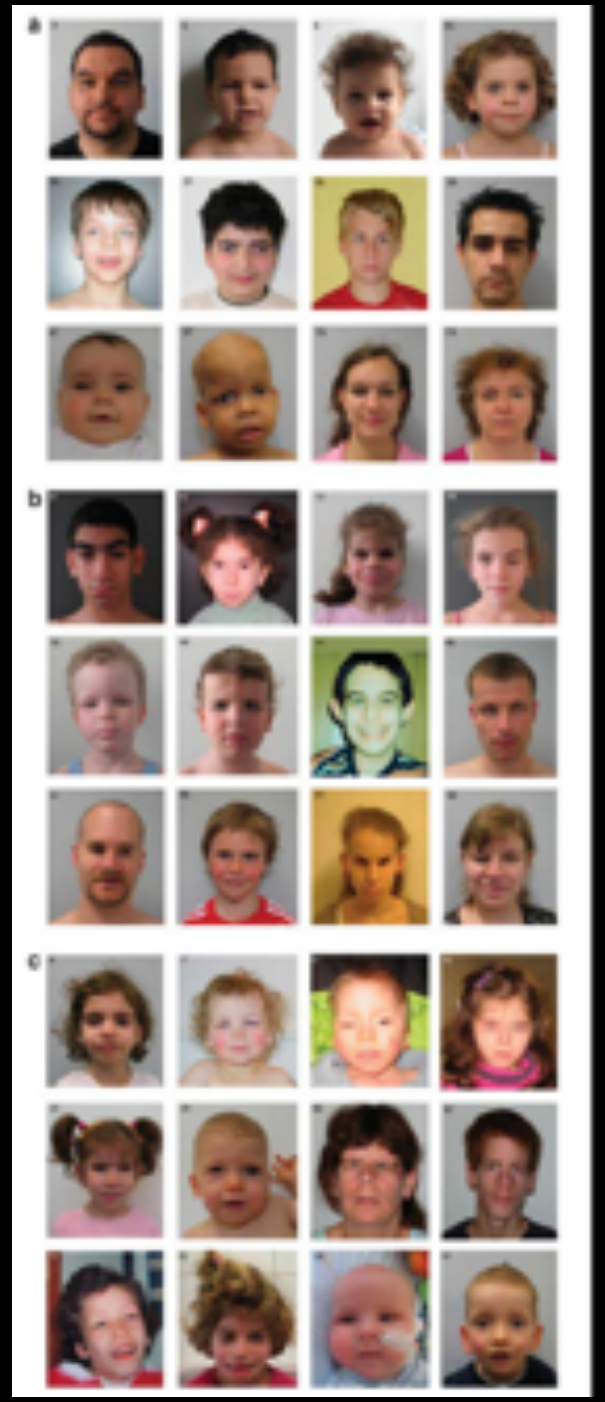
- Deletion involving Rb gene (q14) PLUS adjacent genes
- D Chromosomes (13,14,15) Missing part (-) of long arm (q-)
- 5-15% of retinoblastoma children
- Not inherited
- More often unilateral compared to non deletion Rb
- Depending on the size of the deletion many, many other systemic issues (some life threatening)

Deletion syndrome (?6%)

- Small deletion:
  - Within 13q14
  - Macrocephaly
  - Tall stature
  - Obesity
  - Motor/speech delay
- Medium deletion:
  - 13q12,3q21,3
  - Facial features,Mild-moderate psychomotor delay
  - Short stature
  - Microcephaly
- Large deletion:
  - 13Q12Q31.2
  - Craniofacial dysmorphism
  - Short ststure
  - Microcephaly
  - Mild-severe psychomotor delay
  - Hypotonia
  - Constipation
  - Feeding problems

- Dysmorphic features
  - High and broad forehead
  - Short nose
  - Prominent philtrum
  - Thick, everted lower lip
  - Anteverted earlobes





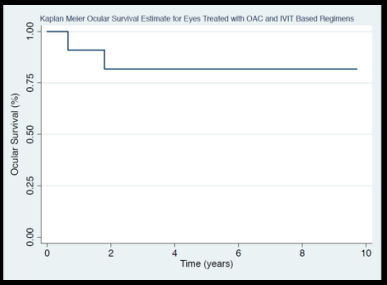
Miller D et al E J Human Genetics 19:947 (2011)

MSKCC Group

- 14 patients
- 7 Unilateral / 7 Bilateral
- 8 Boys/ 6 Girls
- Age Dx: 0.4-24 months
- Birth: 4/14 LBW
- No FH Rb
- F/U: 3.7 yrs mean

Results

- Patient survival: 13/14 (Sepsis with metastasis)
- Ocular Survival: KM: 83%/2 years (1 Bilateral enucleation)
- Heme toxicity: 14 Gr 3, 3 Gr. 4 – One platelet transfusion/ 1 Neupogen
- ERG:
  - IA alone: ERG Better 59%/ ERG Worse 18% ERG Same 23%
  - Ivit Melphalan: 29% worse (>25uV)
  - Ivit Topotecan: None worse



Summary

- Rb Deletion syndrome challenging to manage/ comorbidity
- Modern management with OAC and Intravitreal based regimes give less chemotherapy (<1/10) and shorter time (3 vs 6 months) with higher cure rate than past and no radiation
- Ocular survival 83%
- Patient survival 83%
- No second cancers
- Systemic chemotherapy associated with more neutropenia