# Protein related to Fragile X syndrome may be a new target for blood pressure medicines

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A new study in mice has identified FXR1, a protein in the same family as the one implicated in Fragile X syndrome, as a potential target for creating a new type of blood pressure-lowering medicine, according to preliminary research presented at the American Heart Association's Vascular Discovery: From Genes to Medicine Scientific Sessions 2022. The meeting is being held May 12-14, 2022, in Seattle and is a global exchange of the latest advances in new and emerging scientific research in arteriosclerosis, thrombosis, vascular biology, peripheral vascular disease, vascular surgery and functional genomics.

Fragile X syndrome, or FXS, is the most common known cause of inherited intellectual disability caused by mutations on the X chromosome. The CDC estimates FXS affects 1 in 7,000 males and 1 in 11,000 females born each year in the U.S. FXS may lead to developmental delays, learning disabilities and behavioral problems, with symptoms being more severe among boys compared to girls.

FXS is caused by mutations to the gene FMR1, which codes for an RNA-binding protein FMRP that is believed to play a role in the development of connections between nerve cells in the brain.

FXR1 belongs to the same family of RNA-binding proteins as FMRP and is muscle-specific. RNA-binding proteins help turn genes on and off and are essential to numerous cellular processes.

"In my previous research on FXR1, I expected to see more transcription factors, translation factors, factors that regulate mRNA interact with FXR1," said Amanda St. Paul, lead study author and a Ph.D. candidate at the Lewis Katz School of Medicine at Temple University in Philadelphia. "It was really surprising to find that FXR1 binds to a lot of actin-binding proteins and other proteins involved in the cytoskeleton." Transcription and translation factors are proteins that help turn certain genes on and off. Actin proteins are responsible for the contraction and

relaxation of muscles.

St. Paul and colleagues developed a mouse model where FXR1 can be deleted in smooth muscle cells—the same kind that make up blood vessels in humans. The mice were genetically modified so that the FXR1 gene could be deleted by administering the medication tamoxifen.

With the FXR1 gene deleted, the researchers noted that the vascular smooth muscle cells behaved differently compared to those of the mice with active FXR1.

"We found that vascular smooth muscle cells without FXR1 don't proliferate, they don't adhere, they don't migrate, which are activities dependent on a properly functioning cytoskeleton. And these are all what a vascular smooth muscle cell should be doing," St. Paul said.

Knocking out FXR1 had another consequence that was eye-opening: "When you take away FXR1 from the smooth muscle in these mice, they also had decreased diastolic blood pressure compared to control mice," St. Paul said.

The analysis found that:

- Depleting FXR1 decreased the ability of blood vessel cells to contract; and
- When FXR1 is deleted, the mice had decreased diastolic blood pressure compared to control mice. This was measured using telemetry, an in-vivo measure of blood pressure.

According to St. Paul, these findings suggest that targeting FXR1 in the vascular smooth muscle cells, or the contractile pathway it regulates, may be a promising avenue for the development of anti-hypertensive medications. "A lot of medication targets don't focus on the

cytoskeleton. Since FXR1 is muscle-specific, it gives us a specific target and pathway to examine further," she said. "Millions of people have high blood pressure; finding new ways to improve blood pressure is important."

Future work for St. Paul and colleagues will involve investigating whether FXR1's activity in smooth muscle cells is dependent on its ability to interact with cytoskeletal proteins and if deleting FXR1 is effective in reducing blood pressure in a hypertensive mouse model.

**More information:** American Heart Association's Vascular Discovery: From Genes to Medicine Scientific Sessions 2022

Provided by American Heart Association

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