

## Content

<b>1. General Introduction.....</b>	<b>1</b>
1.1 Immune System .....	3
1.1.1 Innate and Adaptive Immunity .....	3
1.1.2 Major Histocompatibility Complexes .....	7
1.1.3 Antibodies .....	8
1.2 Autoimmunity .....	11
1.2.1 Autoimmune Diseases .....	11
1.3 Systemic Lupus Erythematosus.....	15
1.3.1 Pathogenesis, Prevalence, Genetic and Environmental Contributions ...	15
1.3.2 Autoantibodies variety in SLE patients.....	17
1.3.3 Diagnosis .....	18
1.4 Principal Autoantigen in Systemic Lupus Erythematosus.....	23
1.4.1 Target of Autoantibodies .....	23
1.4.2 TRIM21: Variants, Structure and SLE Relationship.....	24
1.4.3 TROVE2: Variants, Structure and SLE Relationship.....	26
1.5 References .....	29
<b>2. Objectives .....</b>	<b>35</b>
<b>Chapter I:Structural basis for the Functional Mechanism of TRIM21<math>\alpha</math> in Systemic Lupus Erythematosus.....</b>	<b>41</b>
1.1 Monitoring anti-TRIM21 autoantibodies.....	43
1.2 TRIM21 $\alpha$ :IgG complex at equilibrium .....	46
1.3 Conformational dynamics .....	48
1.4 Modelling the recognition .....	51
1.5 Linear epitope mapping.....	55
1.6 TRIM21 $\alpha$ structure .....	58
1.7 Discussion .....	61
1.8 References .....	62
<b>Chapter II: Functional Mechanism of the TROVE2 RNA-binding Protein in SLE .....</b>	<b>65</b>

2.1 Monitoring anti-TROVE2 autoantibodies .....	67
2.2 Dynamic analysis of autoantibodies recognition.....	70
2.3 Modelling the recognition .....	72
2.4 MIDAS motif .....	75
2.5 Discussion .....	78
2.6 References .....	79
<b>Chapter III: Label-free Piezoelectric Biosensor for Determination of Circulating Autoantibodies for Systemic Lupus Erythematosus Diagnosis ..</b>	<b>81</b>
3.1 QCM-D-based anti-TRIM21 biosensor.....	83
3.2 QCM-D-based TROVE2 biosensor.....	85
3.3 Interaction fingerprint pattern .....	88
3.4 Reusability.....	90
3.5 Multiplex assay .....	90
3.6 Biostatistics .....	94
3.7 Discussion .....	95
<b>4. Materials and Methods.....</b>	<b>99</b>
4.1 Serum Samples.....	101
4.2 IgG Purification.....	101
4.3 Quartz crystal microbalance with dissipation monitoring (QCM-D).....	102
4.3.1 Self-Assembly Monolayer (SAM) .....	102
4.3.2 Immobilisation of TRIM21 and TROVE2 on hydrazine chip.....	102
4.3.3 Immobilisation of the N-terminal polypeptides on carboxyl chip.....	103
4.3.4 C-terminal immobilisation of TROVE2 incubated with divalent cations .....	103
4.3.5 Calculation of the $-\Delta f/\Delta D$ ratio with the system at equilibrium.....	104
4.3.6 Calculation of the instantaneous recognition of the proteins and IgGs though the $-\partial f/\partial D$ function.....	105
4.4 Characterization Techniques .....	106
4.4.1 Static Water Contact Angle (CA) Measurements .....	106
4.4.2 Infrared Reflection Absorption Spectroscopy (IRRAS) .....	107
4.4.3 X-ray Photoelectron Spectroscopy (XPS).....	107
4.5 Dual Polarization Interferometry.....	108

4.5.1 Chip treatment.....	108
4.5.2 Determination of the Thickness per molecule.....	109
4.6 Prediction of TRIM21 $\alpha$ structure.....	110
4.7 DVD based immunoassay .....	110
4.8 References .....	111
<b>5. General Discussion.....</b>	<b>113</b>
5.1 References .....	120
<b>6. Conclusions.....</b>	<b>123</b>
<b>7. Appendix.....</b>	<b>129</b>