

## **Detection of nicotinic receptors in normal and diseased brain**

Jens D. Mikkelsen, MD PhD

Neurobiology Research Unit, University Hospital Rigshospitalet, Copenhagen

### Research question and background

Nicotinic acetylcholine receptors (nAChRs) have long been known for their involvement in learning and memory processes, since it was shown that nicotine has pro-cognitive effects in animals and humans. Activation of one particular receptor, the  $\alpha 7$  nAChR, has is probably the most important of these receptors and small molecules activating the receptors have shown promising effects against cognitive deficits seen in both schizophrenia and Alzheimer's disease.

However, the mechanisms behind the beneficial effects of  $\alpha 7$  nAChR agonists at the level of the receptor protein, as well as at the systemic level are poorly understood. Several endogenous proteins and A $\beta$  have been demonstrated to interact with the  $\alpha 7$  nAChR and thereby influence its activation. This research project will focus on functional and pharmacological studies of the  $\alpha 7$  nAChR with emphasis on  $\alpha 7$  nAChR-interacting proteins in both normal and pathological conditions.

### Methods and tissues used

We will use frozen human brain sections from medial prefrontal cortex to determine the distribution of  $^{125}\text{I}$ - $\alpha$ -bungarotoxin binding sites, which will be an indicator of the  $\alpha 7$  nAChR binding sites in the human brain. The distribution and binding levels in patients with Alzheimer's disease and frontotemporal dementia will be compared to non-demented controls. Furthermore, we will in the same material by Western blotting detect proteins that are known to interact with the  $\alpha 7$  nAChR subunit such as  $\beta 2$  nAChR subunit and Lynx-1.

### Results and conclusion

Currently, there are no results in the project.