

Aus dem International Graduate Program Medical Neurosciences  
der Medizinischen Fakultät der Charité – Universitätsmedizin Berlin

DISSERTATION

**The role of microglia in glioma invasiveness**

Zur Erlangung des akademischen Grades  
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## Table of contents

I. List of figures .....	5
II. List of tables.....	6
III. List of abbreviations .....	7
1. Introduction .....	8
1.1. Cancer in general.....	8
1.1.2. The hallmarks of cancer .....	8
1.1.2.1. Self-sufficiency in growth signals.....	8
1.1.2.2. Insensitivity to antigrowth signals.....	9
1.1.2.3. Evading apoptosis.....	9
1.1.2.4. Limitless replicative potential .....	10
1.1.2.5. Sustained angiogenesis.....	10
1.1.2.6. Tissue invasion and metastasis .....	10
1.1.3. Tumor stroma interaction .....	11
1.2. The immune system of the brain .....	11
1.2.1. The origin of microglia.....	12
1.2.2. The function of microglia.....	13
1.2.2.1. Resting or ramified microglia.....	13
1.2.2.2. Activated or amoeboid microglia .....	14
1.3. Brain tumors .....	16
1.3.1. Role of microglia in brain tumors .....	16
1.3.1.1. Immune cell infiltration of intrinsic intracranial tumors .....	16
1.3.1.2. Microglia-glioma cross talk.....	17
1.3.2. Glioma cell evasion of the immune response.....	18
1.4. Matrix metalloproteinases .....	19
1.4.1. Regulation of MMPs .....	20
1.4.1.2. Extracellular proMMP-2 activation cascade .....	22
1.5. The MMPs and cancer.....	23
1.5.1. The role of metalloproteinases in brain tumors.....	23
1.6. Aim of the study .....	24
2. Materials and Methods .....	25
2.1. Materials .....	25
2.1.1. Reagents and Chemicals.....	25
2.1.2. Kits .....	26
2.1.3. Primary antibodies.....	27

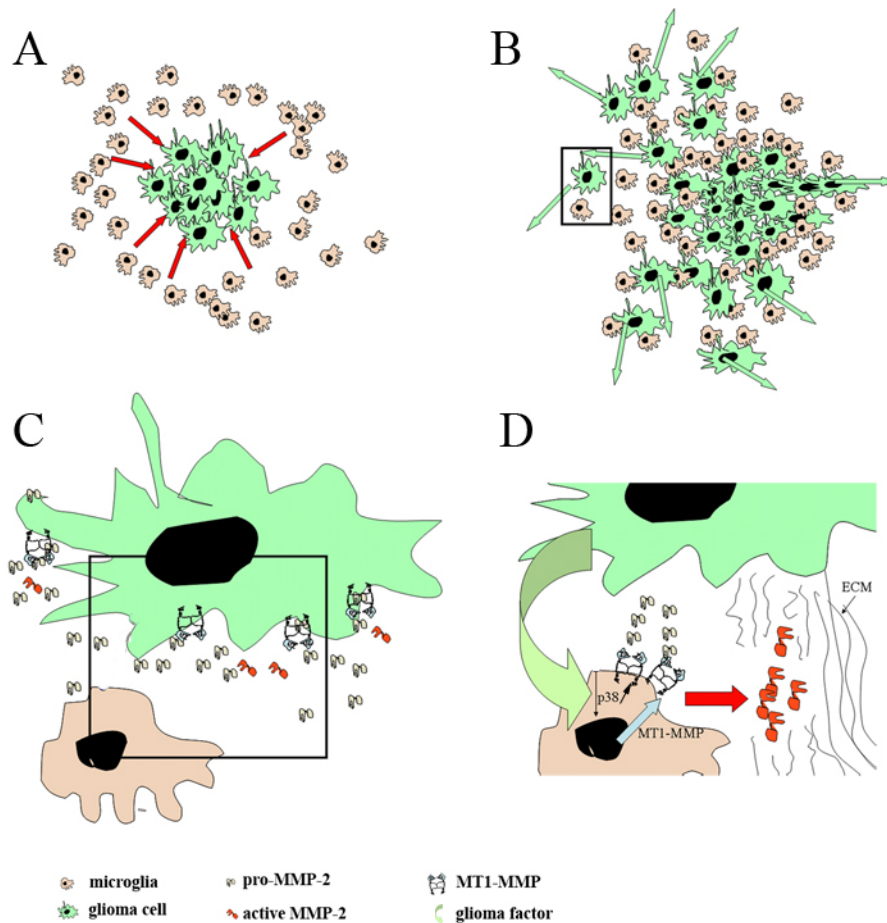
2.1.4. Equipment.....	28
2.1.5. Cell culture equipment .....	29
2.1.6. Cell culture media.....	30
2.1.7. Buffers and Media .....	31
2.1.7.1. Bacteria propagation.....	31
2.1.7.2. Cell culture media.....	31
2.1.7.3. Immunolabeling.....	31
2.1.7.4. Gelatine zymography.....	31
2.1.7.5. Western Blotting.....	32
2.1.8. Software.....	32
2.2. Methods .....	33
2.2.1. Microglial cell culture .....	33
2.2.2. Glioma cell lines.....	33
2.2.3. Amplification of vectors.....	34
2.2.4. G418 sensitivity test .....	34
2.2.5. Transfection of glioma cell lines .....	35
2.2.6. Fluorescence Assisted Cell Sorting (FACS) of EGFP expressing glioma cells.....	36
2.2.7. The organotypical brain slice model .....	38
2.2.7.1. Liposomes.....	38
2.2.7.2. Glioma cell injection into brain slices.....	39
2.2.8. In vivo Inoculation of GL261 cells into C57/BL6 mouse brain.....	39
2.2.8.1. Anesthesia.....	39
2.2.8.2. Glioma inoculation into the mouse brain .....	39
2.2.8.3. Paraformaldehyde fixation .....	40
2.2.8.4. Immunohistochemistry of brain sections (Floating sections).....	40
2.2.9. Immunofluorescence of organotypical brain slice cultures.....	40
2.2.9.1. Tissue preparation for immunolabeling.....	40
2.2.9.2. Immunolabeling.....	41
2.2.10. Microscopy .....	41
2.2.10.1. Two- Photon microscopy .....	41
2.2.10.2. Confocal microscopy.....	41
2.2.10.3. Fluorescence microscopy .....	42
2.2.11. Quantification of glioma cells invasion in organotypical brain slice cultures .....	42

2.2.12. Gelatin zymography .....	43
2.2.13. Western blot.....	43
2.2.13.1. Sample preparation.....	43
2.2.13.2. SDS PAGE .....	44
2.2.13. 3. Semi-dry trans blotting.....	44
2.2.13.4. Immunoblotting .....	45
2.2.14. MT1-MMP activity assay.....	45
2.2.15. Statistical analysis .....	45
3. Results .....	46
3.1. Characterization of the glioma experimental model .....	46
3.1.1. Organotypical brain slice cultures can be selectively depleted of microglia	46
3.1.2. Organotypical brain slice cultures and GL261 glioma cells remain viable	
after clodronate liposome treatment .....	48
3.1.3. Astrocytes and neurons are not affected by clodronate treatment.....	50
3.1.4. Tumor cell migration can be quantified after inoculation of glioma cells	
into cultured brain slices.....	53
3.1.5. Experimental gliomas in organotypical brain slice cultures share features	
with human glioblastomas.....	55
3.2. Glioma invasion directly correlates with microglia density.....	56
3.2.1. In microglia-depleted organotypical brain slice cultures glioblastoma cell	
invasion is impaired.....	56
3.2.2. Co-injection of microglia and gliomas promotes invasion of glioma cells	
3.2.3. LPS stimulation does not increase glioma invasiveness in organotypical	
brain slice cultures.....	60
3.3. Microglia increases MMP-2 activation .....	62
3.3.1. Glioma induced MMP-2 activity is elevated in organotypical brain slice	
cultures containing microglia .....	62
3.3.2. A soluble factor from glioma triggers the activation of MMP-2 in cultured	
microglial cells .....	63
3.3.3. Microglia activates MMP-2.....	64
3.3.4. Iba-1 positive cells are accumulating at experimental gliomas.....	65
3.3.5. The expression of MT1-MMP is increased in microglia surrounding	
gliomas .....	65
3.3.6. Microglial expression of MT1-MMP is up- regulated after stimulation	
with GL261 conditioned medium (GCM).....	66

3.3.7. The MT1-MMP activity is increased after stimulation with GL261 conditioned medium (GCM) .....	68
4. Discussion.....	69
4.1. Organotypical brain slice cultures are an in vitro experimental model which resembles important features of living brain .....	69
4.2. A model for studying human gliomas .....	70
4.2.1. Organotypical brain slice culture is model of choice to study glioma invasion in vitro .....	70
4.2.2. Gliomas in organotypical brain slice cultures are sharing features with human gliomas.....	73
4.3. Microglia depletion .....	74
4.3.1. Microglia .....	75
4.3.2. Astrocytes .....	76
4.3.3. Endothelium .....	76
4.3.4. Neurons.....	76
4.4. Microglia promote tumor invasion.....	77
4.5. MMP-2 activity in gliomas.....	78
4.6. MT1-MMP is expressed predominantly in microglia in mouse gliomas .....	79
4.7. MT1-MMP is up-regulated on microglia when stimulated with GL261 conditioned medium (GCM) .....	80
4.8. GL261 conditioned medium (GCM) up-regulates MT1-MMP in microglia via the p38 MAPK pathway .....	81
5. Summary.....	83
6. References .....	84
Acknowledgements .....	101
Curriculum Vitae .....	102
List of publications .....	103
Meetings with poster presentations .....	104
Eidesstattliche Erklärung.....	105

## 5. Summary

Microglia significantly contribute to the glioma tumor mass by infiltrating primary tumor mass (Fig 5.1. A). The net effect of microglial abundance in gliomas is tumor promoting by inducing the glioma invasiveness (Fig 5.1. B). The result of microglia-glioma cross-talk is escalation of MMP-2 activation and that leads to increased breakdown of ECM proteins which can explain increase of glioma invasiveness (Fig 5.1. C-D). Glioma release a factor which stimulates the production of a major MMP-2 activator- MT1-MMP in microglia. Moreover, the expression of MT1-MMP is mediated by p38 MAPK, which makes this kinase a possible target for therapy of invasive gliomas (Fig 5.1. D).



**Fig. 5.1. Microglia-glioma interaction.** A-B. Microglia are aggregating at the glioma inoculum in organotypical brain slice cultures and their presence increases invasiveness of glioma cells. C. Microglia-glioma cross-talk (enlarged from B). Microglia and glioma cell are close to each other and gliomas are releasing large amounts of inactive proMMP-2. D. Glioma cell releases a factor which stimulates, via p38 MAPK activation, expression of MT1-MMP. Finally, as a result of MT1-MMP over-expression the large amounts of active MMP-2 are released, which are in turn degrading ECM proteins and thereby increase the glioma invasiveness.

**I. List of figures**

Fig. 1.1. Six essential alterations leading to cancer	9
Fig. 1.2. Microglial developmental stages	13
Fig. 1.3. Activation cascade of MMP-2	22
Fig. 2.1. Restriction map and Multiple Cloning Site (MCS) of pEGFP-N1 vector	34
Fig. 2.2. FACS of the EGFP expressing glioma cells	37
Fig. 3.1. Microglia are depleted in cultured brain slices after clodronate liposomes treatment	47
Fig. 3.2. Microglia is present and equally distributed in organotypical brain slice cultures and absent in organotypical brain slice cultures treated with clodronate liposomes	48
Fig. 3.3. Clodronate liposome treatment does not alters cell death in GL261 cells	49
Fig. 3.4. Astrocytes are in a resting state 72h after clodronate liposome treatment of organotypical brain slice cultures	51
Fig. 3.5. Morphology of astrocytes and neurons in organotypical brain slice cultures remain unchanged after clodronate liposome treatment	52
Fig. 3.6. Detection of glioma cells inoculated into cultured brain slices	54
Fig. 3.7. Attributes of human glioblastomas are reflected in organotypical brain slice cultures experimental gliomas	55
Fig. 3.8. GL261 and F98 cells are more invasive in normal (control) organotypical brain slice cultures as compared to microglia depleted organotypical brain slice cultures	57
Fig. 3.9. Density of microglial cells correlates with increased invasive potential of glioblastoma cells	59
Fig. 3.10. LPS treatment does not increase tumor size in organotypical brain slice cultures	61
Fig. 3.11. Supernatant from glioma induce MMP-2 activation by microglia	64
Fig. 3.12. ProMMP-2 from GL261 cells is activated by microglia	65
Fig. 3.13. Iba-1 positive cells overexpress MT1-MMP when associated with experimental gliomas	66
Fig. 3.14. Transcription of MT1-MMP after GL261 conditioned medium (GCM) treatment is up-regulated	67



Fig. 3.15. Increased protein expression and turnover of MT1-MMP after GL261 conditioned medium (GCM) stimulation	67
Fig. 3.16. MT1-MMP activity increase after GL261 conditioned medium (GCM) treatment is mediated by p38 MAPK	68
Fig. 5.1. Microglia-glioma interaction	83

## II. List of tables

Table 1.1. In vivo states of microglia biology and the associated phenotypic characteristics	15
Table 1.2. Matrix Metalloproteinase family members	20
Table 2.1. Distribution of increasing concentrations of G418 in a 24-well plate	35
Table 2.2. Concentration gradient of Lipofectamine 2000 for a transfection in a 6-well plate	36
Table 2.3. Composition of 1% Gelatin 7,5% SDS Polyacrylamide gels	43
Table 2.4. Composition of 10% SDS Polyacrylamide gels	44

### **III. List of abbreviations**

Blood brain barrier (**BBB**)

Carbon dioxide (**CO<sub>2</sub>**)

Enhanced green fluorescent protein (**EGFP**)

Enzyme-linked immunosorbent assay (**ELISA**)

Extracellular matrix (**ECM**)

Extracellular regulated kinase  $\frac{1}{2}$  (**ERK1/2**)

Fluorescence Assisted Cell Sorting (**FACS**)

For example, exempla gratia (**e.g.**)

Glial fibrillary acidic protein (**GFAP**)

Green fluorescent protein (**GFP**)

Griffonia simplicifolia isolectin B4 (**IL-B4**)

Horseshoe peroxidase (**HRP**)

Intra-peritoneal (**i.p.**)

Lipopolysaccharide (**LPS**)

Matrix metalloproteinase (**MMP**)

Matrix metalloproteinase nine (**MMP-9**)

Matrix metalloproteinase two (**MMP-2**)

Membrane type of matrix metalloproteinase type one (**MT1-MMP**)

Mitogen activated protein kinase (**MAPK**)

Polymerase chain reaction (**PCR**)

Reverse transcriptase PCR (**RT-PCR**)

Revolutions per minute (**rpm**)

Room temperature (**RT**)

Sodium dodecyl sulphate polyacrylamide gel electrophoresis (**SDS-PAGE**)

## Curriculum Vitae

**PERSONAL INFORMATIONS**

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**Birthplace** Belgrade, Yugoslavia

**EDUCATION**

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- **2002** until now, working at Department for Cellular Neurosciences in Max-Delbrück-Centrum für Molekulare Medizin as a member of **Prof. Kettenmann** working group. I work in the field of Neurooncology and Immunology. For my work I use regular cell and molecular biology techniques, immunocytochemistry and imaging techniques.
- **2001-2002**, I was working in one of the best hospitals in Yugoslavia- Military Medical Academy (VMA), beside my regular activities there, as a General practice doctor, I volunteered in laboratories at Experimental Medicine department in order to get familiar with ordinary and scientific lab work.

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**Eidesstattliche Erklärung**

Ich versichere an Eides statt, dass ich die vorliegende Dissertation

The role of microglia in glioma invasiveness

Selbst und ohne unzulässige Hilfe Dritter verfasst habe, dass sie auch in Teilen keine Kopie anderer Arbeiten darstellt und die benutzten Hilfsmittel sowie die Literatur vollständig angegeben sind.

Berlin, den

Darko Markovic