



Département de psychiatrie  
Centre de neurosciences psychiatriques  
Site de Cery  
CH-1008 Prilly - Lausanne

# Centre de Neurosciences Psychiatriques

## CNP SEMINAR

### ANNOUNCEMENT

Friday, June 30, 2017, 14:00

“Perineuronal net instability and neurological disorders”

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**Salle Forel**

**Hôpital Psychiatrique de Cery  
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During early postnatal development, different brain regions exhibit transient critical periods (CP) of heightened plasticity (Hensch, 2005). Beyond such CP, learning capacity is reduced and regenerative potential greatly limited. On the other hand, mis-timing of CP and aberrant plasticity are linked to neurodevelopmental disorders. Previous studies have identified particular extracellular matrix structure – perineuronal nets (PNNs) – as a ‘brake’ on plasticity. Here I present several lines of evidence suggesting that PNNs are in fact dynamic structures, and that their turnover plays an active role in plasticity control and injury response. First, I describe a novel mouse model in which reciprocal inhibition within parvalbumin (PV)-expressing interneuron is selectively impaired (PV-alpha1 KO mice). This excitatory-inhibitory (E-I) imbalance upon PV+ cells results in enhanced baseline gamma oscillations (30-80Hz) and PNN turnover. Subsequently, enhanced cortical plasticity is observed in these mice. Second, in a rat model of post-traumatic epileptogenesis, a loss of PNN and its binding factor, Otx2, is found to precede the loss of intracortical inhibition and seizure activities (Hsieh, Lee et al., 2016). Third, in another mouse model in which Otx2 is mutated so that its binding to PNN is disrupted, we report a global delayed PNN maturation and CP closure (Lee, Bernard, Ye et al., 2017). Therefore, PNN integrity is tightly regulated by neuronal activities and extracellular factors in normal brain development and upon injury. Mis-regulation in PNN turnover could be responsible for a wide range of neurological disorders.

#### Selected publications:

1. Hensch TK. **Critical period plasticity in local cortical circuits.** Nat Rev Neurosci. 2005 Nov; 6(11):877-888.
2. Hsieh TH, Lee HH et al. **Trajectory of parvalbumin cell impairment and loss of cortical inhibition in traumatic brain injury.** Cereb Cortex. 2016 Nov 30. [Epub ahead of print]
3. Lee HH, Bernard C, Ye Z et al. **Genetic Otx2 mis-localization delays critical period plasticity across brain regions.** Mol Psychiatry. 2017 May; 22(5):680-688.