

TABLE OF CONTENTS

Zusammenfassung	I
Résumé	IV
Summary	VII
Table of contents	IX

Chapter 1 – Introduction: key concepts and methods	1
1.1 Cell surface receptors	1
1.2 G protein-coupled receptors (GPCRs)	2
1.2.1 GPCR classification	2
1.2.2 GPCR signaling	4
• Signaling via heterotrimeric G-proteins	4
• Signaling via GPCR kinases and arrestins	6
• Biased signaling	6
• GPCR basal activity	7
1.2.3 Structure-function relationships and structural properties of GPCRs	7
1.3 Protease-activated receptors (PARs)	12
1.3.1 Mechanism of activation	12
1.3.2 PAR1 and PAR2 signaling	13
1.3.3 PARs in health and disease	15
1.4 Cell adhesion	18
1.4.1 Integrins	18
• Integrin signaling	19
• The adhesome	21
• Fibronectin-binding integrins in wound healing	21
• PAR-regulation of integrin affinity	22
1.5 Atomic force microscopy (AFM)	23
1.5.1 AFM-based single molecule force spectroscopy (SMFS)	23
1.5.2 AFM-based single cell force spectroscopy (SCFS)	25
1.6 References	28

Chapter 2 – Structural properties of human PAR1	39	Chapter 4 – Conclusion and perspectives	131
2.1 Structural properties of PAR1 changing upon binding of a strong antagonist	39	4.1 Conclusion	131
2.1.1 Author contributions	39	4.2 Outlook into translation	133
2.1.2 Summary	40	4.3 References	135
2.1.3 Introduction	41	Chapter 5 – Acknowledgements	137
2.1.4 Results	43	Appendix	
2.1.5 Discussion	53		
2.1.6 Methods	56		
2.1.7 Acknowledgments	64		
2.1.8 Supplementary data	65		
2.1.9 Cover	70		
2.1.10 References	71		
2.2 Structural properties of PAR1 changing upon binding of a peptide-mimetic antagonist	76		
2.2.1 Contributors	76		
2.2.2 Summary	77		
2.2.3 Introduction	78		
2.2.4 Results	79		
2.2.5 Discussion	86		
2.2.6 Methods	88		
2.2.7 Acknowledgments	89		
2.2.8 Supplementary data	90		
2.2.9 References	91		
Chapter 3 – PARs in early cell adhesion	93		
3.1 In fibroblasts PARs promote $\alpha 5\beta 1$ integrin-mediated adhesome assembly to strengthen early cell adhesion	93		
3.1.1 Author contributions	93		
3.1.2 Summary	94		
3.1.3 Introduction	95		
3.1.4 Results	97		
3.1.5 Discussion	108		
3.1.6 Methods	112		
3.1.7 Acknowledgments	117		
3.1.8 Supplementary data	118		
3.1.9 References	126		