# Molecular imaging at the synaptic level: the role of synaptic zinc in traumatic brain injury and neurodegenerative disease

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**Principal Investigators**

Per Malmberg

**Institution**

Chalmers University of Technology

**Contact information of lead PI**
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Sweden

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Molecular imaging at the synaptic level: the role of synaptic zinc in traumatic brain injury and neurodegenerative disease

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**Research Abstract**

The brain is not static during life. It is changing and reforming connections, pathways and synapses during events of learning and memory but also during injury and aging. This phenomenon is described as neuroplasticity and altered neuroplasticity may be the main cause behind neurodevelopmental and neurodegenerative disorders such as Alzheimer’s disease and autism spectrum disorders. The last few years a number of studies have indicated the

importance of zinc in regulating ion channels and intracellular pathways involved in neuroplasticity and also learning and memory. However very little is known about the role synaptic zinc plays in neuronal signal transduction and to gain a full understanding of the role synaptic zinc plays in memory formation a better understanding of different zinc reservoirs in the synapses is needed. This cannot be accomplished with the current methodology, using stains and fluorescent probes, and we propose to develop a nano-bio chemical imaging methodology for direct observation of synaptic interfaces with >10 nm spatial resolution using algorithms for image fusion of molecular, elemental and contrast data from NanoSIMS, Coherent anti-Stokes Raman scattering (CARS), and Helium-ion microscopy (HIM). Using this method we aim to measure changes in synaptic zinc and cell membrane lipids and correlate this information to dynamic changes observed in cells and tissue related to traumatic brain injury and neurodegenerative disease. This project therefore aims to (1) Establish the nanobio-imaging approach as an accurate and superior method for measuring endogenous metals at the synaptic level by combining information from nano-SIMS, super resolution CARS, and SIMS-HIM using image fusion. (2) Examine cell models and then simple animal models as well as rat and mouse models, to establish a baseline for synaptic zinc and lipids in cells and animals. HIM and NanoSIMS will be used to measure the zinc in nanometer regions of the cells to create molecular and elemental maps of a healthy neuron to understand the role of synaptic zinc in neuronal communication. (3) Determining changes in zinc concentration and kinetics in synaptic zones in relation to traumatic brain injury as well as neurodegenerative disease to obtain a molecular understanding of the damaged and diseased neuron. The development of these methods to measure lipids and zinc changing at the synapse level will lay the foundation to examine processes such as memory formation, brain injury and neurodegenerative diseases and in the future correlate them with changes in protein content in the synapse.

**Further information available at:**

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