Summary

In this paper a characterization of two new splice variants of mouse Panx1 was conducted, an extended (mPanx1ext) and a truncated form (mPanx1tru). Their mRNA expression in various tissue was compared to that of wildtype Panx1 (mPanx1wt). All three forms showed different expression levels depending on tissue type. Over-expression analysis in N2a cells showed that the two new Panx1 proteins showed no distinct cellular expression. Presumably they were degraded shortly after the translation. This result was confirmed by Western blot analysis. The two new alternative splice forms of Panx1 meet no detectable function(s) in the mouse, according to the knowledge this work.

The focus of this thesis was the establishment of an experimental model of ischemia using metabolic inhibition and subsequent analysis of Panx1 function. Thus isolated neuronal cultures were stressed by ischemia and their metabolic activity and cytotoxicity was determined. Neurons of Panx1-KO animals and WT neurons blocked by MFQ under ischemic conditions during an early phase were better protected than WT neurons. In a second approach, the electrophysiological behavior of WT and Panx1-KO hippocampal slices were measured under ischemic conditions on the basis of field potentials. This approach confirmed a protective effect of the Panx1-KO phenotype, since these slices respond less sensitively on the applied ischemic conditions compared to WT sections. The network regulating effect of GABA\textsubscript{A} receptors in ischemic conditions was mediated about 40% by the by the presence of Panx1 channels. These two results confirm that Panx1-KO sections can adapt better to ischemia than those expressing the Panx1 channel.

Finally an expression analysis of hypoxia and plasticity related transcripts was performed on hippocampal slices incubated with and without MI. This analysis shows that the Panx1-KO leads to a significant destabilization of the transcriptome under MI.
In conclusion after evaluating all submitted experiments and the recent literature, a regulatory effect of Panx1 protein on the hippocampal network under ischemia can be described. Taking into account the known channel biophysical properties, expression pattern and (patho)physiological relevance, it can be concluded that Panx1 a potential target for therapeutic intervention early after an ischemic attack. The work presented here is a building block for further, more clinically relevant biomedical understanding the function(s) of Panx1 in the nervous system.