

Table of contents

Acknowledgments 1

Abstract 2

Table of contents..... 3

Abbreviations 5

1. Introduction..... 8

 1.1 The hemostatic system..... 8

 1.1.1 Primary hemostasis 8

 1.1.2 Secondary hemostasis 9

 1.1.3 Fibrin formation and fibrinolysis 11

 1.2 The complement system 13

 1.2.1 The classical pathway 14

 1.2.2 The lectin pathway 14

 1.2.3 The alternative pathway..... 15

 1.2.4 Effector functions of the complement system..... 16

 1.2.5 Interaction with the adaptive immune system 17

 1.2.6 Regulation of the complement system 17

 1.3 Crosstalk between the complement and the hemostatic system..... 19

 1.3.1 Interactions between the complement and the coagulation system 19

 1.3.2 Interactions between the complement and the fibrinolytic system..... 20

 1.3.3 Shared regulatory proteins..... 21

 1.4 Pathophysiological aspects of the complement system 22

 1.4.1 Complement in cardio and- cerebrovascular disease 22

 1.4.2 Complement in diabetes 24

 1.5 MASP-1 26

 1.5.1 MASP-1 in coagulation 27

2. Aim and rationale of the project 29

3. Published results 30

 3.1 MASP-1 of the complement system promotes clotting via prothrombin activation..... 30

 3.2 MASP-1 Induced Clotting – The first Model of Prothrombin Activation by MASP-1 40

 3.3 Plasma levels of mannan-binding lectin-associated serine proteases MASP-1 and MASP-2 are elevated in type 1 diabetes and correlate with glycaemic control 54

4. Unpublished results..... 61

4.1 The effect of MASP-1 on clot fibrinolysis 61

4.1.1 Background and aim 61

4.1.2 Materials and methods 61

4.1.3 Results 62

4.1.4 Discussion 63

4.2 MASP-1 enhances clot formation in a microvascular flow model 64

4.2.1 Background and aim 64

4.2.2 Materials and methods 66

4.2.3 Results 67

4.2.4 Discussion 68

5. General discussion..... 70

6. References 74

7. Declaration of originality 91

8. Curriculum Vitae..... 92

9. Appendix..... 95