Genomic Approaches Towards Better Understanding and Treating DM

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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.

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

- ATCAACGAGATAGGTTTCCCATACGTA
- CAGAGTTTAGAGATGAGATCGATAGAT
- CAGAGTTGAGAGCAGTAGGATATTAGA
- ATAGATGCGAGAGAGGGGGTTTATAAT
- CTGCTGAGAGTAGCTGCTGCTAGAGTT
- ACGAGACCGCGCTTTCGCTTTTTAAAGGG

Flow-cell → Tissues or cells → mRNA

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

(myotonia) arrhythmia? insulin resistance?
We also study where RNA is located in the cell

Muscle cells

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

![Image of DM muscle cells with Toxic RNA](Thurman Wheeler, Charles Thornton)

**Nerve cell**

![Image of Nerve cell](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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Ultimately, our goal is to better understand DM so that we can effectively treat it.

What are the downstream consequences of CTG repeat expansions?

- Can we destroy or prevent the RNA from being made?
- Can we prevent MBNL from sticking to the RNA?
- Can we remove or shorten the CTG repeats?

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