

# Contents

**Acknowledgements .....i**

**Abstract..... iii**

**Résumé..... v**

**Contents .....vii**

**Chapter 1      Introduction..... 1**

    1.1    Tissue engineering..... 1

        1.1.1    Engineered tissues for transplantation ..... 1

        1.1.2    In vitro tissue-engineered 3D models ..... 2

    1.2    The extracellular matrix..... 3

        1.2.1    Main components of the ECM ..... 4

        1.2.2    Cell-ECM interactions and remodeling..... 5

        1.2.3    Role of the ECM in wound healing ..... 6

    1.3    Growth factors interactions with the ECM..... 7

    1.4    Approaches to recreate the ECM ..... 8

        1.4.1    Poly(ethylene glycol) as a biopolymer for engineering scaffolds ..... 9

        1.4.2    Enzymatically cross-linked PEG hydrogel platform ..... 9

    1.5    Vascularization and tissue engineering models ..... 10

        1.5.1    Regulation of angiogenesis ..... 11

        1.5.2    The role of the extracellular matrix in angiogenesis ..... 12

        1.5.3    Angiogenic growth factors ..... 12

    1.6    Motivation and objectives..... 13

    1.7    References..... 14

**Chapter 2      Modular poly(ethylene glycol) matrices for controlled 3D-localized cell differentiation .....19**

    2.1    Introduction..... 19

    2.2    Results and Discussion..... 21

        2.2.1    Design of streptavidin/biotin-based growth factor-presenting TG-PEG hydrogels..... 21

        2.2.2    Production and characterization of streptavidin-modified TG-PEG hydrogels ..... 22

        2.2.3    Biotinylation of BMP-2 ..... 23

        2.2.4    Binding and release of rhBMP-2-biotin from Gln-streptavidin hydrogels..... 26

        2.2.5    Osteogenic differentiation of C2C12 cells on hydrogels with immobilized BMP-2 ..... 27

        2.2.6    Localized 3D osteogenic differentiation of mesenchymal stem cells..... 28

2.3	Conclusion .....	32
2.4	Experimental Section .....	32
2.5	References .....	37
<b>Chapter 3</b>	<b>Engineered poly(ethylene glycol) matrices for cell-dependent proteolytic release of growth factors.....</b>	<b>39</b>
3.1	Introduction .....	39
3.2	Results and Discussion .....	41
3.2.1	Design of a proteolytically degradable streptavidin peptide linker .....	41
3.2.2	Production and characterization of the degradable streptavidin linker .....	42
3.2.3	Binding of biotinylated proteins to streptavidin hydrogels.....	44
3.2.4	Release of rhBMP-2-biotin from streptavidin hydrogels.....	46
3.2.5	Osteogenic differentiation of cells in streptavidin hydrogels .....	47
3.2.6	Degradable linkers for the immobilization and release of growth factors.....	51
3.3	Conclusion .....	52
3.4	Experimental Section .....	53
3.5	References .....	56
<b>Chapter 4</b>	<b>Evaluation of growth factors modulating angiogenesis .....</b>	<b>59</b>
4.1	Introduction .....	59
4.1.1	Objective .....	61
4.2	Results and discussion .....	61
4.2.1	Anti-angiogenic effect of netrin-4 on the chicken CAM .....	61
4.2.2	Effects of ephrins and VEGF on the chicken CAM .....	63
4.2.3	Casting of the CAM with polyurethane for $\mu$ CT quantification .....	65
4.2.4	Effects of ephrins cell migration.....	66
4.3	Conclusion .....	69
4.4	Experimental Section .....	70
4.5	References .....	72
<b>Chapter 5</b>	<b>Conclusion .....</b>	<b>75</b>
5.1	Achieved results .....	75
5.1.1	Streptavidin linker for the controlled and localized immobilization of growth factors .....	75
5.1.2	MMP-sensitive streptavidin linker for cell-dependent release of immobilized growth factors.....	76
5.1.3	Growth factors modulating angiogenesis .....	76
5.2	Future developments .....	78
5.3	References .....	80
<b>Bibliography .....</b>		<b>83</b>
<b>Curriculum Vitae .....</b>		<b>91</b>
<b>List of publications .....</b>		<b>93</b>