Additional evidence on western blot, histology, and electrophysiology

Although not my areas of expertise, a FAR-from-exhaustive quick search led me to evidence of "recycled" western blot and histology images, and electrophysiological data. I have consulted several Columbia and non-Columbia neurobiologists familiar with western blot, histology, and electrophysiology. All agree with my assessment below.

As shown below, the sets of Actin band appear identical in the study on the P301S mouse model (Giannopoulos et al., 2018, Aging Cell) and the study on the htau mouse model (Giannopoulos et al., 2015, Biological Psychiatry). The pGSK3α and β bands appear the same (with slightly different light intensity) as well. See bands circled in red rectangular boxes below.

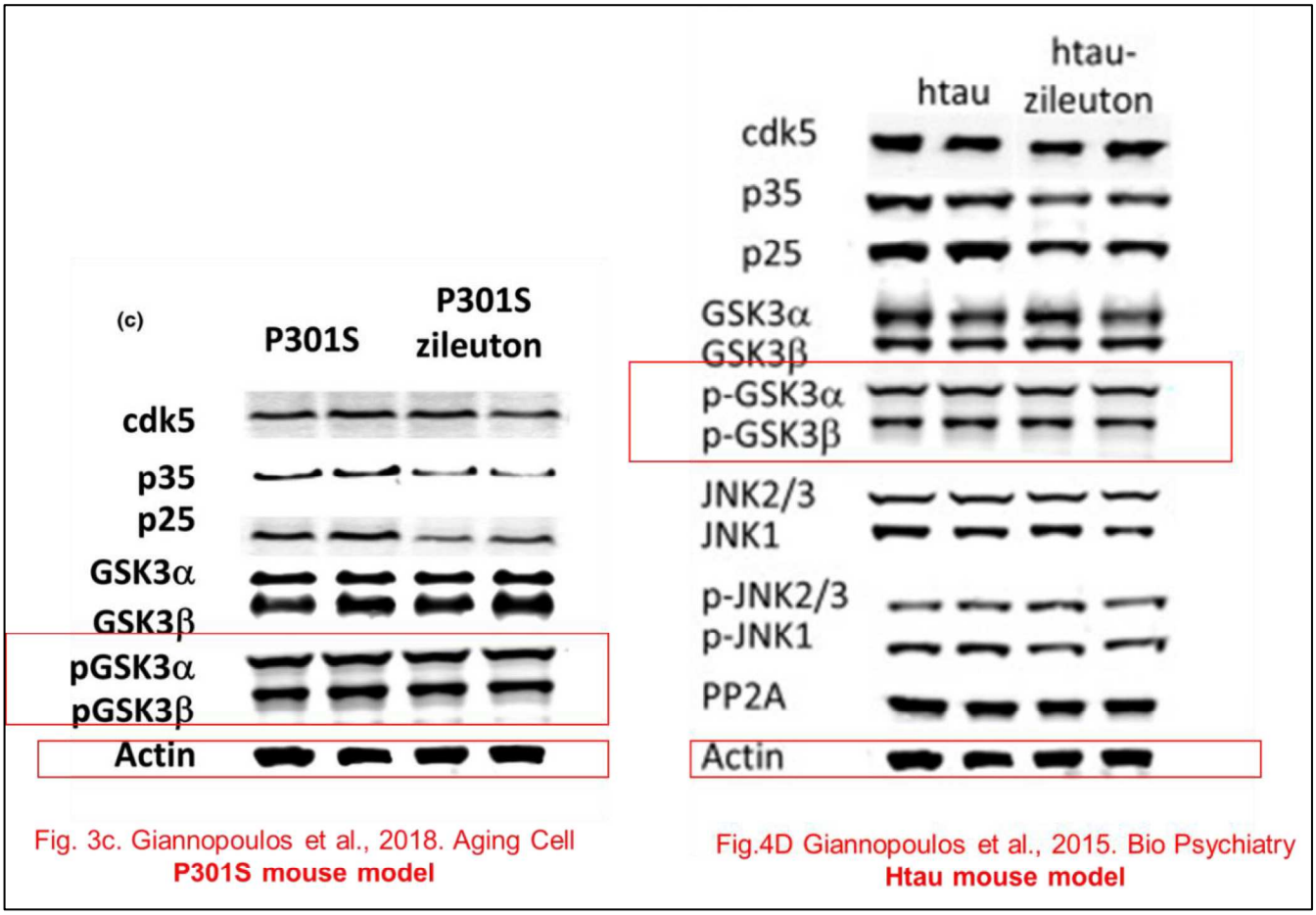

Fig. 3c. Giannopoulos et al., 2018. Aging Cell
P301S mouse model

Fig.4D Giannopoulos et al., 2015. Bio Psychiatry
Htau mouse model

The 2018 Aging cell paper also contain an image (Fig 4C) a part of which appears to be identical to part of Fig 6A in Giannopoulos et al., 2019, Molecular Neurobiology. Please see bands circled in red rectangular boxes below (next page). Identical CD45 and Actin bands appear in both figures, although the gel images are supposedly from two different mouse models (P301S and htau).

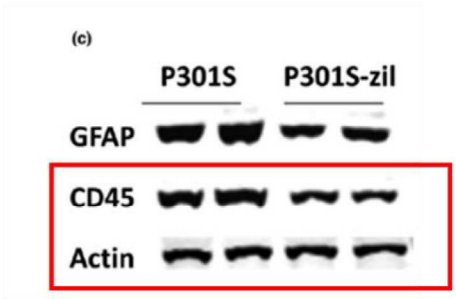

Fig 4C. Giannopoulos et al., 2018. Aging Cell
P301S mouse model

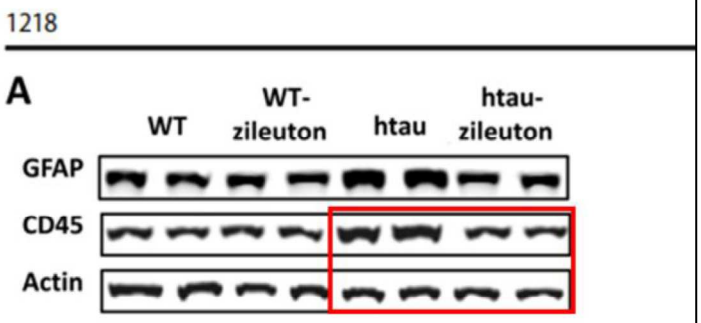

Fig 6A. Giannopoulos et al., 2019. Molecular Neurobiology
Htau mouse model

Below is Fig 5C of the Giannopoulos et al., 2019, Molecular Neurobiology paper. WT and htau-zileuton PSD95 images appear to be mirror images (flipped). See blue boxes. WT and WT-zileuton MAP2 images are completely identical (red box).

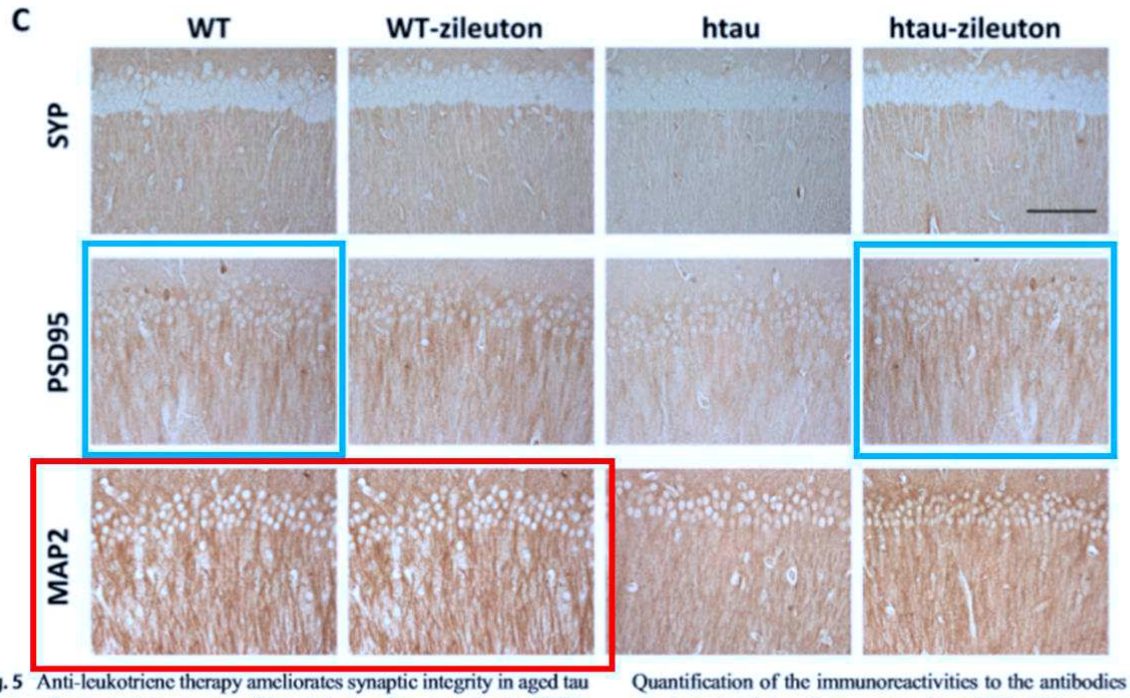

Fig. 5 Anti-leukotriene therapy ameliorates synaptic integrity in aged tau mice. **a** Representative western blot analysis of synaptophysin (SYP), post-synaptic density protein 95 (PSD-95), and microtubule-associated protein 2 (MAP2) in brain cortex homogenates from wild type (WT) and htau mice receiving zileuton or vehicle for 16 weeks. **b** Quantification of the immunoreactivities to the antibodies shown in the previous panel ($n = 6$ per group; $^*p < 0.05$). Values represent mean ± SEM (*one-way ANOVA*). **c** Representative images of brain sections from htau mice receiving zileuton or vehicle immunostained with SYP, PSD-95, and MAP2 antibodies (*scale bar 100 μm*)

In Fig 4C of Giannopoulos et al., 2018 Molecular Neurobiology, WT and WT-5LO SYP images seem to be identical, with the WT-5LO one slightly shifted to the left. See blow.

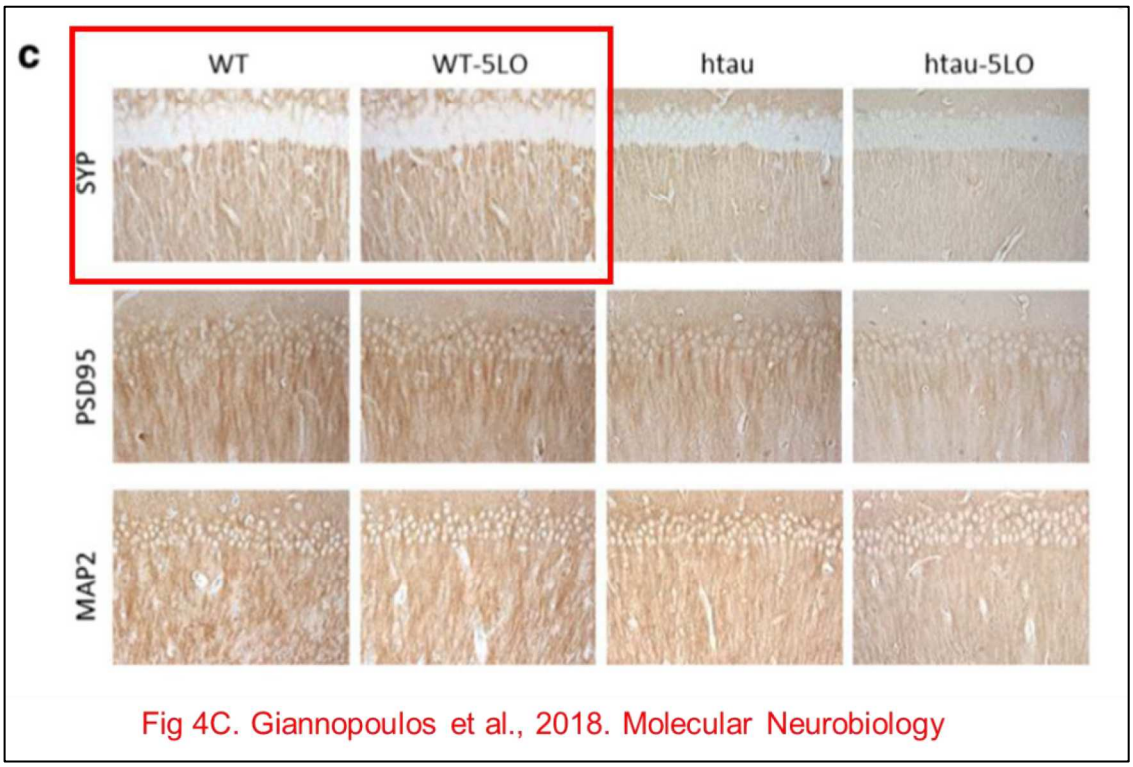

Fig 4C. Giannopoulos et al., 2018. Molecular Neurobiology

See graphs on the next page. In two studies that tested genetic and pharmacological rescue strategies using the 3xTg mouse model (Giannopoulos et al., 2013. Biological Psychiatry; Giannopoulos et al., 2014. Molecular Psychiatry), one study used 3xTg/FLAPKO mice and MK-591 treatment, to compare with WT and 3xTg mice, the other study used 3xTg/5LOKO mice and zileuton treatment, also to compare with WT and 3xTg mice. As shown on the next page, Fig 6. in Giannopoulos et al., 2013. Biological Psychiatry and Fig 5. in Giannopoulos et al., 2014. Molecular Psychiatry appear to contain identical electrophysiological data. Panel a in the 2013 paper appears identical to panel a of the 2014 paper; panel b in the 2013 paper appears identical to panel b in the 2014 paper; panels c in the 2013 paper appears identical to panel c in the 2014 paper-----despite the use of different genetic and pharmacological treatment groups in the two studies. While it might be reasonable to justify recycling WT and 3xTg data (if clearly stated), it is puzzling that WT and 3xTg data are NOT exactly the same in panel D and panel E of each paper.

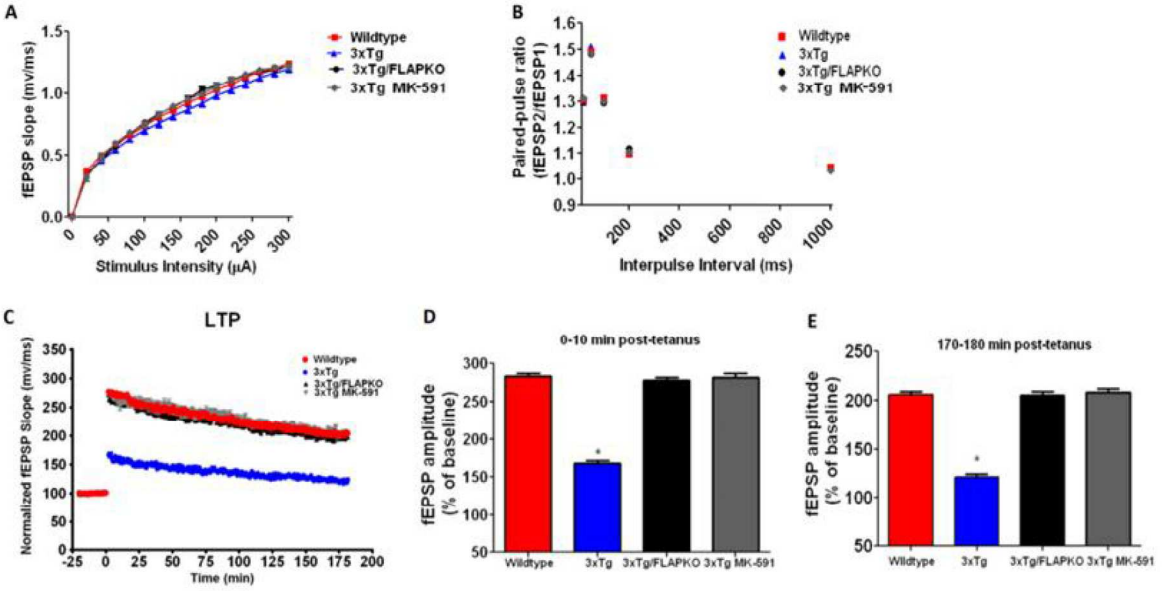

Fig 6. Giannopoulos et al., 2013. Biological Psychiatry

Wildtype and 3xTg mice, 3xTg mice genetically deficient for FLAP (3xTg-FLAPKO), and 3xTg mice treated with MK-591 at 6 months of age.

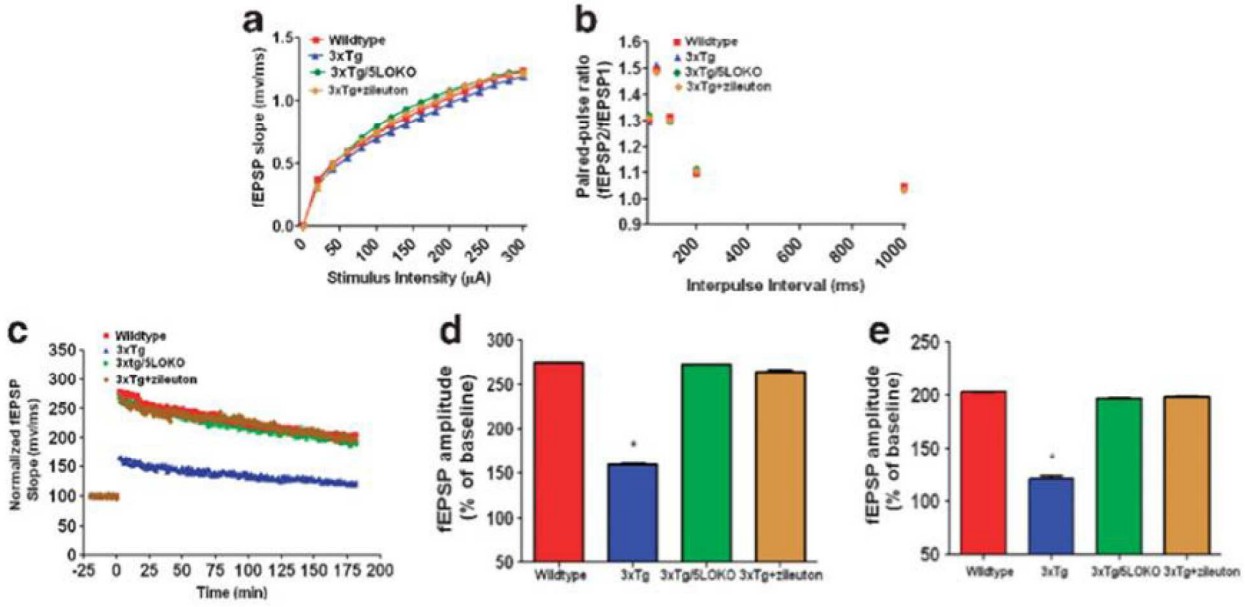

Fig 5. Giannopoulos et al., 2014. Molecular Psychiatry

Wildtype (WT),3xTg, 3xTg mice genetically deficient for 5LO (3xTg/5LOKO) and 3xTg+zileuton mice at 6 months of age.

References:

Giannopoulos, P.F., Chiu, J., and Pratico, D. (2018). Antileukotriene therapy by reducing tau phosphorylation improves synaptic integrity and cognition of P301S transgenic mice. Aging Cell *17*, e12759.

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Giannopoulos, P.F., Chu, J., Sperow, M., Li, J.G., Yu, W.H., Kirby, L.G., Abood, M., and Pratico, D. (2015). Pharmacologic inhibition of 5-lipoxygenase improves memory, rescues synaptic dysfunction, and ameliorates tau pathology in a transgenic model of tauopathy. Biol Psychiatry *78*, 693-701.

Giannopoulos, P.F., and Pratico, D. (2018). Overexpression of 5-Lipoxygenase Worsens the Phenotype of a Mouse Model of Tauopathy. Mol Neurobiol *55*, 5926-5936.

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Giannopoulos, P.F., Chu, J., Joshi, Y.B., Sperow, M., Li, J.G., Kirby, L.G., and Pratico, D. (2014). Gene knockout of 5-lipoxygenase rescues synaptic dysfunction and improves memory in the triple-transgenic model of Alzheimer's disease. Mol Psychiatry *19*, 511-518.