
Table Of Contents

Chapters	Page No.
List of Figures	(i)
List of Tables	(iv)
List of Abbreviations.....	(v)
Abstract.....	(viii)
CHAPTER ONE	
1. Introduction.....	1
1.1 Oligodendrocytes biology and function.....	1
1.2 Disorders of central nervous system and oligodendrocytes.....	2
1.3 Regulation of oligodendrocyte behaviour	4
1.4 Growth Factor receptor regulation of OPC behaviour.....	5
1.5 The role of Integrins in regulating OLG behavior CNS.....	6
1.6 Receptor Tyrosine Kinases (RTK) activated intracellular signaling cascades.....	7
1.7 Integrin activated intracellular signaling cascades.....	9
1.8 Role of Lipid Rafts in the Stabilization of PDGFR α and Integrins interaction.....	10
1.9 Cytoskeleton of oligodendrocytes.....	11
1.10 Glioblastoma multiforme.....	11
1.11 Anoikis resistance in glioma.....	12
1.12 Role of PDGFR α in glioma.....	13
1.13 Role of lipid rafts in glioma.....	13
1.14 Rationale of the study.....	14
1.15 Hypothesis of the study.....	15
1.16 Objectives of the study.....	16
1.17 Significance of current study.....	16

CHAPTER TWO

2. Materials and Methods	17
2.1 Oligodendrocyte Progenitor Cells isolation and culture	17
2.2 Glioma Cell Line	19
2.3 Agarose drop cell migration assay	19
2.4 Immunocytochemistry	20
2.5 Protein Extraction, Protein Quantification and Western Blotting.....	21
2.6 Immunoprecipitation	23
2.7 Cell surface receptor biotinylation and internalization assay	24
2.8 Lipid raft staining	24
2.9 Anoikis assay	25
2.10 Actin cytoskeleton fraction	25
2.11 Treatment Groups	25
2.12 Microscopy, quantification and statistical analysis	27

CHAPTER THREE

3. To study the combinatorial effects of PDGF and ECM on OPC migration	28
3.1 Introduction.....	28
3.2 Plan of work.....	29
3.3 Results.....	29
3.3.1. Individual effects of PDGF-A and ECM on OPC migration	29
3.3.2. Physiological concentration of PDGF-A require FN engagement to augment OPC migration.....	30
3.3.3. Physiological concentration of PDGF-A require FN engagement to promote F-actin and filopodia formation.	31
3.3.4. Higher concentration of PDGF-A doesn't require FN engagement to augment OPC migration.....	32
3.4 Discussion.....	47

CHAPTER FOUR

4. To study the Role of PDGFRα in Integrin switching	53
4.1 Introduction.....	53
4.2 Plan of work.....	54
4.3 Results.....	54
4.3.1. Dose-dependent effect of PDGFR α activation on $\alpha v\beta 1$ and $\alpha v\beta 3$ integrins expression.....	54
4.3.2. Time-dependent effects of PDGFA on $\alpha v\beta 1$ and $\alpha v\beta 3$ integrins expression.....	55
4.3.3. Role of pERK1/2 and actin cytoskeleton in PDGFR α activation mediated integrin switching ($\alpha v\beta 1$ and $\alpha v\beta 3$).....	56
4.3.4. PDGFR α inhibition modulates integrin switching during anoikis resistance in C6 glioma cells	56
4.3.5. PDGFR α and $\alpha v\beta 3$ integrin uncouples during anoikis resistance.....	57
4.4. Discussion.....	72

CHAPTER FIVE

5. To study PDGFRα and Integrin interaction: role of Lipid rafts	78
5.1 Introduction.....	78
5.2 Plan of work.....	79
5.3 Results.....	79
5.3.1. PDGF-A increased lipid raft in OPCs	79
5.3.2. PDGFR α activation mediated lipid raft-actin interaction	80
5.3.3. Lipid raft depletion by FB1 decreased the PDGF-A mediated effects on OPCs.....	80
5.3.4. PDGF-A reverts the effects of M β CD on OPCs.....	81
5.3.5. Lipid raft internalization regulates PDGFR α - $\alpha V\beta 3$ interaction in C6 glioma cells.....	81
5.4. Discussion.....	94
6. Summary.....	98
Bibliography.....	107
List of Publications.....	129