NEWS

Community Newsletter: Chromatin regulators; dysregulated protein synthesis; microglia and myelin

BY **MICHAEL FERGENSON**

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In this week's issue of Community Newsletter — our last for 2022 — we highlight tweets discussing research that uncovered a new function of autism-linked chromatin regulators, a mechanism behind restricted and repetitive behaviors in fragile X mice, and a previously unknown role for microglia.

Up first is a new **preprint** that provides "evidence that autism-associated chromatin regulators **ALSO regulate tubulin**," tweeted its lead investigator, **Helen Willsey**, assistant professor of psychiatry at the University of California, San Francisco. *Spectrum* **profiled** Willsey in November.

> Check out our new????pre-print????!! Here we provide evidence that autism-associated chromatin regulators ALSO regulate tubulin. ????**https://t.co/csRX1Z0xHP pic.twitter.com/Is8eaefhfq**
>
> — Helen Willsey (@goodfrognosis) **December 8, 2022**

The five chromatin regulators that are most strongly linked to autism — ADNP, CHD8, CHD2, POGZ and SUV420H1/KMT5B — all seem to co-localize with tubulin, a cytoskeleton protein, in frog embryos and in human cells. The work "highlights the importance of **functional exploration of risk genes** to help clarify pleiotropy" rather than relying on the annotated function of genes, Willsey wrote.

> Overall, this work brings up the limitations of relying on annotated function to identify convergent pathological mechanisms and highlights the importance of functional exploration of risk genes to help clarify pleiotropy. As ever, the future is frogs ????!
>
> — Helen Willsey (@goodfrognosis) **December 8, 2022**

"We work with **deficiency and pathogenic mutations** in CHD2 and other chromatin regulators in iPSC models and have noted altered expression of genes associated with cytoskeleton, adhesion, migration for many--will be looking for that theme now," tweeted **Kristen Kroll**, professor of developmental biology at Washington University School of Medicine in St. Louis.

> Very cool--we work with deficiency and pathogenic mutations in CHD2 and other chromatin regulators in iPSC models and have noted altered expression of genes associated with cytoskeleton, adhesion, migration for many--will be looking for that theme now.
>
> — Kristen Kroll (@Krolllab) **December 9, 2022**

Kroll said she "would love to **recommend this work** on Faculty Opinions once it's out," prompting thanks from Willsey, who replied, "excited to **see what you discover** for CHD2 and similar chromatin regulators!"

> Awesome thank you!! Excited to see what you discover for CHD2 and similar chromatin regulators!
>
> — Helen Willsey (@goodfrognosis) **December 9, 2022**

This "**really important preprint** . . . highlights the need to revisit our assumptions about functional annotations of genes involved in Autism Spectrum Disorders," tweeted **Tomasz Nowakowski**, assistant professor of neurological surgery at the University of California, San Francisco. In August, *Spectrum* explored research into newly discovered functions of autism-linked genes that **upend**

the genes' conventional classifications.

> Really important preprint from **@goodfrognosis** - highlights the need to revisit our assumptions about functional annotations of genes involved in Autism Spectrum Disorders. Previously, these genes were assumed to only regulate gene expression. It turns out that they do a lot more! **https://t.co/kNDNLKf86P**
>
> — Nowakowski_Lab (@LabNowakowski) **December 9, 2022**

Another **preprint** that generated excitement on Twitter this week linked restricted and repetitive behaviors in fragile X model mice to dysregulated protein synthesis at cortico-striatal synapses, specifically in a class of GABAergic neurons in the striatum.

"Excited to share our last work from **@KlannLab** where we **unveiled cell-type specific changes** in the striatal medium spiny neurons underlying the expression of RRBs in FXS mice!" tweeted **Francesco Longo**, researcher at the University of Gothenburg in Sweden.

> Excited to share our last work from **@KlannLab** where we unveiled cell-type specific changes in the striatal medium spiny neurons underlying the expression of RRBs in FXS mice! A great collaboration with **@CarterAG**, **@NicTritsch**, and **@BagniClaudia** labs! 1/5 **https://t.co/KibaODhlj2**
>
> — Francesco Longo (@fran_longo17) **December 9, 2022**

Matthew Kraushar, professor of genome regulation at the Max Planck Institute for Molecular Genetics in Berlin, Germany, called the work an "**awesome story**: protein synthesis abnormalities in specific synapses in the striatum driving motor phenotypes in FXS/ASDs."

> awesome story: protein synthesis abnormalities in specific synapses in the striatum driving motor phenotypes in FXS/ASDs
>
> super strong work from **@KlannLab** and colleagues!

> ???????????? **https://t.co/fCr4QEOkGL**
>
> — Matthew L. Kraushar (@MatthewKraushar) **December 10, 2022**

Another new **study** alert on Twitter this week tied microglia to myelin maintenance. “We reveal a **novel role for microglia** in regulating myelin growth & integrity, required to maintain healthy myelin once it’s formed,” tweeted **Niamh McNamara**, graduate student in **Veronique Miron’s** lab at the University of Edinburgh in Scotland, about the paper, published 14 December in *Nature*. Myelin, which aids signal conductance between neurons, is **deficient in some forms of autism**.

> Overall, we reveal a novel role for microglia in regulating myelin growth & integrity, required to maintain healthy myelin once it’s formed. This has important implications for ageing & neurodegenerative disease, where we know microglia are dysregulated & myelin pathology occurs. **pic.twitter.com/m5CNcBhC3m**
>
> — Niamh McNamara (@niamh_mc_namara) **December 14, 2022**

“Extremely cool and interesting findings: **loss of microglia** leads to myelin hyper- and de-myelination, oligodendrocyte cholesteryl ester accumulation and upregulation of cholesterol synthesis genes!” tweeted **Leyla Akay**, graduate student in the Tsai Laboratory at the Massachusetts Institute of Technology in Cambridge.

> Wow! Extremely cool and interesting findings: loss of microglia leads to myelin hyper- and de-myelination, oligodendrocyte cholesteryl ester accumulation and upregulation of cholesterol synthesis genes! Such exciting results ???? **https://t.co/5So6x5xh3S**
>
> — Leyla Akay (@leyla_aakay) **December 14, 2022**

That’s it for this week. Our next Community Newsletter will go out on 8 January, 2023. If you have any suggestions for interesting social posts you saw in the autism research sphere, feel free to send an email to **michael@spectrumnews.org**.

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