

BBB seminar (BMED380)



Thursday, January 18. 14:30 at the BBB, Auditorium 4

The C1q family synaptic organizers: Unlocking therapeutic potential for neuropsychiatric and neurological disorders

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Numerous neuropsychiatric and neurodevelopmental disorders, including schizophrenia, Alzheimer's disease, and autism spectrum disorders, are believed to arise from synaptopathies characterized by synaptic loss or dysfunction. Despite extensive research, the mechanisms underlying synaptic damage and potential avenues for repair remain elusive. Synaptic organizers, which play crucial roles in synapse formation, maturation, and elimination, can be categorized into two main classes: cell adhesion molecules (*e.g.*, neurexin and neuroligin) and secreted diffusible molecules (*e.g.*, Wnt and FGF). We have proposed a third class known as extracellular scaffold proteins (ESPs), exemplified by Cbln1 and neuronal pentraxin 1 (NP1), which act as scaffolds at the synaptic cleft [1]. For example, Cbln1, a member of the C1q family, is released from presynaptic neurons in an activity-dependent manner [2] and promptly facilitates synapse formation by binding to GluD2 glutamate receptors in the adult cerebellum *in vivo* [3]. Furthermore, through the combination of structural elements from Cbln1 and NP1, we have designed a synthetic synaptic organizer, CPTX, which effectively restores synapses, spatial and contextual memory, as well as locomotion in mouse models of Alzheimer's disease and spinal cord injury [4]. In this seminar, I will provide an overview of the current understanding regarding the C1q family of synaptic organizers and explore the potential development of novel therapeutic agents for the treatment of neuropsychiatric and neurological disorders.

References:

1. Yuzaki M. *Annu Rev Physiol* 80:243-262, 2018.
2. Hirai H et al., *Nat Neurosci* 8:1534-41, 2005; Ibata K et al., *Neuron* 102:1184-1198, 2019.
3. Matsuda K et al., *Science* 328: 363-368, 2010; Elegheert J et al., *Science* 353:295-299, 2016.
4. Suzuki K et al., *Science* 369:eabb4853, 2020.

Chairperson: Hongyu Zhang (hongyu.zhang@uib.no), Dept. of Biomedicine