## Life Sciences Seminar

# Morphological determinants of cortical GABAergic interneuron myelination

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Cortical GABAergic fast-spiking parvalbumin-positive (PV) interneurons are frequently myelinated with a proximally-biased topography and account for a substantial fraction of neocortical myelin. Conversely, somatostatin-positive (SOM) interneurons contribute only modestly to myelin content in the cerebral cortex. Previous studies have demonstrated that myelinating glia are sensitive to fiber caliber for initiating axonal wrapping, however the majority of studies have focused on the peripheral nervous system or have been performed in cell culture settings. Given the substantial differences in axonal morphology between local PV+ and SOM+ interneurons, we therefore sought to examine whether cortical interneuron myelination might be related to axonal morphology in vivo. We now demonstrate that segmental axonal myelination of cortical interneurons is strongly predicted by the joint combination of interbranch-point distance and local axon caliber in both mouse and human neocortex. We further explored the robustness of this model by either increasing PV+ interneuron size with cell-type specific deletion of Tsc1 or reducing PV+ interneuron size by cell-type specific deletion of Ube3a. In both cases, although the frequency of myelinated segments was significantly altered, the joint combination of interbranch-point distance and local axon caliber remained highly predictive of myelin topography. Lastly, we considered regular-spiking SOM+ cells, which normally have relatively shorter interbranch distances and thinner axon diameters than PV+ cells, and are rarely myelinated. Enlargement of SOM+ cell size by cell type-specific deletion of Tsc1 dramatically increased the frequency of myelinated axonal segments and with a topography accurately predicted by the model. Together, our results suggest that local axonal morphology is an important determinant underlying the topography of cortical GABAergic interneuron myelination.

**Friday, January 17, 2020 01:00pm - 02:00pm**
Seminar Room, Lab Building East

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