FSHD Type 2: Differences and Similarities to FSHD1

Rabi Tawil, MD

4th FSHD Patient Day

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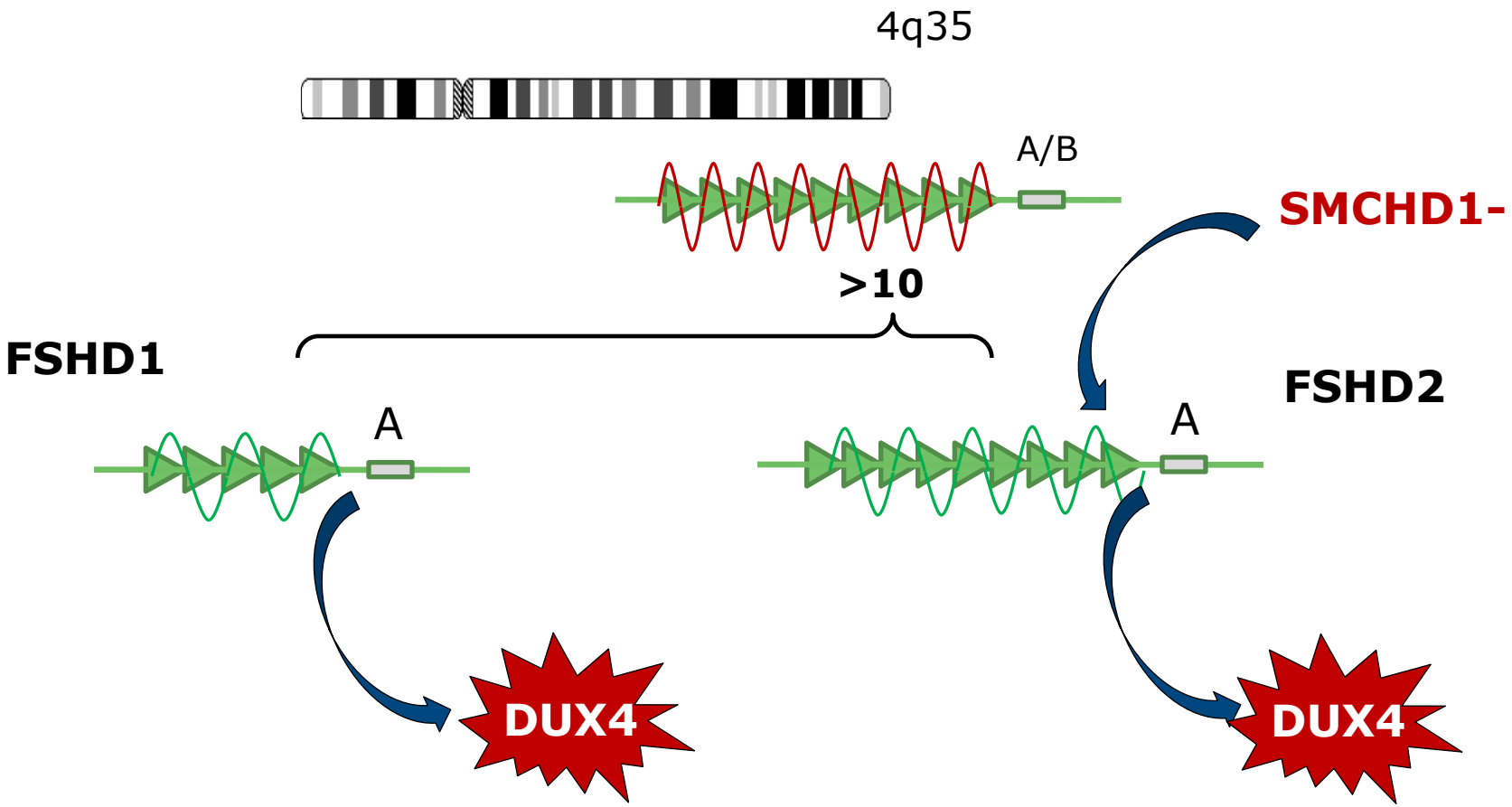
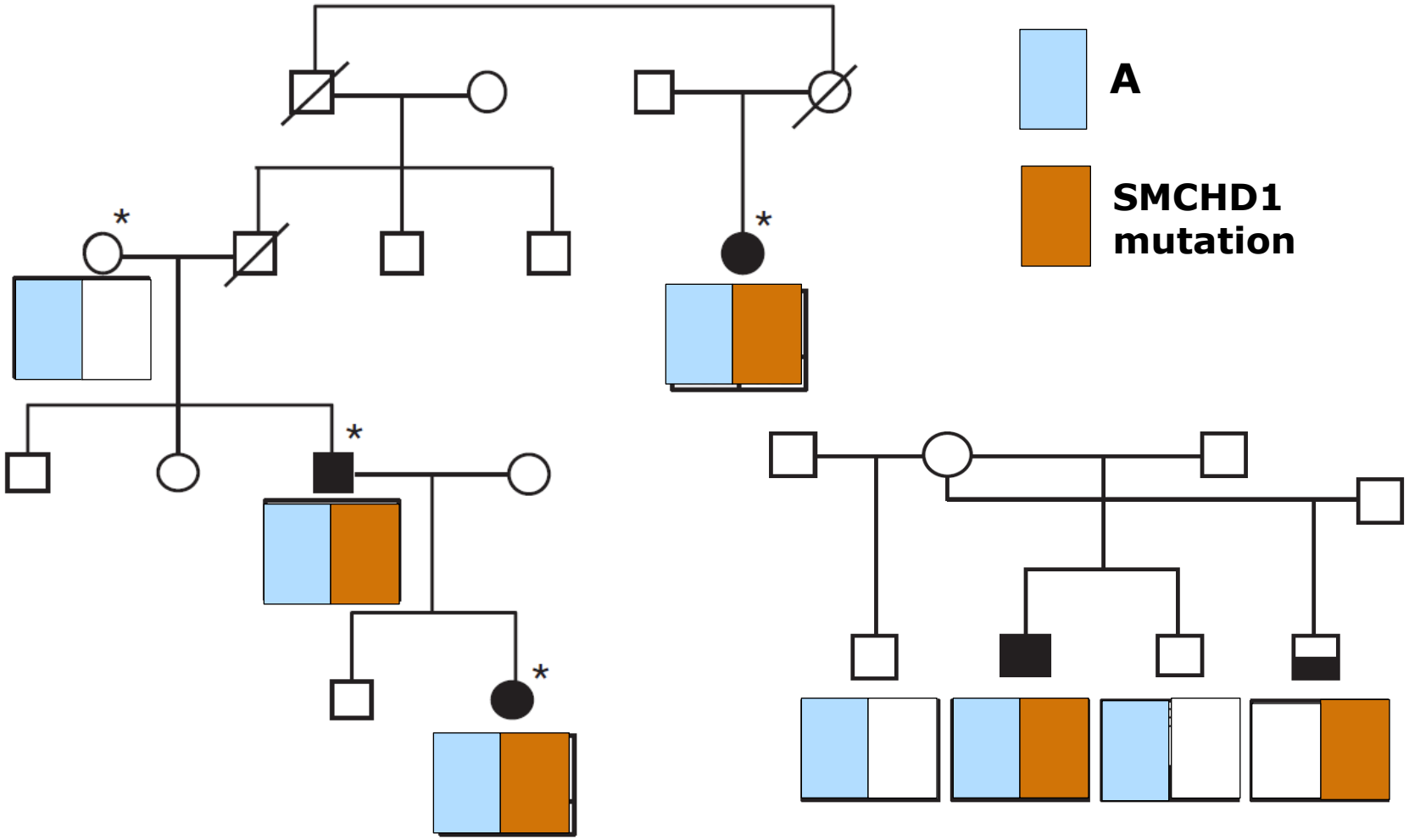
FSHD2

- Described in about 2002: Individuals with FSHD2 looked like typical FSHD but genetic testing showed they had no loss of the number of repeat DNA sequences on chromosome 4
- However, like FSHD1, there were signs that the DNA structure was looser on the tip of chromosome 4 and also like FSHD1, one of their 2 copies of chromosome 4 has the **A** sequence at the tip.

FSHD2: Genetic defect



FSHD2 is a Digenic Disease



Chance of Inheritance in FSHD2

- Because FSHD2 results from the chance of inheriting two separate genetic predisposition, the inheritance pattern is complicated and depends on the genetic profile of the parents.
- Chance of inheritance can vary from less than 25% to about 50%
- Like FSHD1, the disease of FSHD2 is very variable

Clinical Features of FSHD2 vs FSHD1

- 33 individuals with FSHD2 from 27 families were studied
- Average age at symptom onset: 26 years (range: 0-60)
- The initial symptoms:
  - Scapular weakness: 61%
  - Foot weakness: 27%
  - Facial weakness: 10%
  - Hip girdle weakness: 3%

Clinical Features of FSHD2 vs FSHD1

- On examination:
  - Scapular weakness: 100%
  - Foot weakness: 79%
  - Facial weakness: 94%
- Overall disease severity was not different between males and females
- Hearing loss: 18%
- Retinal vascular disease not observed in FSHD2
- Inheritance 20/33 are sporadic (about 30% in FSHD)

FSHD2: Conclusions

- FSHD1 and 2 are clinically indistinguishable as far their clinical features.
- FSHD2, as a group, tend to be less affected
- No retinal vascular disease was seen in FSHD2
- However, since the SMCHD1 gene is responsible for how tightly bound the DNA structures are on different chromosome, could the mutations in that gene that FSHD affect genes on other chromosomes?

FSHD2: Conclusions

- There is no evidence that families with FSHD2 have other associated medical conditions
- 80% of FSHD2 can be accounted for by mutations in the SMCHD1 gene
- Other genes are likely to be discovered
- Knowledge about these other genes is very important in understanding FSHD in general and may suggest other ways of treating FSHD

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