Genomic Approaches Towards Better Understanding and Treating DM

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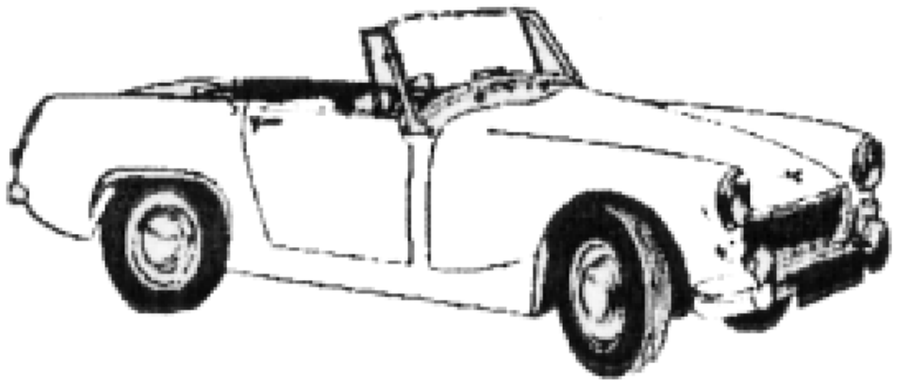
LABORATORY

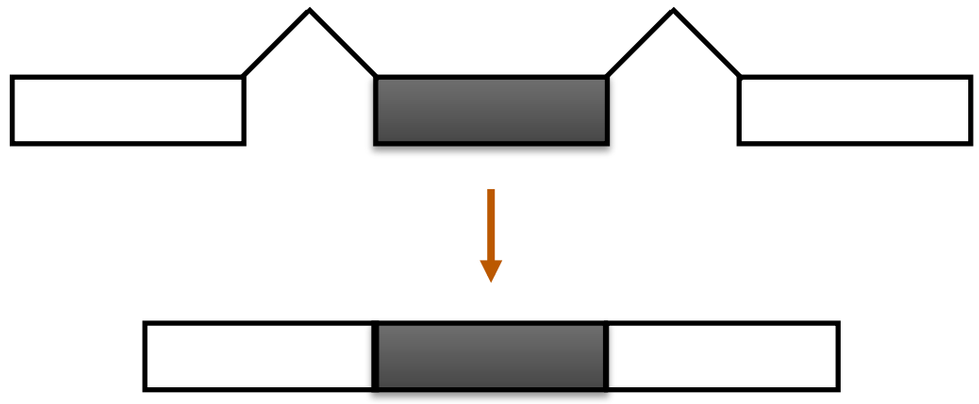
NIH DIRECTOR'S EARLY INDEPENDENCE AWARD

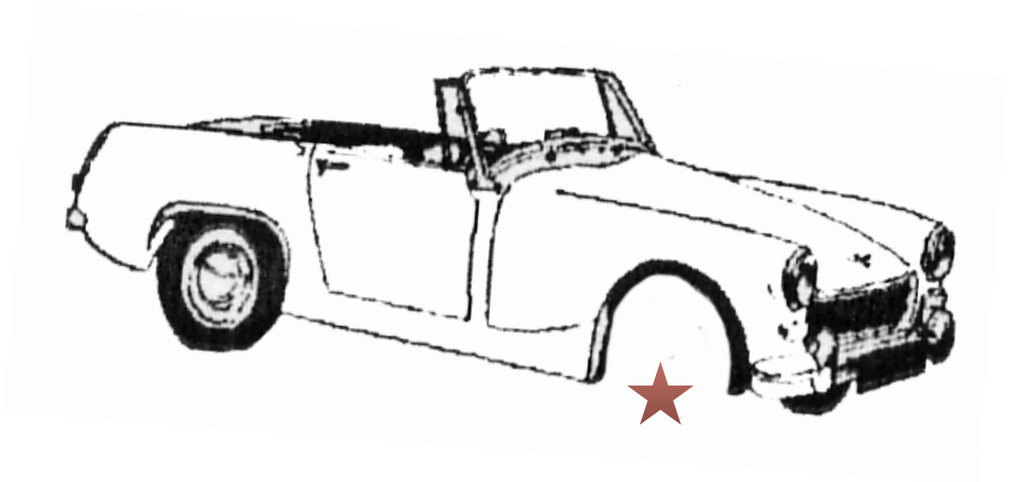
Taking the 10,000 foot view

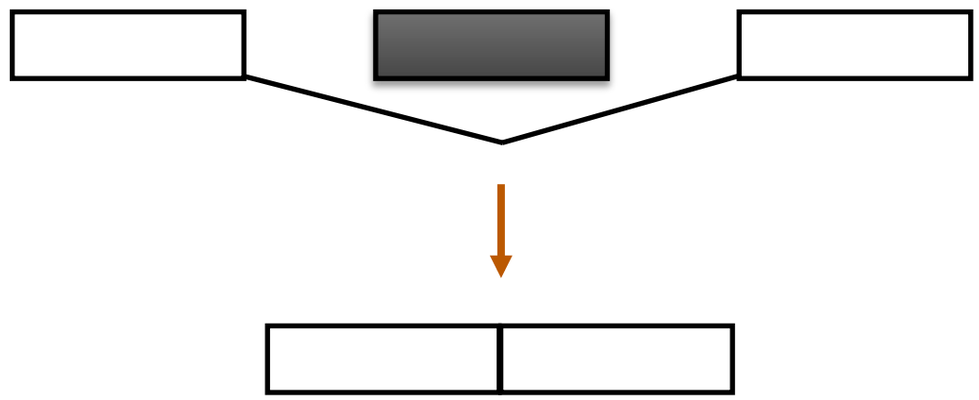
- There are ~30,000 genes in the human genome
- Hundreds to thousands of molecular changes occur in DM
- Using high throughput and computational approaches, we can study many of these changes

An analogy





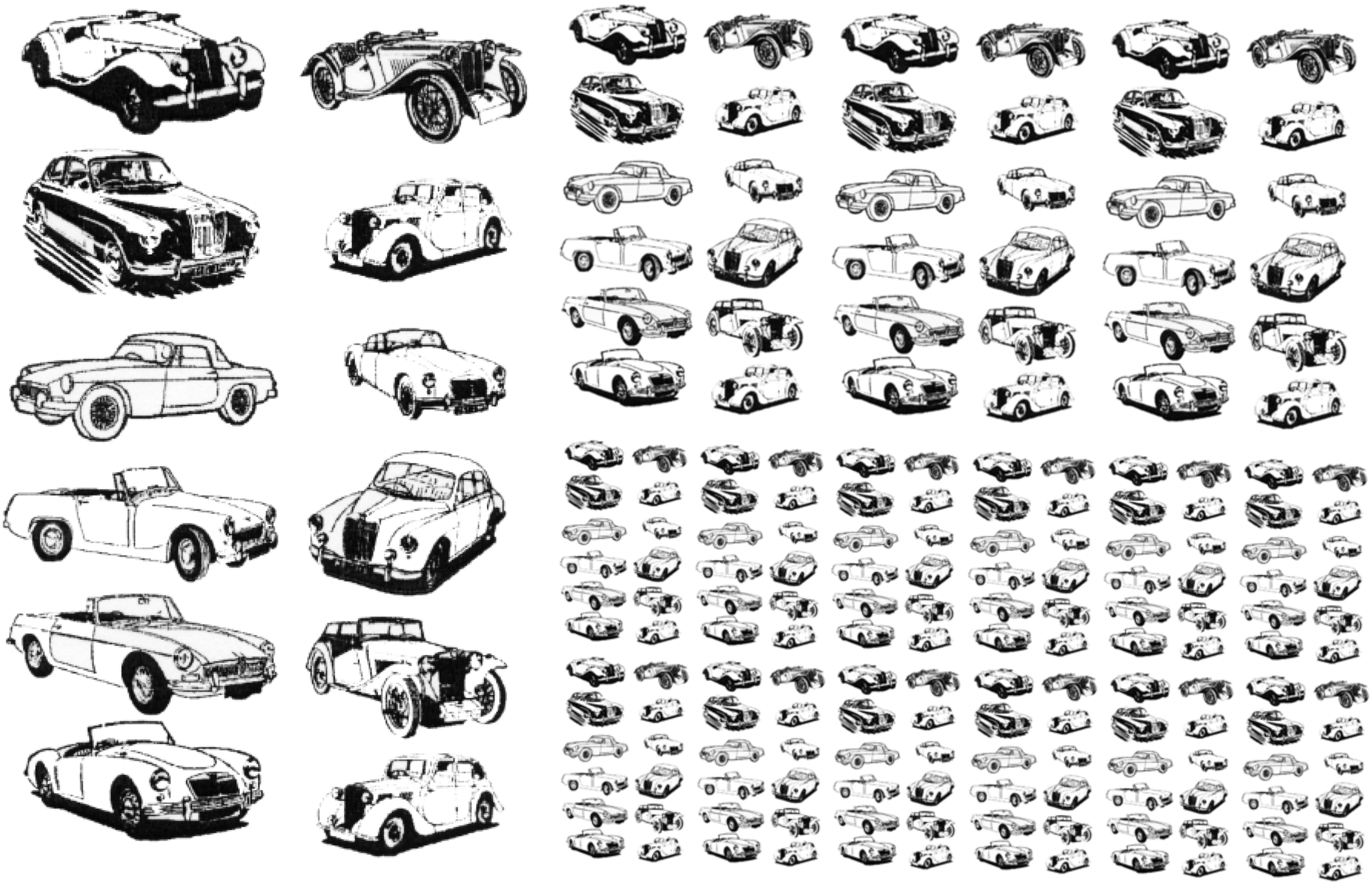




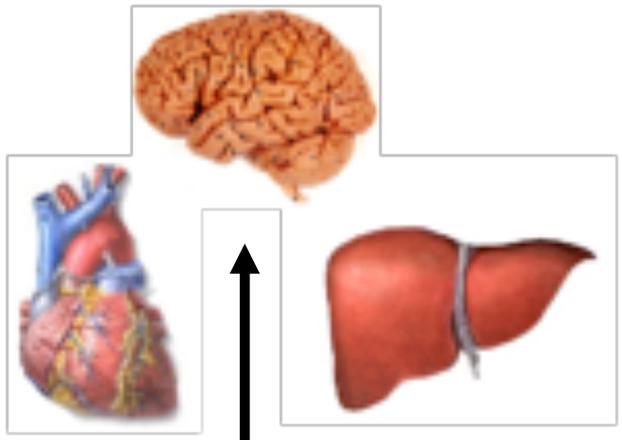
"Different" cars

Different RNA isoforms

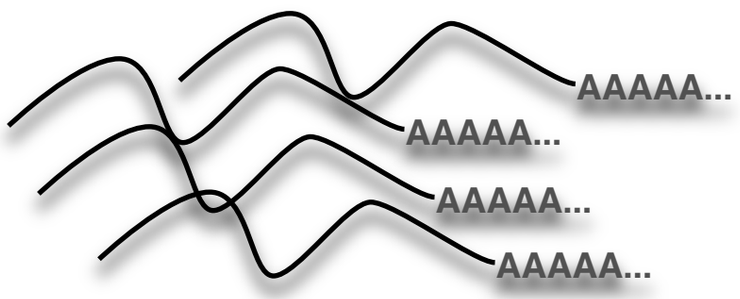
We try to look at ALL the RNA isoforms in the cell



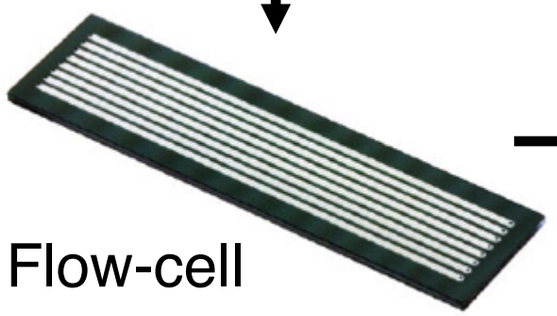
Deep sequencing and computational tools allow us to observe thousands of RNA splicing changes



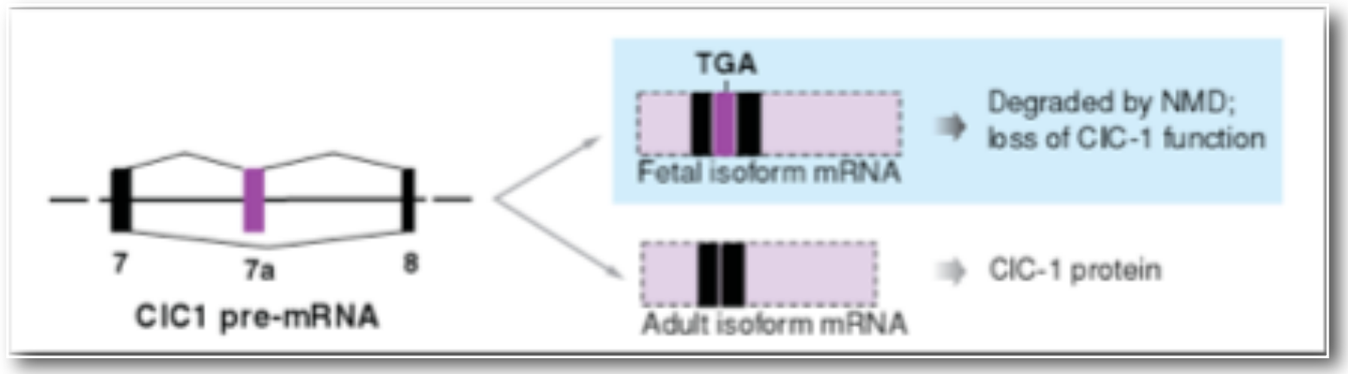
Tissues or cells



mRNA



Flow-cell



Chloride channel 1,
Cardiac troponin T,
Insulin receptor,
etc.

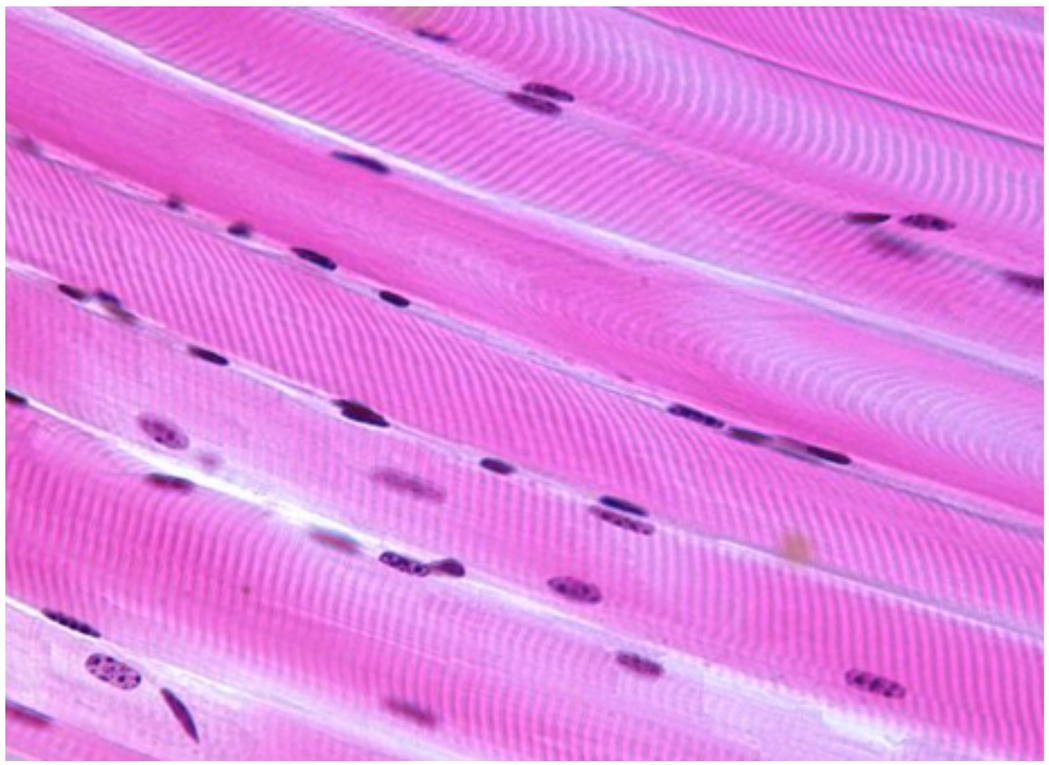
(myotonia)
arrhythmia?
insulin resistance?

Millions of sequences that tell us the identity and quantity of RNA species

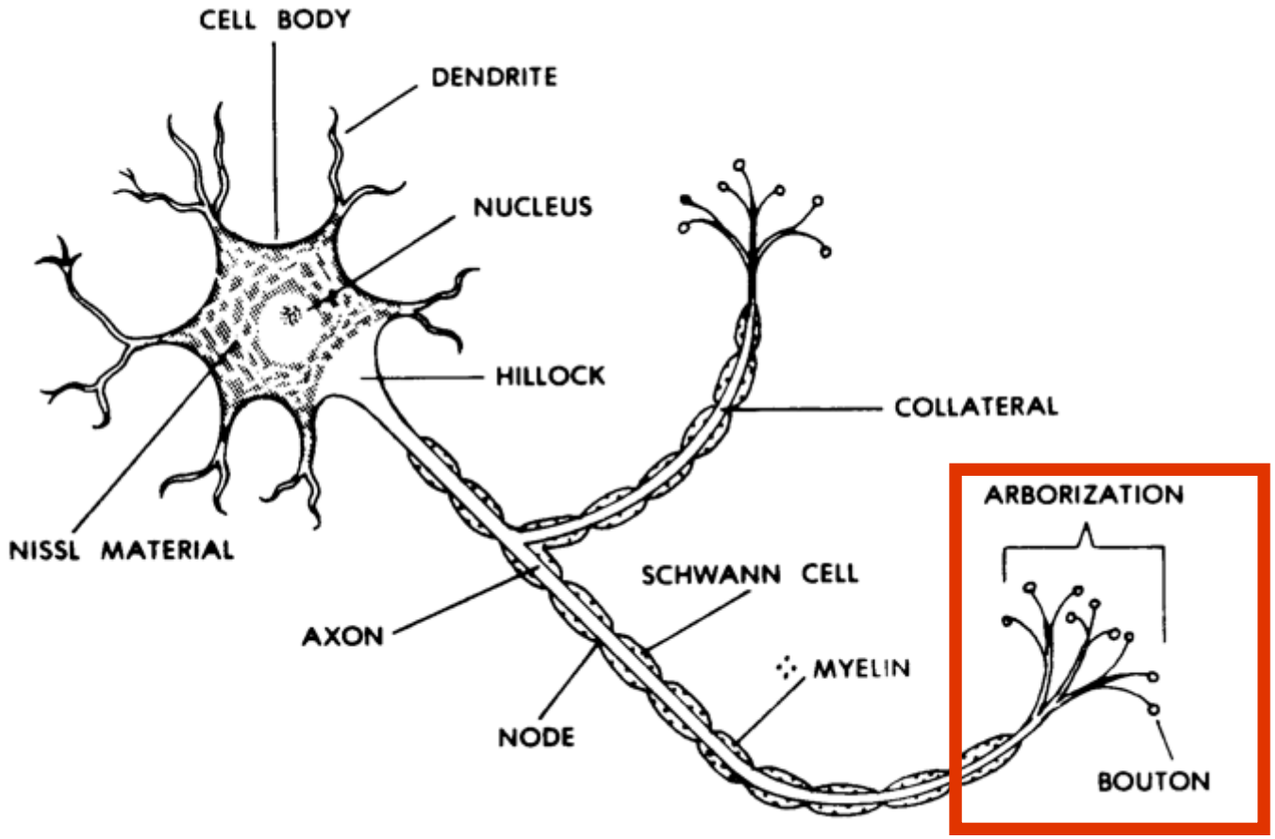
```
ATCAACGAGATAGGTTTCCCATACGTA
CAGAGTTTAGAGATGAGATCGATAGAT
CAGAGTTGAGAGCAGTAGGATATTAGA
ATAGATGCGAGAGAGGGGGTTTATAAT
CTGCTGAGAGTAGCTGCTGCTAGAGTT
ACGAGACGCGCTTCGCTTTTAAAAGGG
...
```

We also study where RNA is located in the cell

Muscle cells



Nerve cell

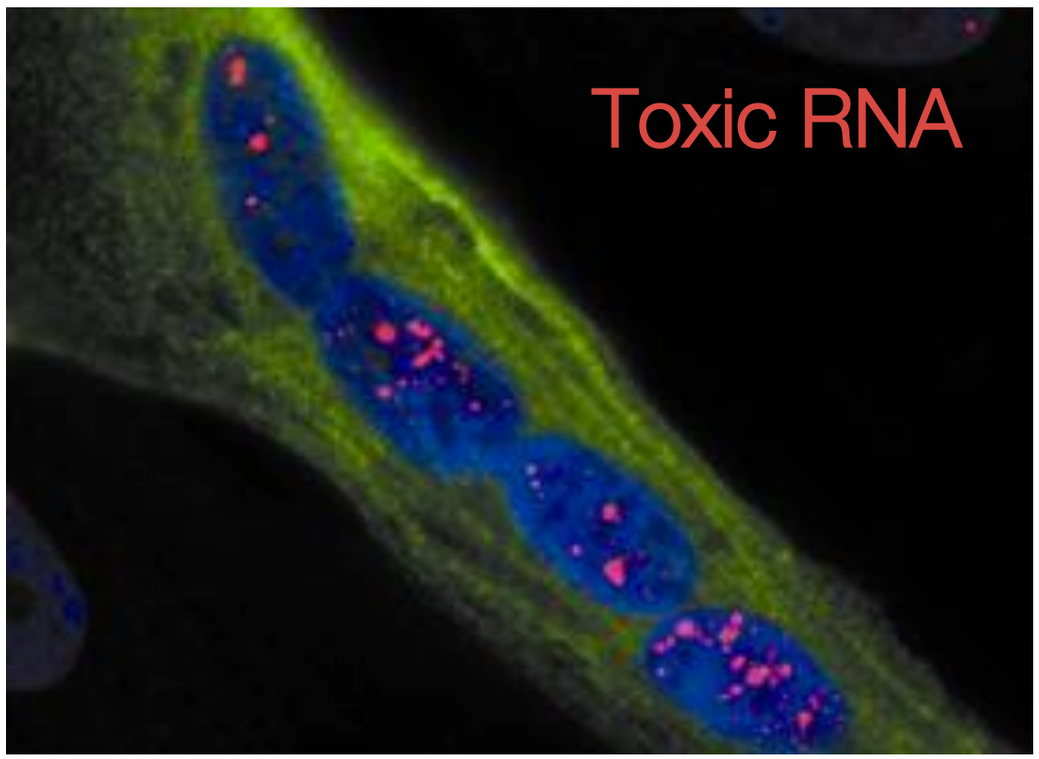


RNA can be carried to specific places in the cell before it is used to make protein, and

Muscleblind may participate in this process

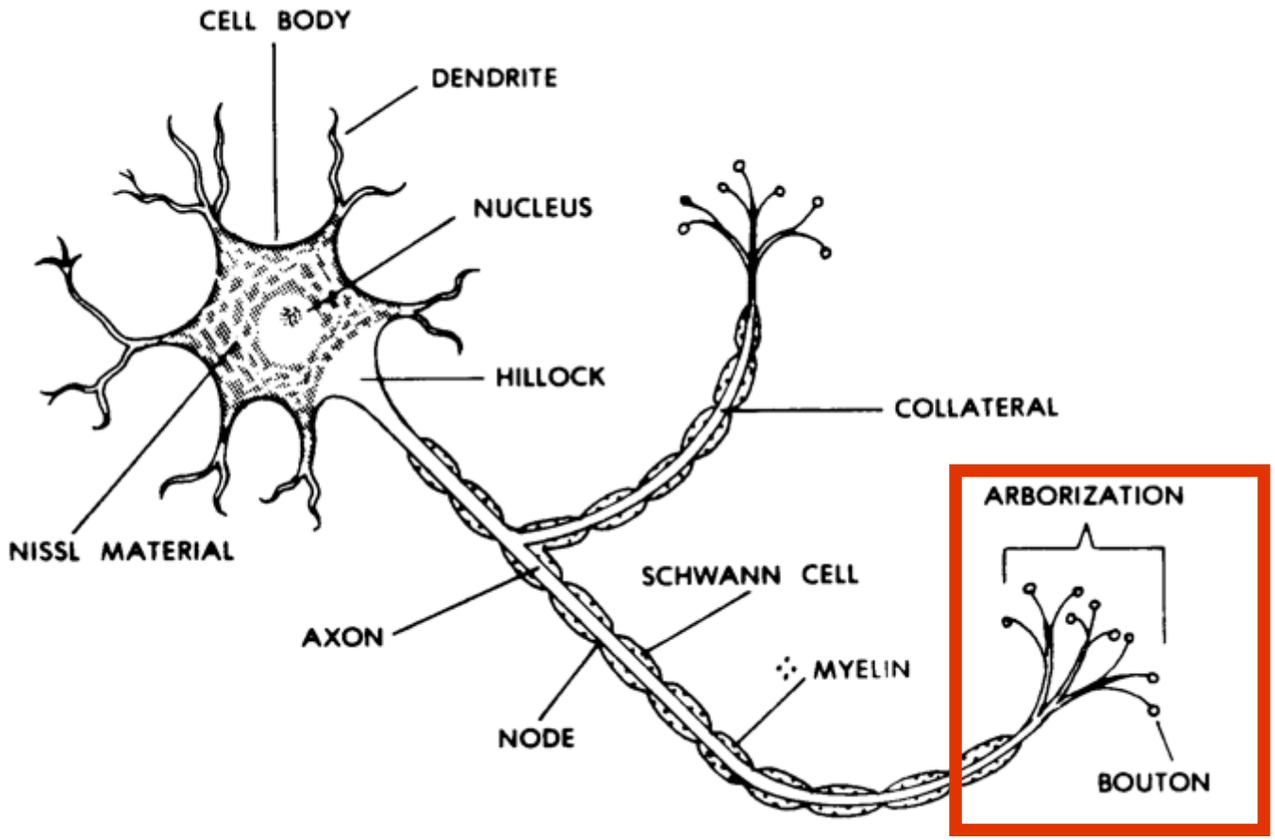
We also study where RNA is located in the cell

DM muscle cells



Thurman Wheeler, Charles Thornton

Nerve cell



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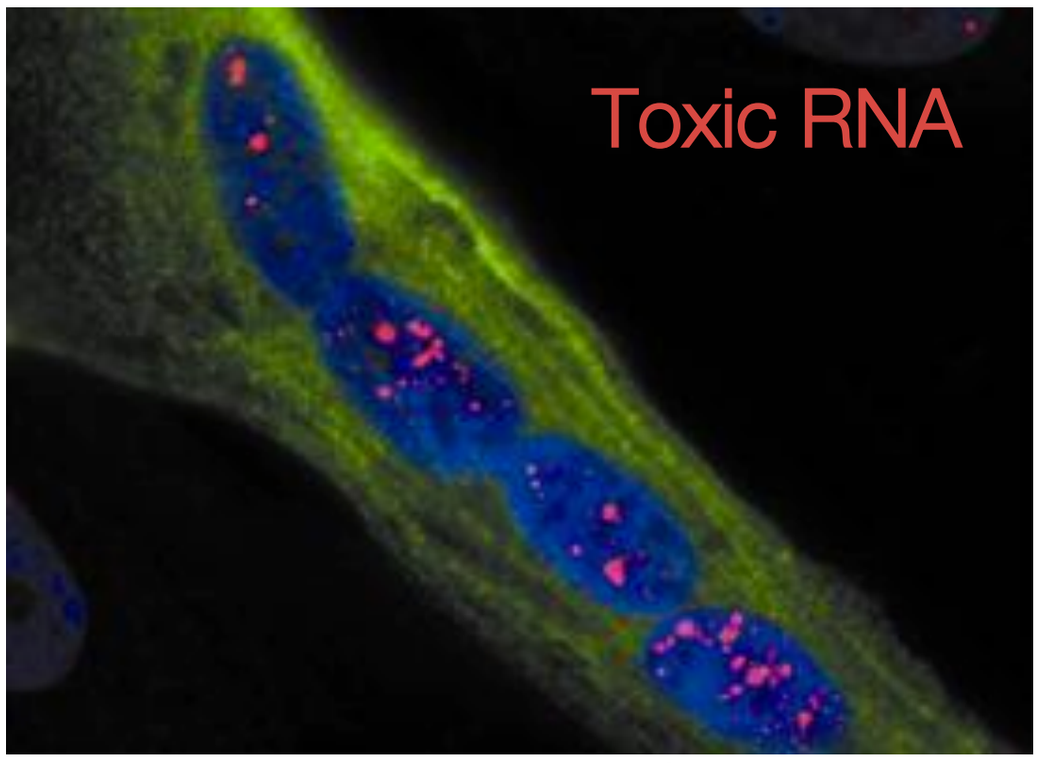

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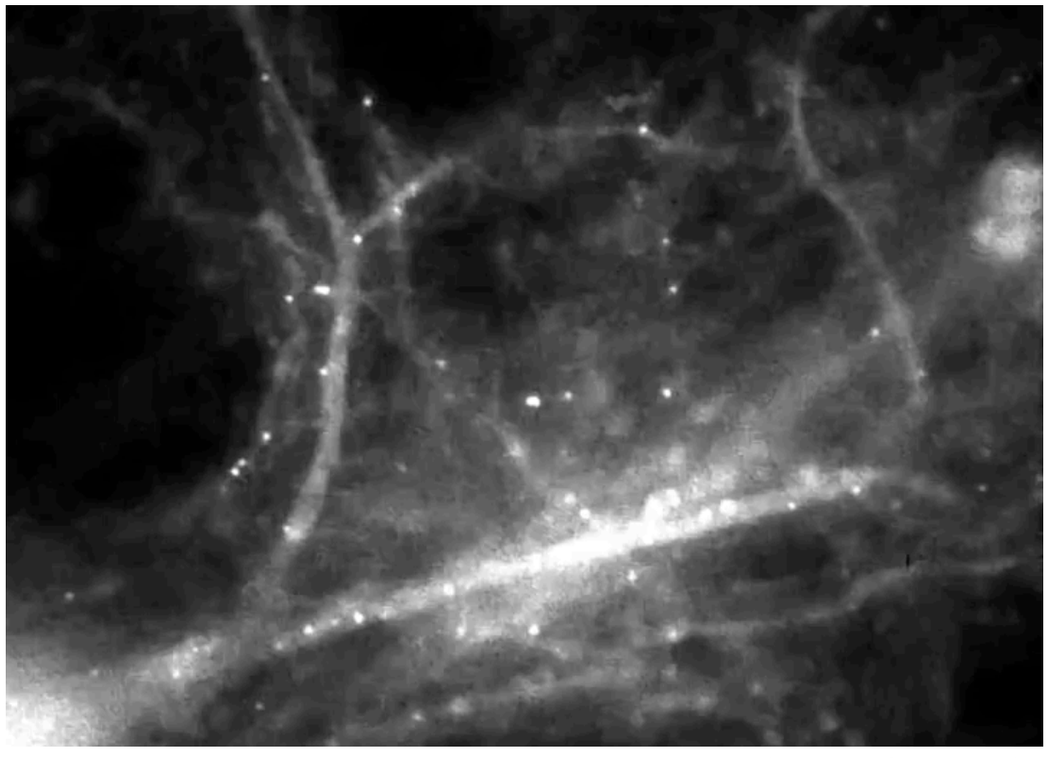
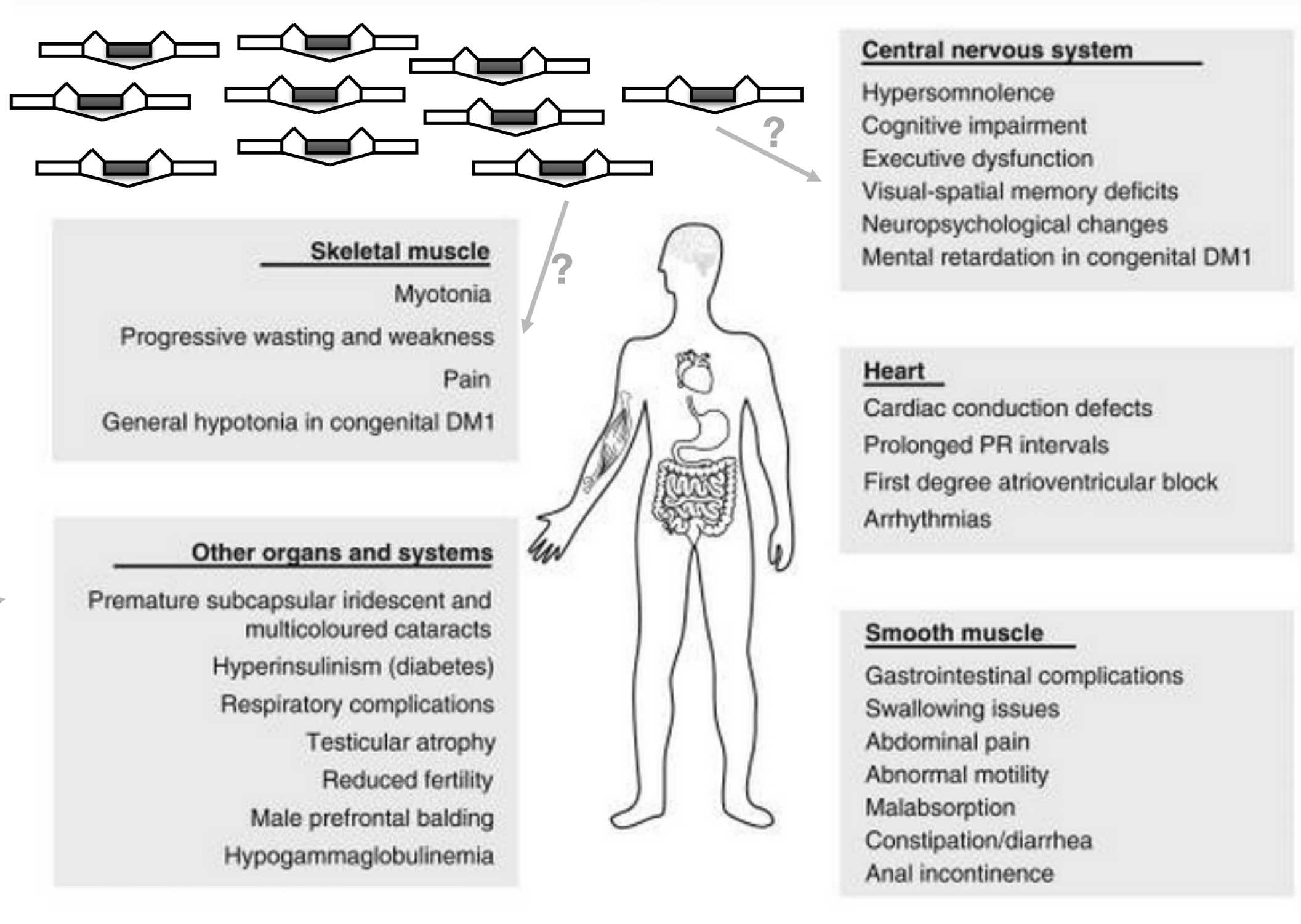


Park et al 2014 (Rob Singer)

RNA can be carried to specific places in the cell
before it is used to make protein, and
Muscleblind may participate in this process

We try to study how ALL RNAs move and localize in the cell…

…so that we can better connect molecular events with the symptoms experienced in DM



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Illumina
Shujun Luo
Gary Schroth

MIT Biomicro Center

Swanson Biotechnology Core

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Ultimately, our goal is to better understand DM so that we can effectively treat it

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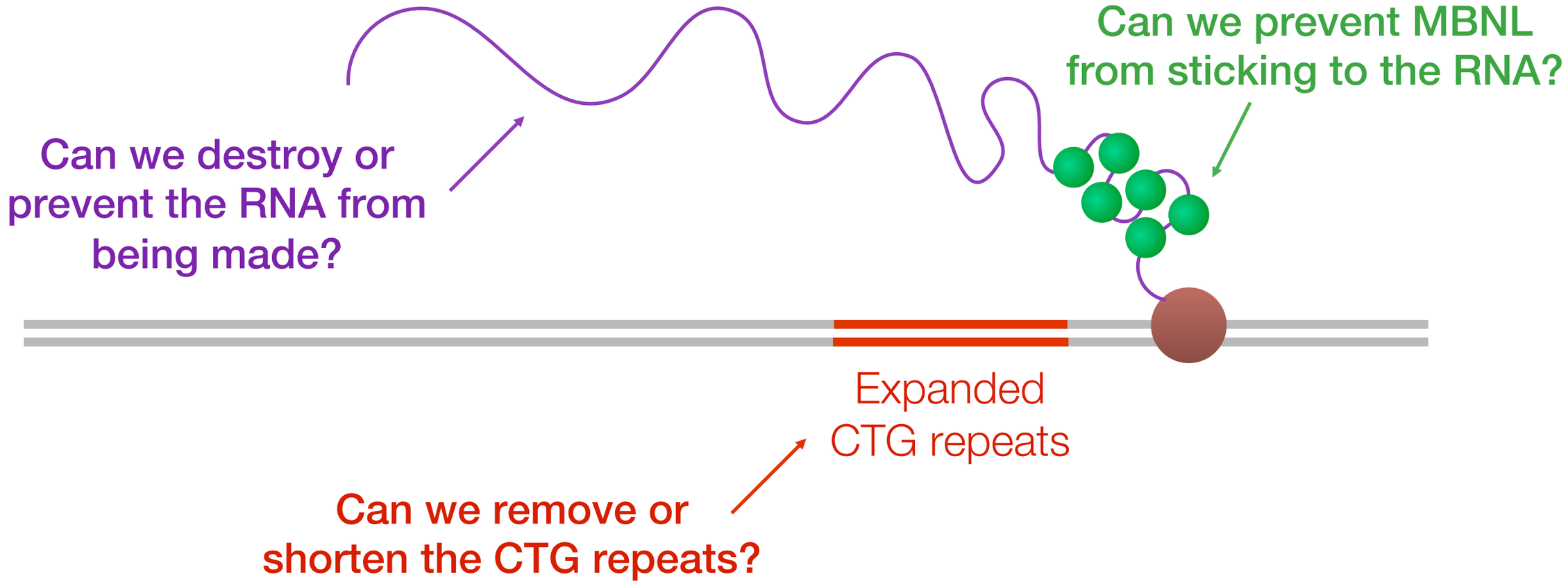
What are the downstream consequences of CTG repeat expansions?



When we have molecules that can do these things, can we make sure they get to the right cells in the body?