

CONTENTS

1. INTRODUCTION 1

1.1. Architecture of the lung..... 1

1.2. Physiology of the lung 1

1.3. Acute respiratory distress syndrome 3

1.3.1. Pathophysiology 3

1.3.2. Animal models..... 4

1.4. Ventilator-induced lung injury 5

1.4.1. Pathophysiology 5

1.4.2. Lung protective ventilation..... 8

1.5. Intracellular mechanisms of converting mechanical stimuli 10

1.5.1. Responses to mechanical forces 10

1.5.1.1. Cell death..... 10

1.5.1.2. Pro-apoptotic pathways 10

1.5.1.3. Anti-apoptotic pathways..... 13

1.5.1.4. Mitogen-activated protein kinase pathways 15

1.6. Aim of the study 17

2. MATERIALS AND METHODS 18

2.1. Materials 18

2.1.1. Equipment..... 18

2.1.2. Reagents 19

2.2. Methods 20

2.2.1. Animal models..... 20

2.2.2. Protein isolation from lungs 22

2.2.3. Measuring protein concentration..... 23

2.2.4. SDS polyacrylamide gel electrophoresis 23

2.2.5. Protein blotting 25

2.2.6. Protein visualisation 25

2.2.7. RNA isolation 27

2.2.8. Measuring RNA concentration..... 28

2.2.9. cDNA synthesis 28

2.2.10. Real-time polymerase chain reaction 29

2.2.11. Cryosections - immunohistochemistry	30
2.2.12. Statistical analysis	32
3. RESULTS.....	33
3.1. Protein expression analysis.....	33
3.1.1. The mitogen-activated protein kinases	33
3.1.2. PI3K-Akt pathway	33
3.1.3. Markers of cell death	34
3.2. Gene expression analysis.....	35
3.3. Immunohistochemistry	38
4. DISCUSSION.....	40
5. ABSTRACT	48
6. ZUSAMMENFASSUNG	49
7. ABBREVIATIONS	50
8. REFERENCES	54
9. ERKLÄRUNG ZUR DISSERTATION	68
10. DANKSAGUNG	69