Developing a cell-free DNA-based biomarker for FSHD

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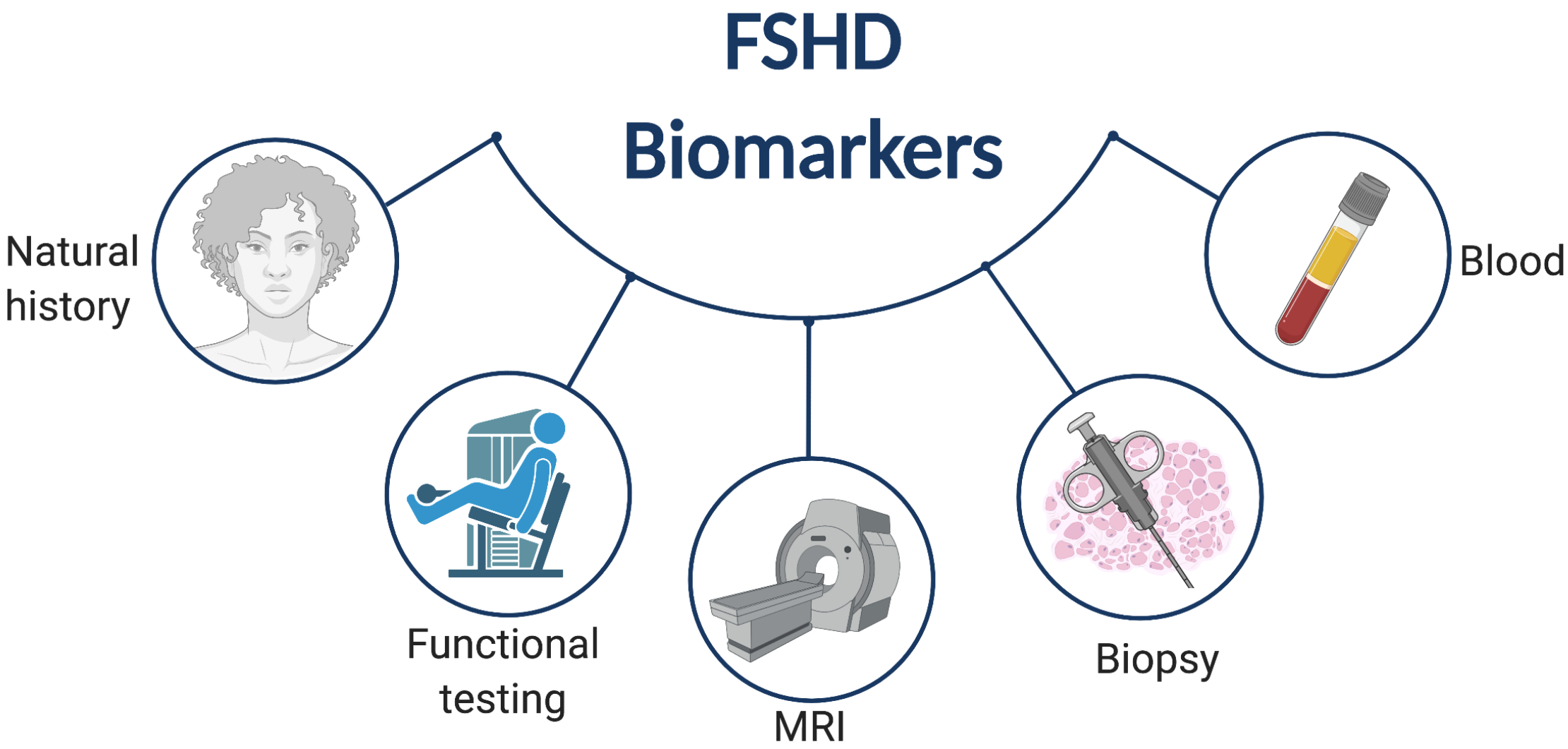
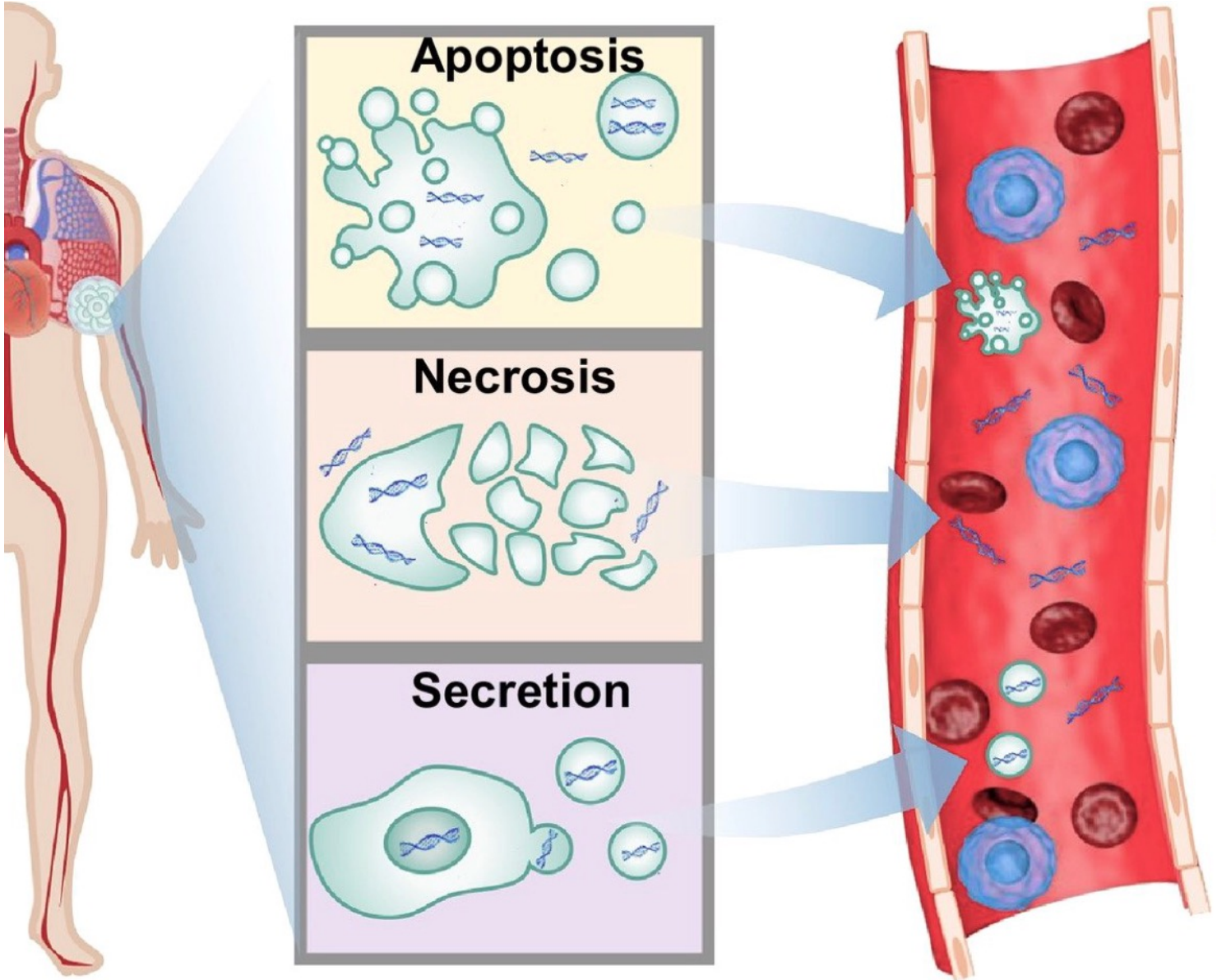


Cell-free DNA as an FSHD biomarker

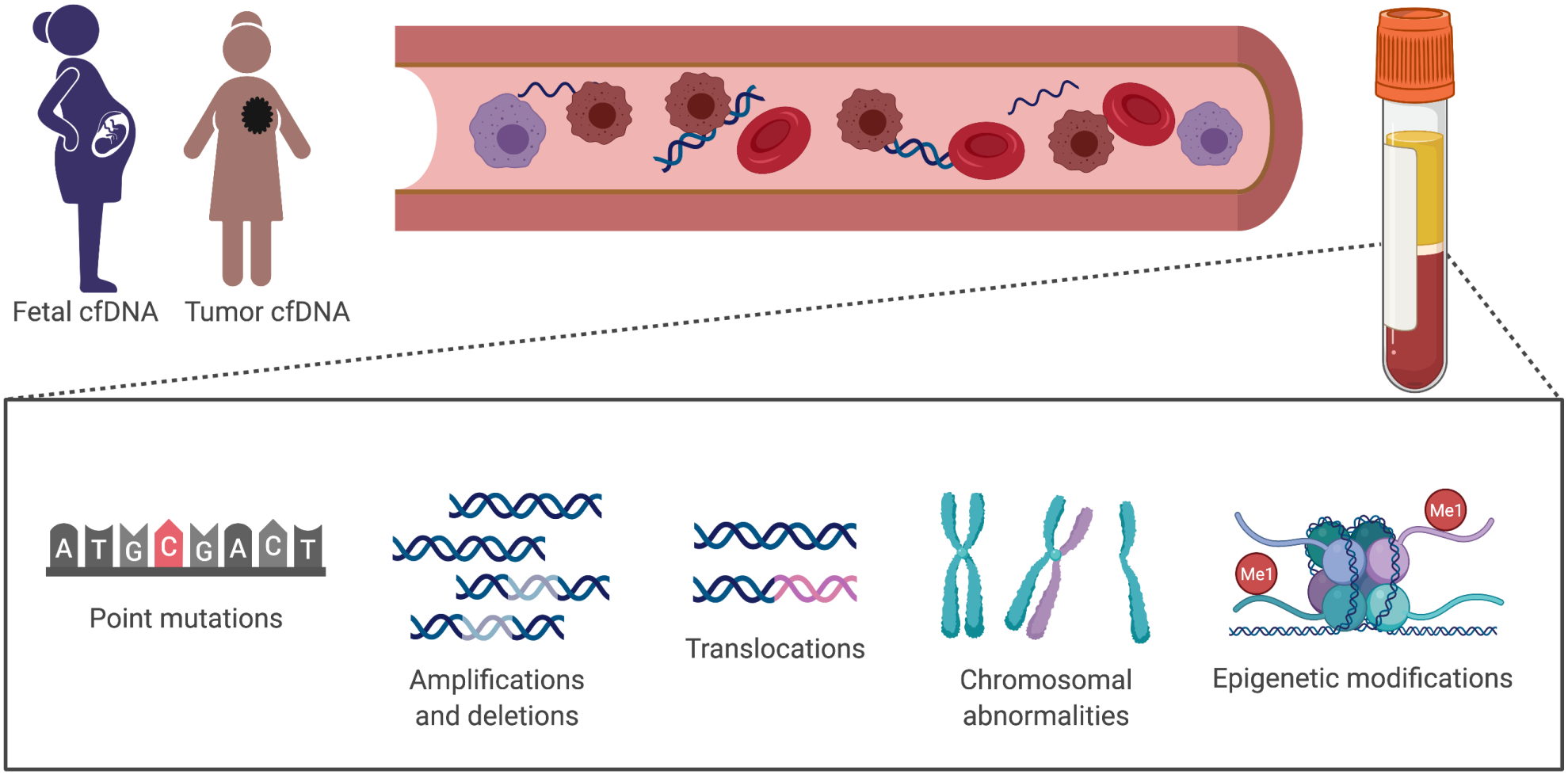
What is cell-free DNA?

- DNA that is released into the blood from cells all over the body
- Dynamic snapshot



Luo et al, 2021

cfDNA is widely used in clinical diagnostics



cfDNA from muscle cells in FSHD?

- DUX4-induces muscle cell death, which might release muscle DNA fragments into the blood stream.
- We could look for DUX4 and DUX4-induced gene expression patterns
- Monitor FSHD in real time?
- Data from Dan Miller and Premi Haynes at UW (4 unaffected and 12 FSHD-affected individuals; Leo Wang) - Caveats

Conclusions

- Promising differences in patterns of cfDNA between individuals with FSHD and control cohort.
- Both D4Z4 repeats and the rest of the genome can be leveraged.

Future Directions

- Sample collection from much larger cohort (n=50 per group)
  - Statistically well-powered to both test identified signatures and discover new ones
- Once signature established, look for opportunities to pair with clinical trials
- Assay cost optimization through scaling and capture of relevant DNA

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