

# Contents

<b>Index of abbreviations.....</b>	
<b>1 Introduction.....</b>	<b>1</b>
1.1 Acid-sensing ion channels belong to the degenerin/epithelial Na <sup>+</sup> channel family .....	1
1.2 Expression sites and functions of ASICs and BASIC .....	3
1.2.1 Expression sites .....	3
1.2.2 Physiological functions and pathophysiological roles of ASICs.....	3
1.3 Structure of ASICs and BASIC .....	4
1.4 Electrophysiological properties of ASICs and BASIC .....	5
1.5 Neuropeptides and venom toxins modulate ASICs .....	7
1.5.1 FMRFamide and related neuropeptides .....	7
1.5.2 Endomorphins and dynorphins.....	9
1.5.3 Venom toxins .....	10
<b>2 Aim.....</b>	<b>11</b>
<b>3 Materials and methods.....</b>	<b>12</b>
3.1 Materials.....	12
3.1.1 Standard chemicals .....	12
3.1.2 The neuropeptides.....	12
3.1.3 Molecular biological materials .....	17
3.2 Molecular biology .....	17
3.2.1 Preparation, linearization and purification of plasmid DNA.....	17
3.2.2 Synthesis and purification of mRNA .....	18
3.3 Electrophysiological recordings .....	18
3.3.1 Preparation of oocytes.....	18
3.3.2 Injection of oocytes.....	19
3.3.3 The two-electrode voltage clamp technique .....	20
3.3.4 The TEVC set-up.....	21
3.3.5 Solutions for two-electrode voltage clamp recordings .....	21
3.3.6 Experimental protocols .....	22

3.3.7 Choosing the conditioning and activation pH for ASIC1a, ASIC1b and ASIC3 .....	24
3.3.8 Data analysis.....	25
<b>4 Results.....</b>	<b>27</b>
4.1 Experiments on ASIC4 and BASIC expressing oocytes.....	27
4.1.1 There is no direct agonist for ASIC4 among the 109 screened neuropeptides .....	27
4.1.2 There is no direct agonist for BASIC among the 109 screened neuropeptides .....	29
4.2 Experiments on ASIC1a, ASIC1b and ASIC3 expressing oocytes.....	31
4.2.1 Dynorphin A(1-13) and dynorphin A(1-17) pre-application increased currents of ASIC1a .....	31
4.2.2 YFMRFamide pre-application decreased current amplitude and slowed desensitization of ASIC1b.....	37
4.2.3 Endomorphin-1 and YFMRFamide pre-applications slowed ASIC3 desensitization .....	42
4.3 Comparing RPRFamide's, FMRFamide's and YFMRFamide's effect on ASIC3 desensitization .....	50
<b>5 Discussion.....</b>	<b>52</b>
5.1 The search for direct agonists .....	52
5.1.1 Discussion of the results.....	52
5.1.2 Limitations .....	53
5.2 The search for new modulators.....	53
5.2.1 Discussion of the results.....	53
5.2.2 Limitations .....	54

5.2 Conclusion.....	56
<b>6 Summary .....</b>	<b>57</b>
<b>7 References .....</b>	<b>58</b>
<b>Auflistung eigener Publikationen.....</b>	<b>65</b>
<b>Danksagung .....</b>	<b>66</b>
<b>Erklärung § 5 Abs. 1 zur Datenaufbewahrung.....</b>	<b>67</b>
<b>Eidesstattliche Erklärung über den Eigenanteil gemäß § 5 Abs. (1) und § 11 Abs. (3) 12. der Promotionsordnung .....</b>	<b>68</b>