

Fragile X Research and Treatment Center Newsletter

April 2023



Meet The Team



Nina Gross, PhD, is a basic neuroscientist who works in the bench lab. Her research focuses on understanding the molecular mechanisms underlying FXS and autism. Her lab helped make determining FMRP and FMR1 mRNA levels in the blood possible!



Matilyn Shanahan received her B.S. and M.S. in Biochemistry & Molecular Biology from Wright State University. She conducts benchtop experiments on patient blood samples to measure their FMRP levels and sequence the gene responsible for expressing FMRP, FMR1.

Fragile X Results Spotlight

A sensitive and reproducible qRT-PCR assay detects physiological relevant trace levels of *FMR1* mRNA in individuals with Fragile X syndrome

DNA → mRNA → Protein
"transcription" "translation"

What we did:

- Collected blood from 77 individuals with FXS (55 male, 22 female), 29 premutation carriers ("PMC"; 2 male, 27 female), and 32 typically-developing controls ("TDC"; 26 male, 6 female)
- Used a new method to detect FMR1 mRNA levels in the blood

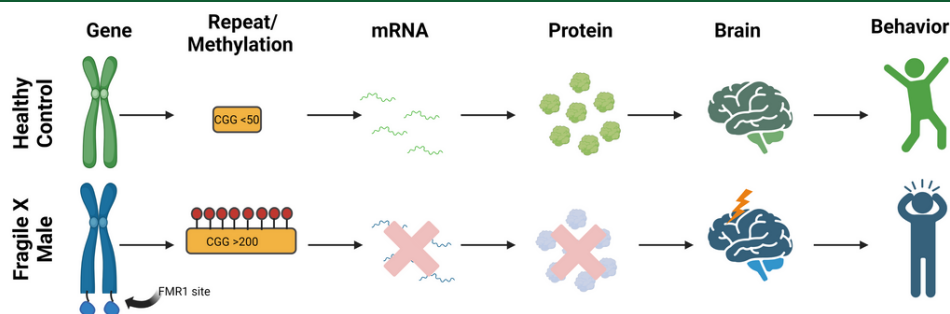
What we found:

- Our assay for detecting FMR1 mRNA is:
 - Highly sensitive - it can detect very low levels of mRNA
 - Highly reproducible - values are the same when tested again
- mRNA levels are:
 - Lower in FXS males than FXS females or non-FXS males
 - Lower in full mutation males than mosaic males
 - Higher in PMC females than FXS females and TDC females
 - Strongly related to FMRP levels in FXS, but not PMC or TDC
 - Related to IQ in FXS participants who have any FMR1 mRNA



Why this matters:

- FMR1 mRNA is required for the body to make FMRP
- Some full mutation FXS males have trace levels of FMR1 mRNA, consistent with our findings of trace FMRP levels in some males
 - This means the FMR1 gene is not always completely "turned off"
 - Standard diagnostic blood tests for FXS may not be sensitive enough to detect subtle variations in how the gene is working
- FMR1 mRNA may have "dose effect" on outcomes like IQ



Find the full article here:

<https://www.nature.com/articles/s41598-023-29786-4>