

## Trimethyltin-induced hippocampal degeneration in developing rats: Modulation of reelin expression and endogenous neurogenesis

Amelia Toesca, Valentina Corvino, Maria Concetta Geloso and Fabrizio Michetti

Institute of Anatomy and Cell Biology, Università Cattolica del S. Cuore, Largo Francesco Vito 1, 000168, Rome, Italy

Trimethyltin (TMT) is a neurotoxicant inducing in rats selective neuronal death, mainly localised in hippocampal regions. Reelin is an extracellular matrix glycoprotein essential for the radial migration of cortical neurons during development and for the integration of dentate granular cell progenitors. In the hippocampus, reelin modulates the synaptic plasticity, its expression being down-regulated as brain maturation is completed (reviews 1-3). We analyzed the expression of reelin, and the modulation of neurogenesis, in the postnatal rat hippocampus during TMT-induced neurodegeneration. BrdU-analysis indicated an enhancement of hippocampal neurogenesis in the subgranular zone of TMT-treated rats (P21 and P28), the newly generated cells differentiating essentially towards neurons. Immunohistochemistry and Real-time PCR revealed that reelin expression remained almost unmodified in treated rats, while a time-dependent down-regulation in the hippocampus of control rats was observed, as expected. Quantitative analysis of reelin-IR cells evidenced, in treated animals, a persistent reelin expression in the stratum lacunosum moleculare of Cornu Ammonis and in the molecular layer of Dentate Gyrus. Thus TMT treatment enhances endogenous neurogenesis and prevents the physiological developmental decrease of reelin. These results hint at the possibility that both phenomena, in an integrated or distinct manner, might play a role in the tissue response to brain injury.

### References

- [1] Geloso et al. (2011) *Neurochem Int* 58: 729-738.
- [2] Corvino et al. (2013) *Neurochem Res* 38: 240-253.
- [3] Frotscher (2010) *Trends Neurosci* 33: 407-414.

### Key words

Trimethyltin, Hippocampal neurodegeneration, Reelin, Endogenous neurogenesis, Brain development.