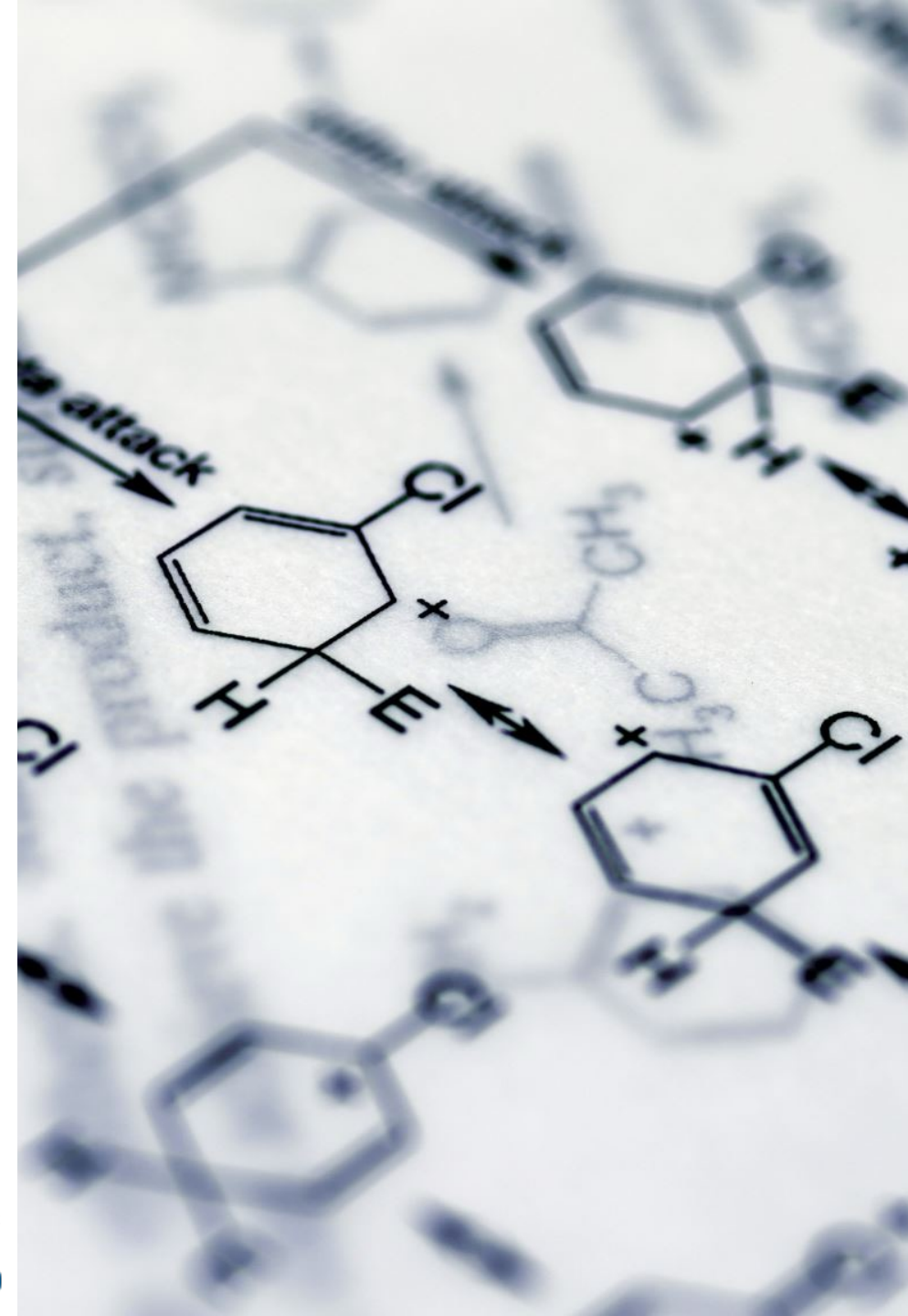


**6TH CENTRAL - EASTERN EUROPEAN CONGRESS ON CELL
FREE DNA AND MEDICAL PRACTICE
7-8TH MARCH 2024**

**MITOCHONDRIAL DNA COPY NUMBER AS A
MINIMALLY-INVASIVE DIAGNOSTIC BIOMARKER OF
GLIOMAS**

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Andor Karácsony, Dávid Adorján, Bálint Nagy, Álmos Klekner,
István Balogh, Beáta Soltész

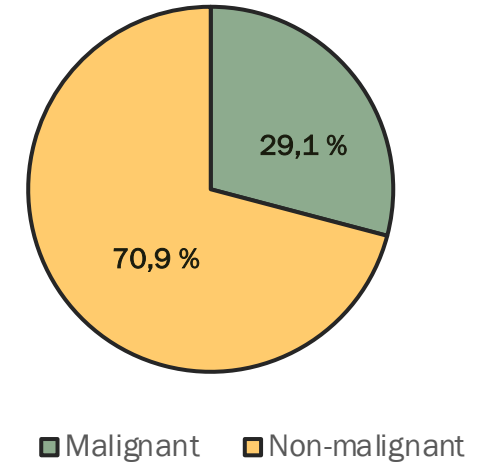
University of Debrecen, Hungary



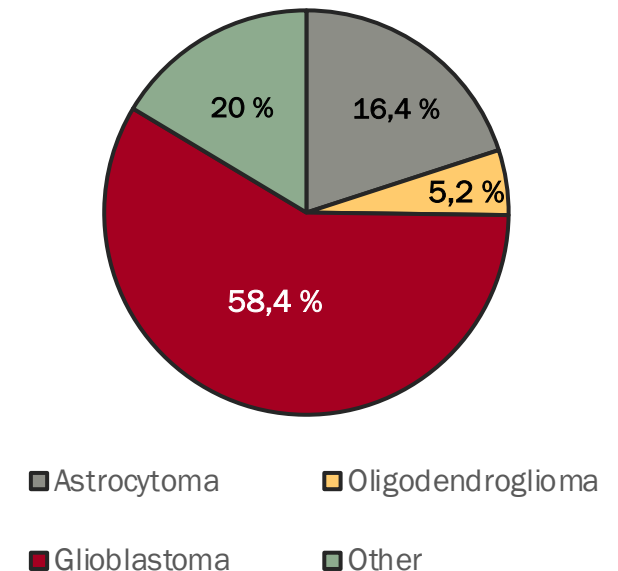
Gliomas

- Brain tumors are relatively rare
 - 2000-2020: 35 839 malignant brain tumor cases in Hungary
- The most common central nervous system tumors are gliomas
- Origin: glial- or precursor cells
- WHO classification, 2021:
 - *Gliomas, glioneural and neural tumors.*
 - Adult-type diffuse gliomas
 - *Astrocytoma (IDH-mutant)*
 - *Oligodendroglioma (IDH-mutant, 1p/19q codeleted)*
 - *Glioblastoma (IDH-wildtype)*

Tumors of the central nervous system



Gliomas



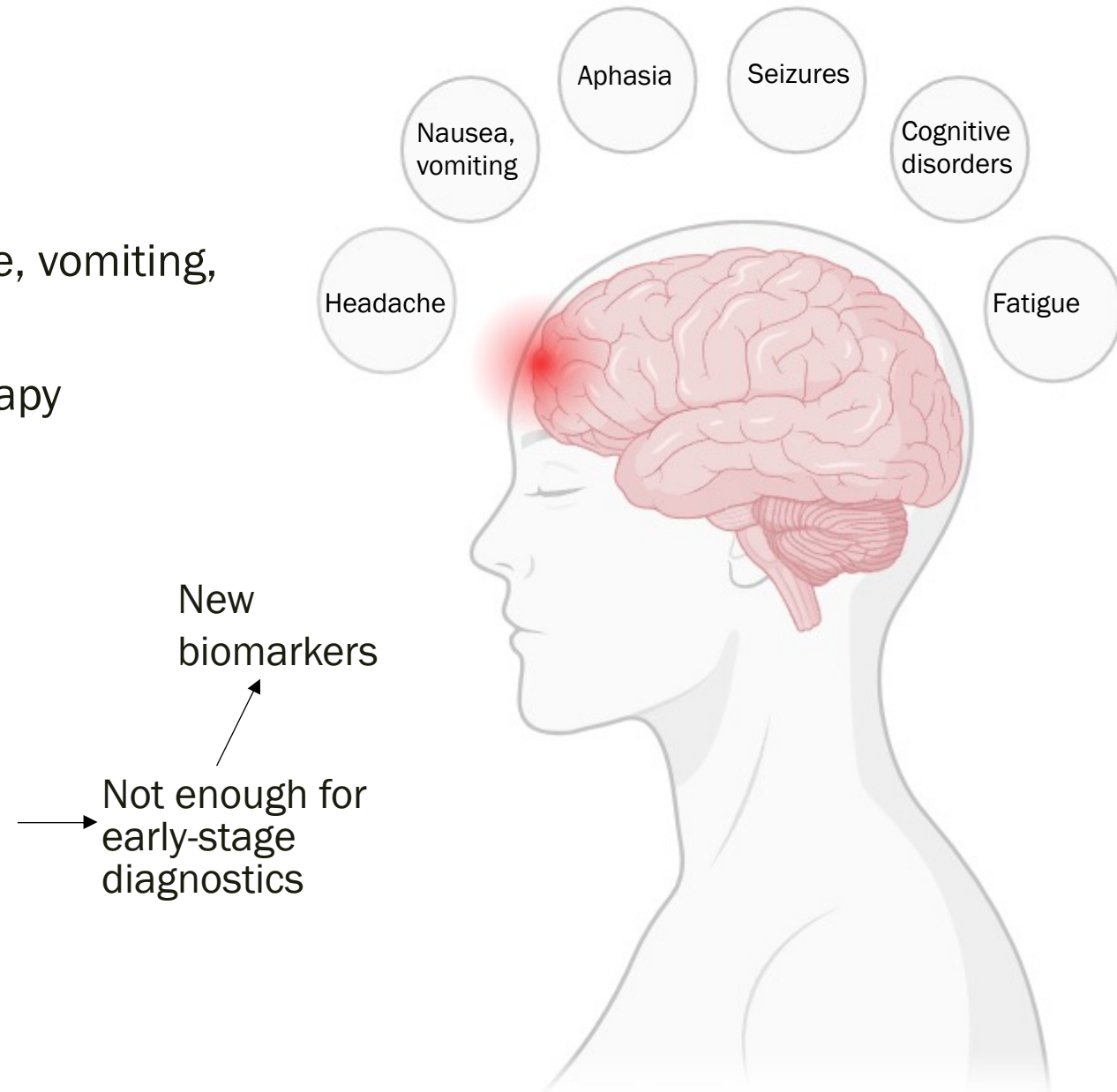
Adult-type diffuse gliomas

	Astrocytoma, IDH-mutant	Oligodendroglioma, IDH-mutant, 1p/19q codeleted	Glioblastoma, IDH-wild type
Grades	2, 3, 4	2, 3	4
Altered genes	<i>IDH1</i> , <i>IDH2</i> , <i>ATRX</i> , <i>TP53</i> , <i>CDKN2A/B</i>	<i>IDH1</i> , <i>IDH2</i> , 1p/19q, <i>TERT</i> promoter, <i>CIC</i> , <i>FUBP1</i> , <i>NOTCH1</i>	<i>IDH</i> -wild type, <i>TERT</i> promoter, 7/10 chromosomes, <i>EGFR</i>
Associated hereditary syndromes	Neurofibromatosis 1	Rubinstein-Taybi syndrome	Li-Fraumeni syndrome
Cell characteristics	<ul style="list-style-type: none"> - Slow growth - Low mitotic activity - High rate cell differentiation 	<ul style="list-style-type: none"> - Atypical cell nucleus - Higher mitotic activity - Enhanced cellular pleomorphism 	<ul style="list-style-type: none"> - Necrosis - Microvascular proliferation

Glioblastoma

- The most common, aggressive primary malignancy of the brain
- Generally fatal outcome
- Risk factors are not characterised
- Symptoms are not specific (headache, fatigue, vomiting, neurocognitive slowing, etc.)
- Treatment: surgery, radiation and chemotherapy
- Currently used biomarkers:

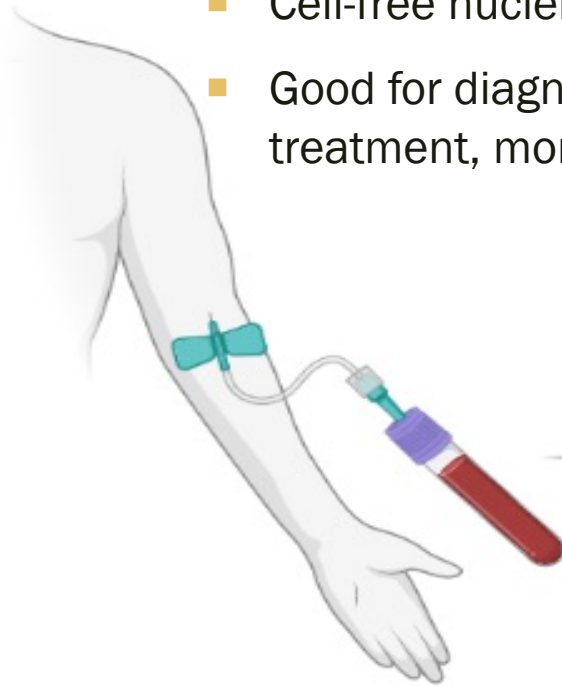
Marker	Modification
<i>ATRX</i>	Mutation or deletion
<i>IDH</i>	Missense mutation of Arginine 132 or 172
<i>MGMT</i>	Promoter methylation
<i>CDKN2A</i>	Homozygotic deletion
<i>p53</i>	Mutation
<i>PI3K</i>	Activation mutation
<i>PTEN</i>	Mutation or deletion
<i>RB</i>	Mutation or deletion
<i>TERT</i>	Promoter methylation



Liquid versus tissue biopsy

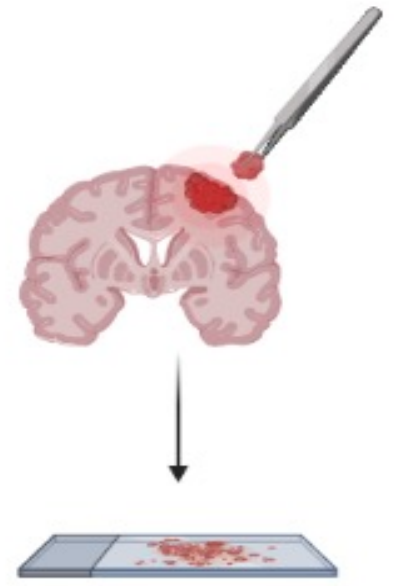
■ Liquid biopsy:

- Minimally-invasive
- Cheaper
- Repeatable
- Shows the heterogeneity of the tumour
- Cell-free nucleic acids are accessible
- Good for diagnosing, staging, choosing treatment, monitoring the patient

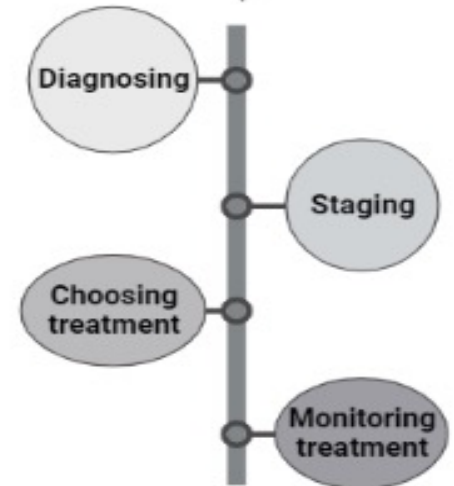


■ Tissue biopsy:

- Gold standard
- Hardly repeatable
- Causes discomfort
- Time consuming
- High financial costs
- Invasive
- Risky



bio
radar



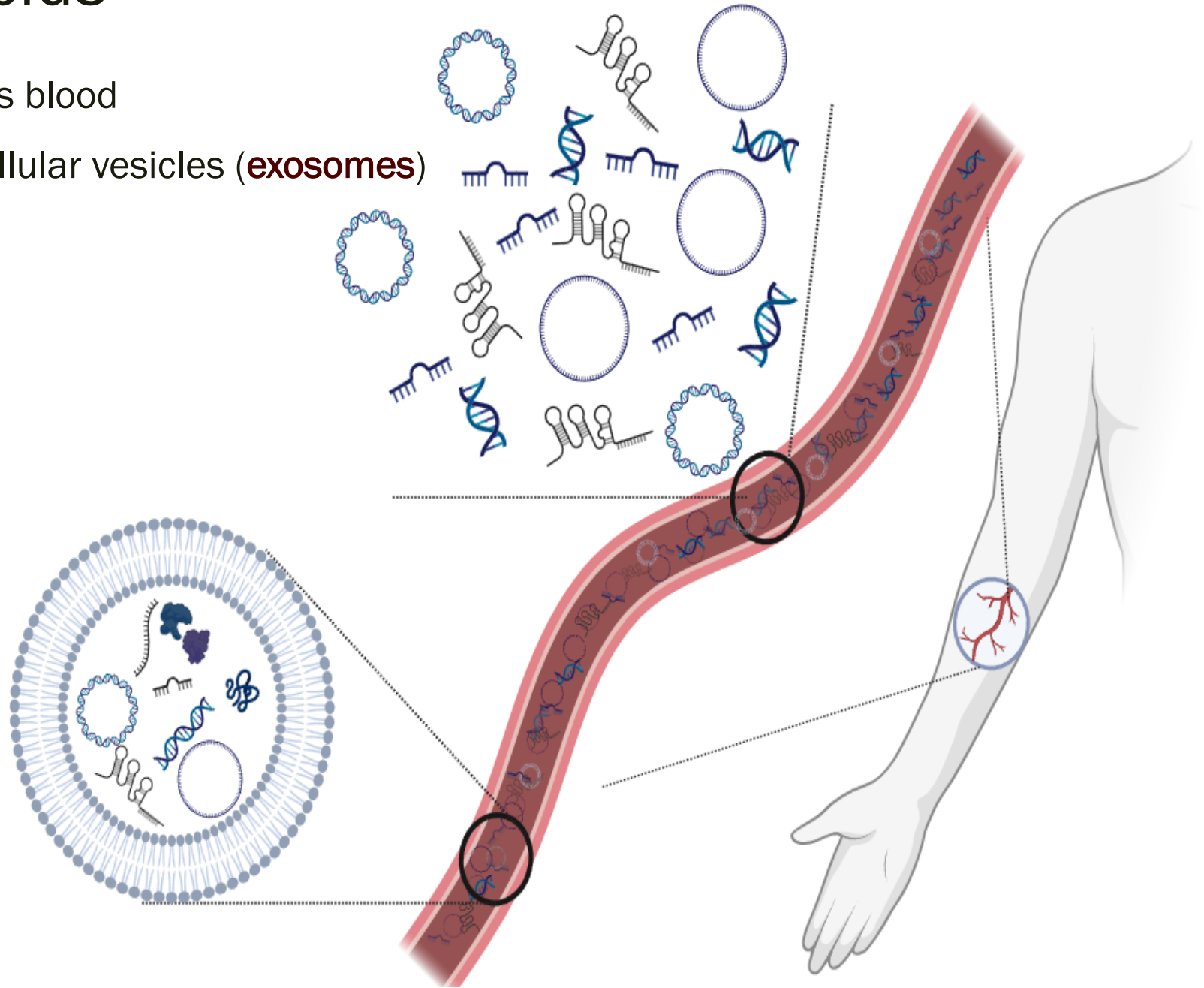
Cell-free nucleic acids

- Present in biofluids, such as blood
- Can be packed into extracellular vesicles (**exosomes**)

Released by necrosis,
apoptosis or active
secretion

Cargo: DNAs and RNAs

Altered levels can be
associated with
diseases



Aim of the study I.



To measure and compare the mtDNA copy number in the tissue and blood of glioma patients.



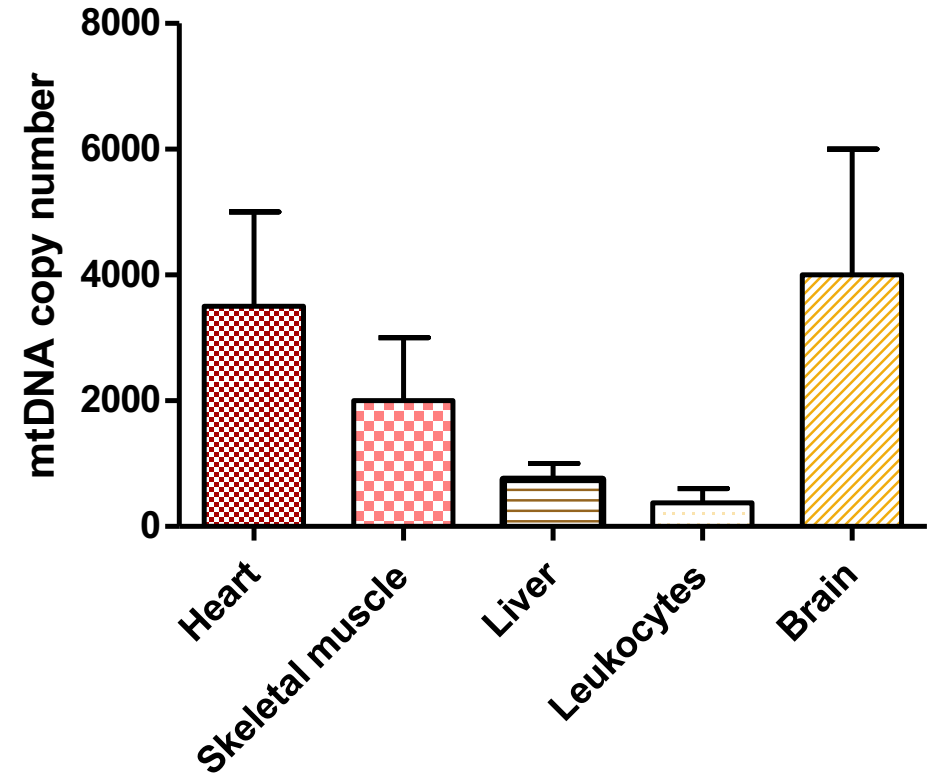
To measure and compare the mtDNA copy number in the tissue and blood of glioma patients and meningioma.



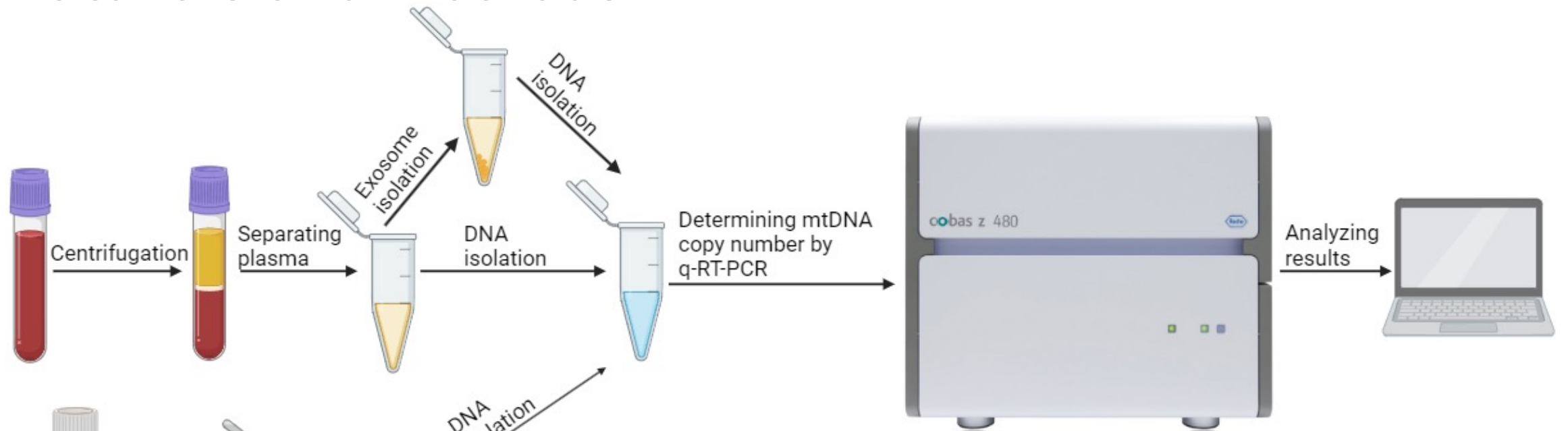
To examine whether the mtDNA copy number shows a correlation with the presence of the tumour and with a copy number detectable in the tumour tissue itself.

Mitochondrial DNA copy number

- Mitochondrial DNA copy number varies according to cell type
- Dysfunction can play roles in cancer
- Deregulation of energy production in cells can be associated with the development of cancer
- Higher mtDNA copy numbers might have a positive effect on prolonged overall survival



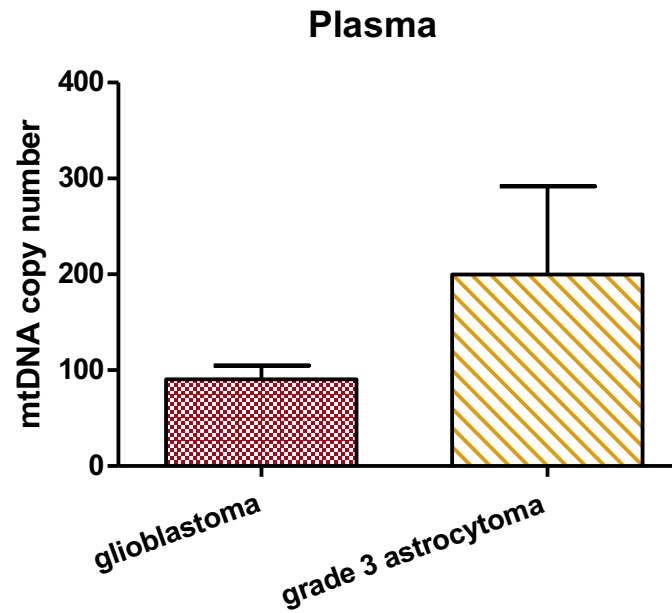
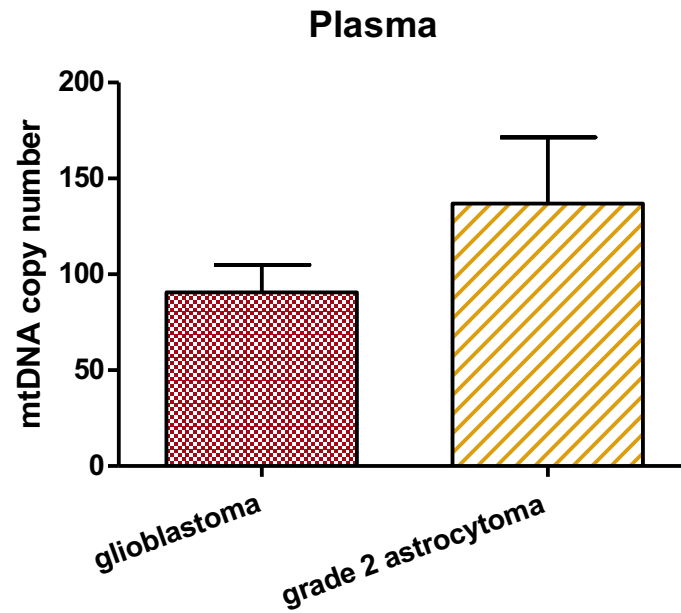
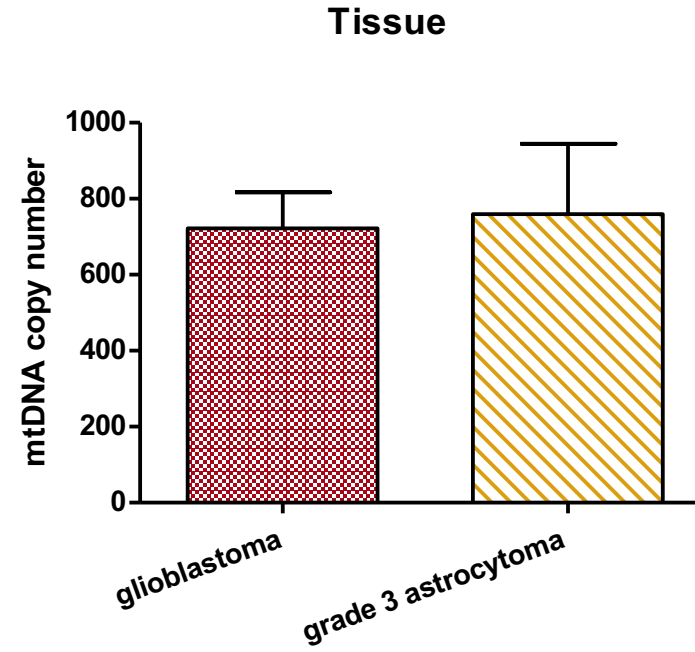
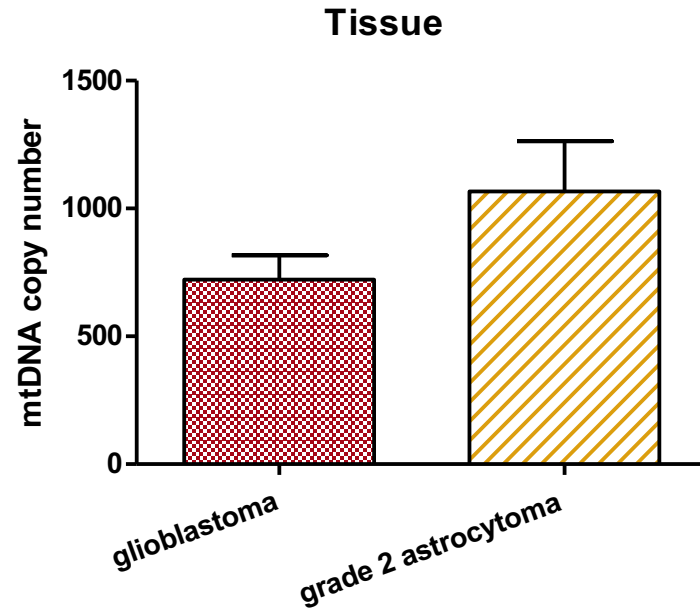
Materials and methods



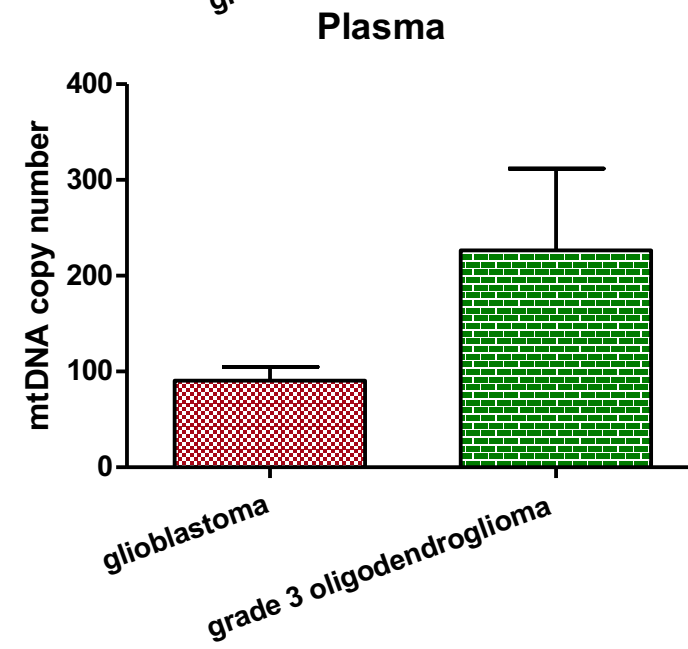
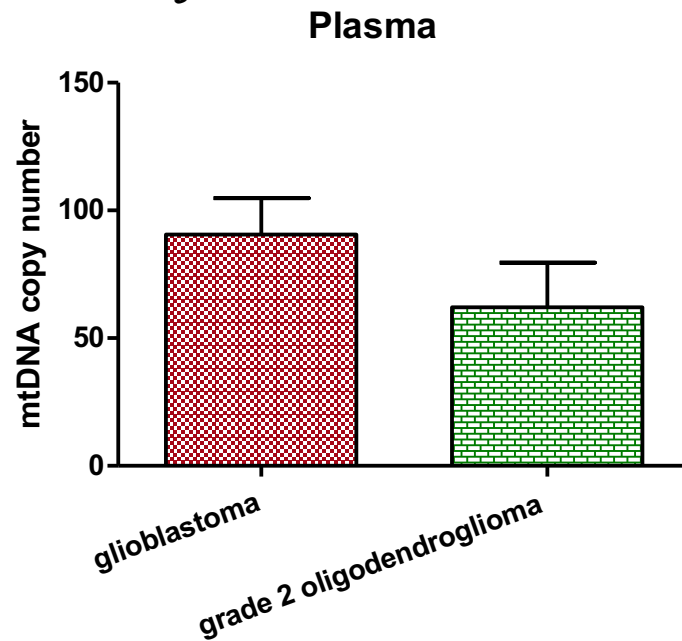
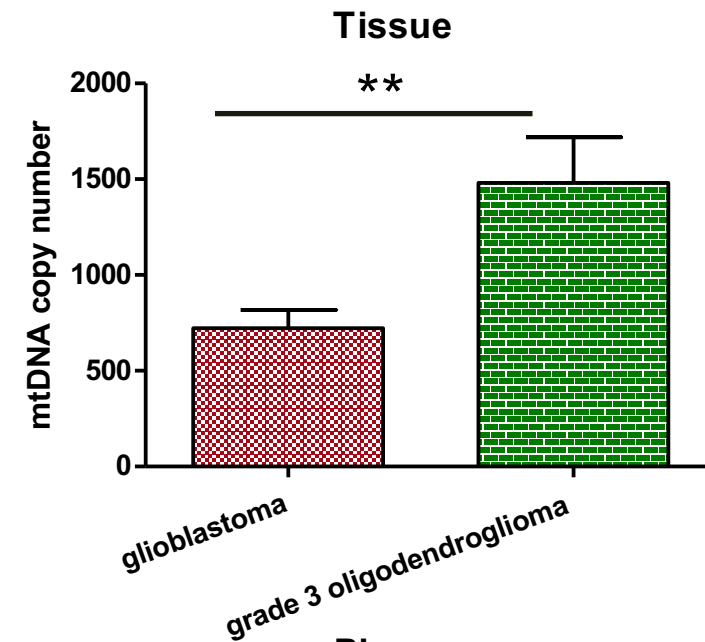
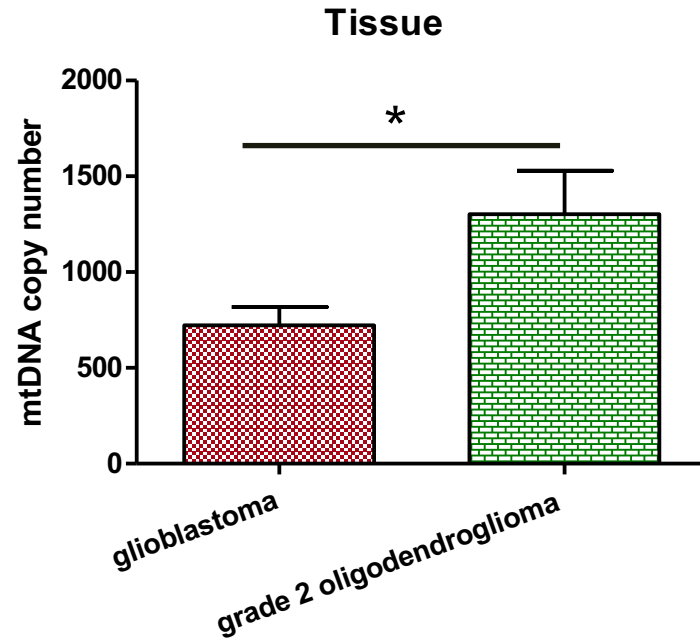
Plasma samples	
Diagnosis	Number of samples
Meningioma	9
Grade 2 astrocytoma	9
Grade 3 astrocytoma	10
Grade 2 oligodendroglioma	8
Grade 3 oligodendroglioma	9
Glioblastoma	8
Non-tumor control	5
Total	58

Tissue samples	
Diagnosis	Number of samples
Meningioma	11
Grade 2 astrocytoma	12
Grade 3 astrocytoma	8
Grade 2 oligodendroglioma	13
Grade 3 oligodendroglioma	9
Glioblastoma	23
Total	76

Results I.

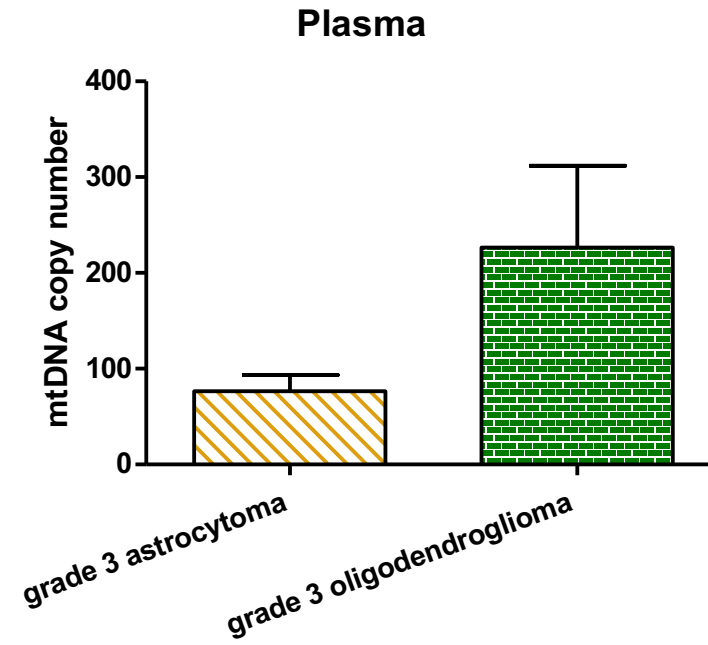
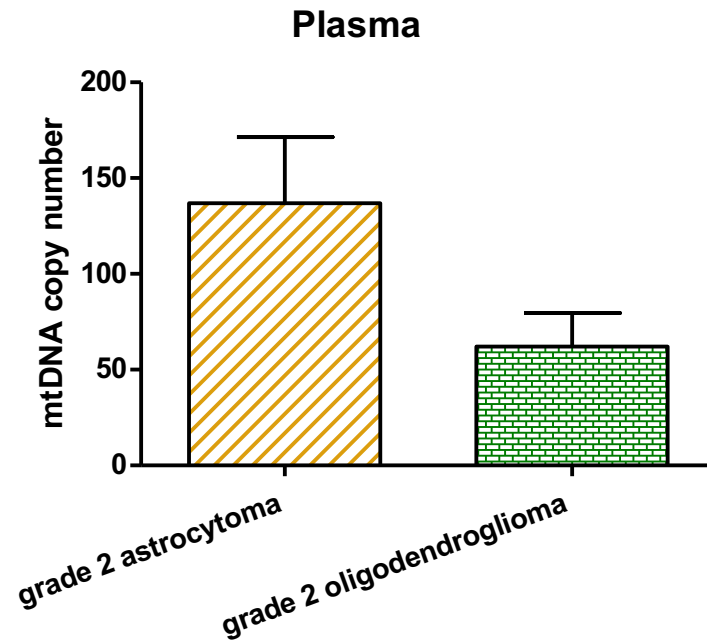
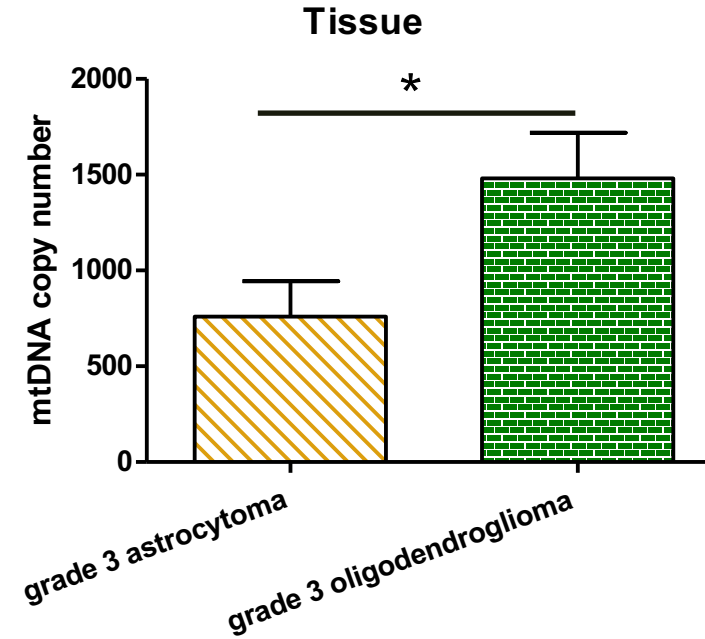
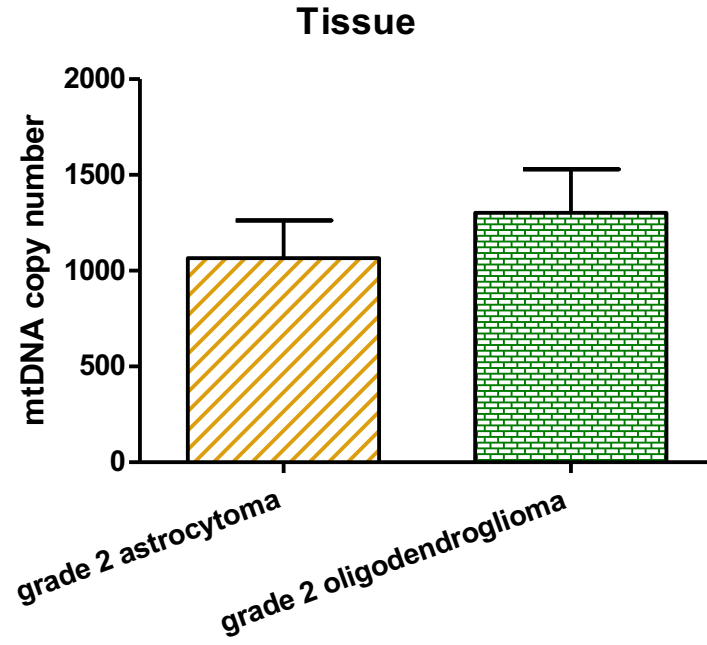


Results II.

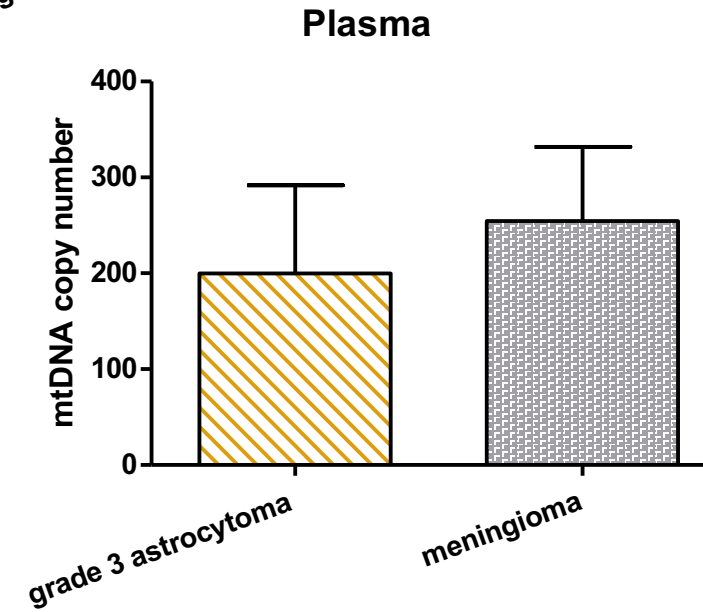
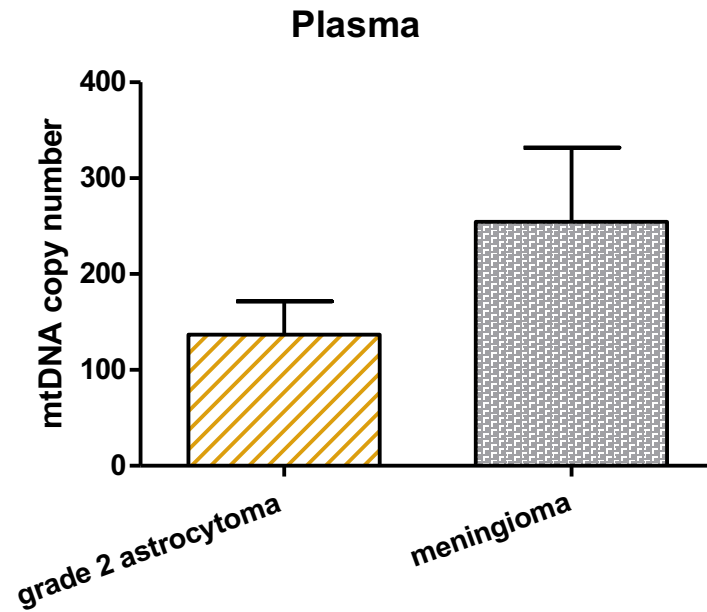
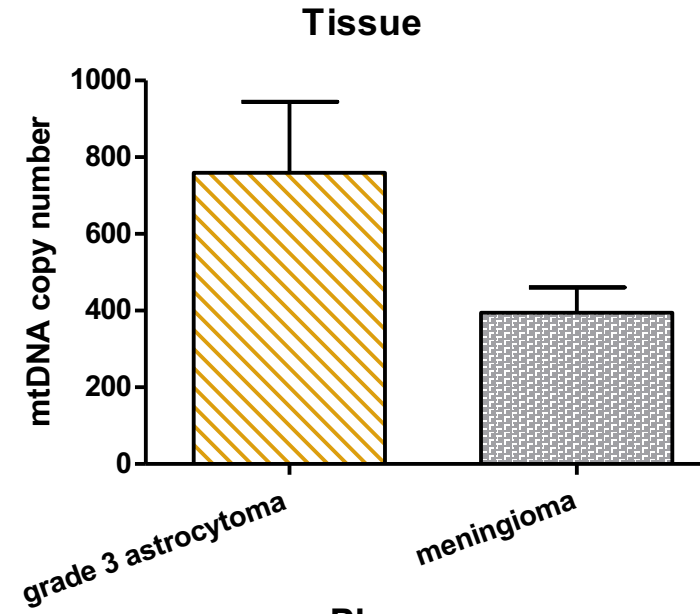
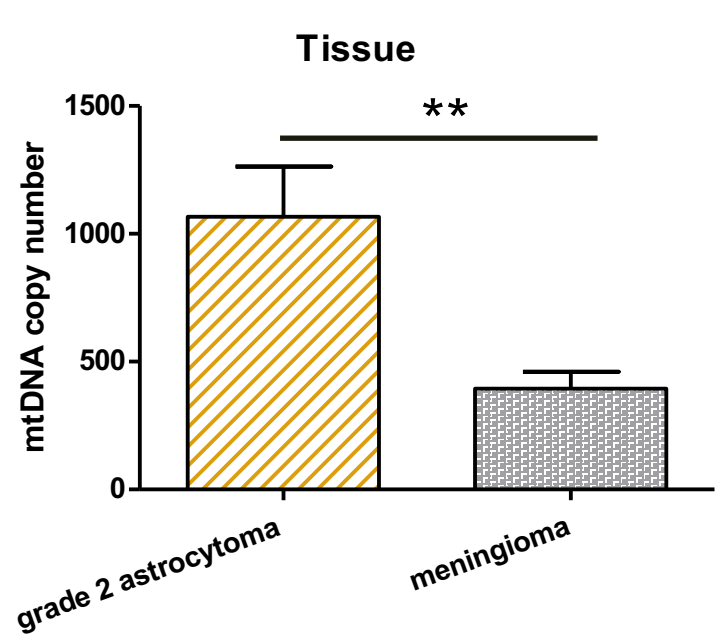


* $p < 0.05$
** $p < 0.01$

Results III.

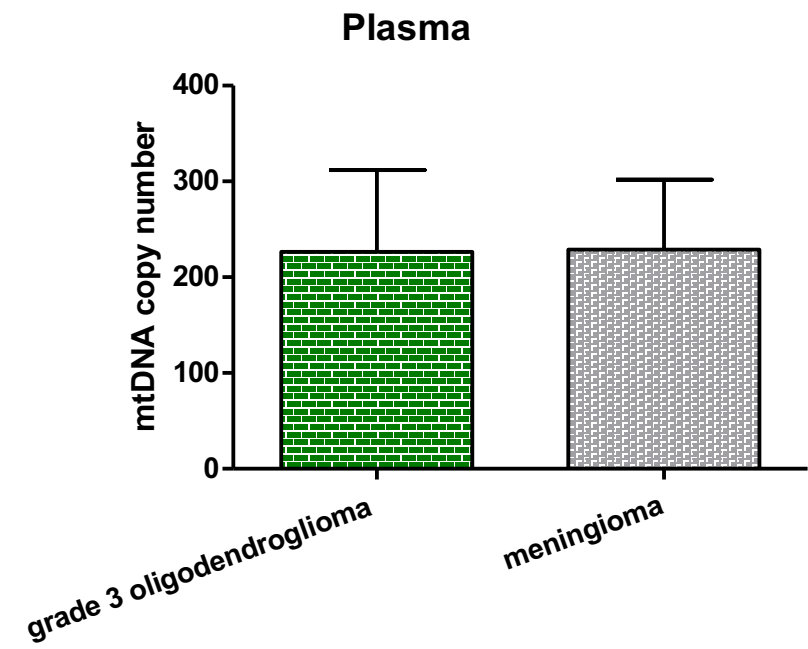
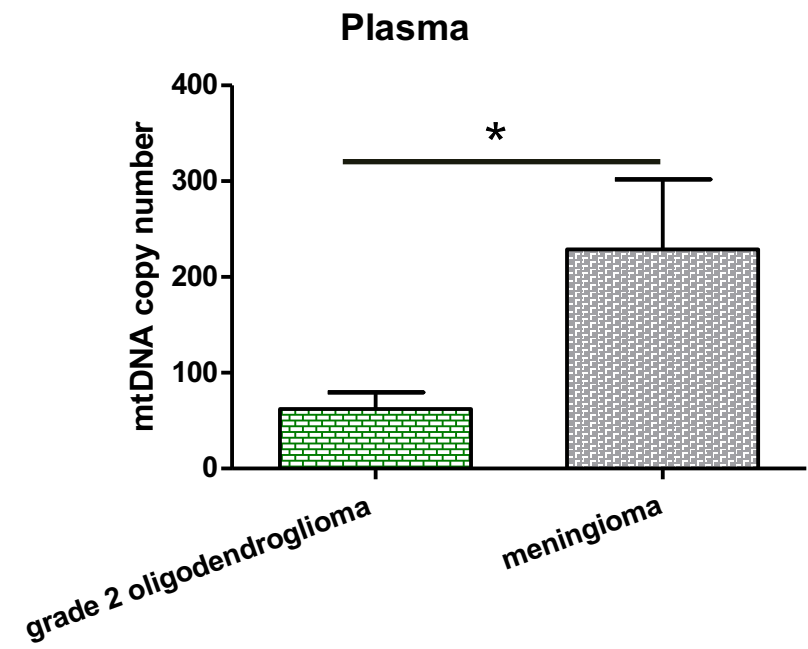
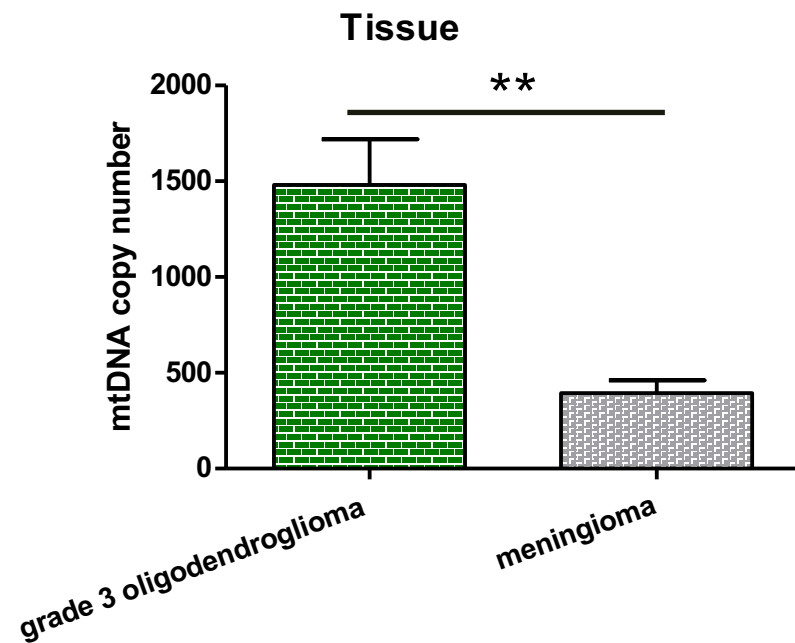
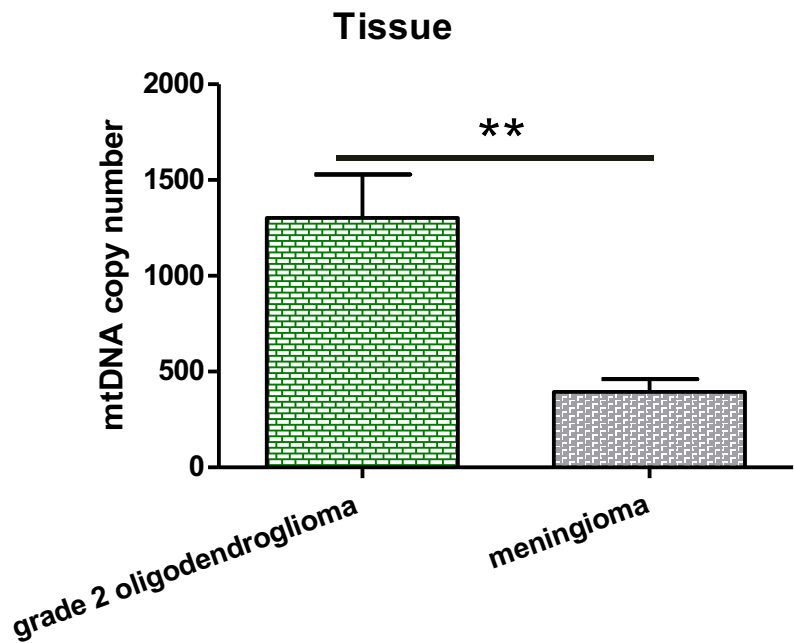


Results IV.



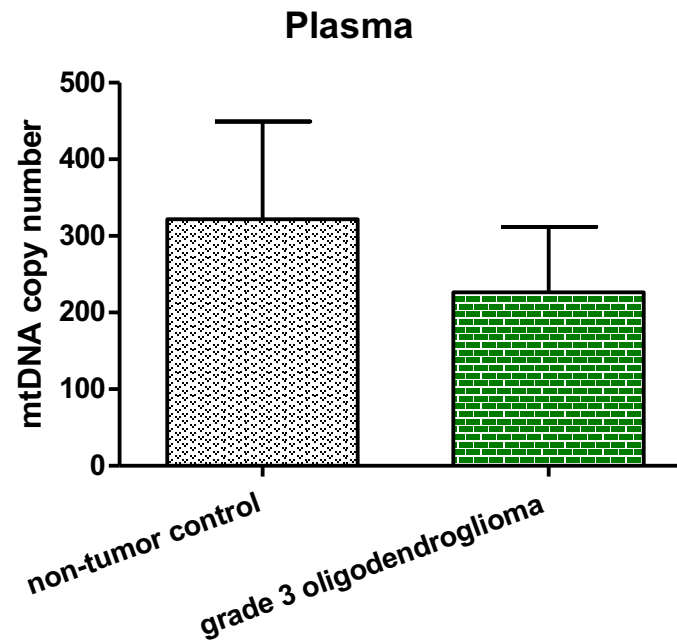
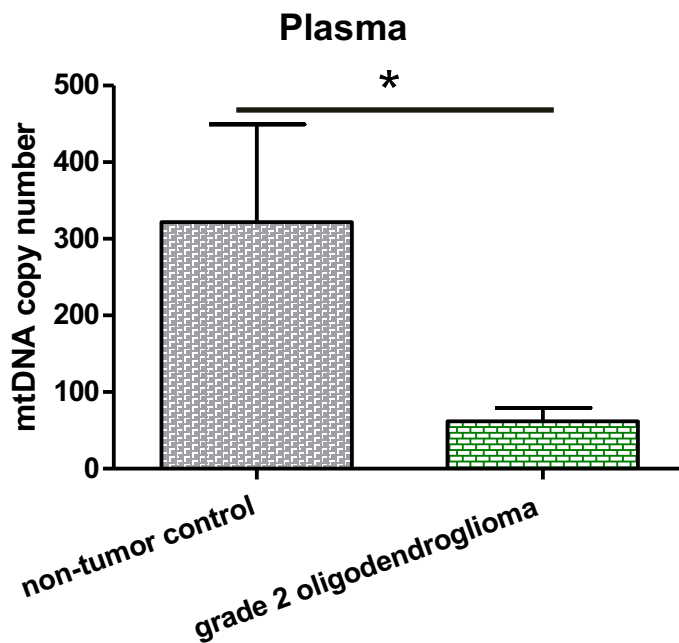
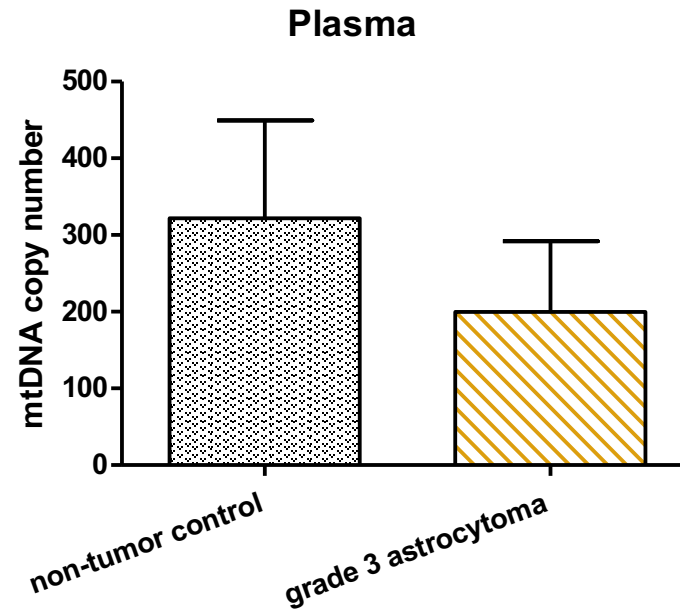
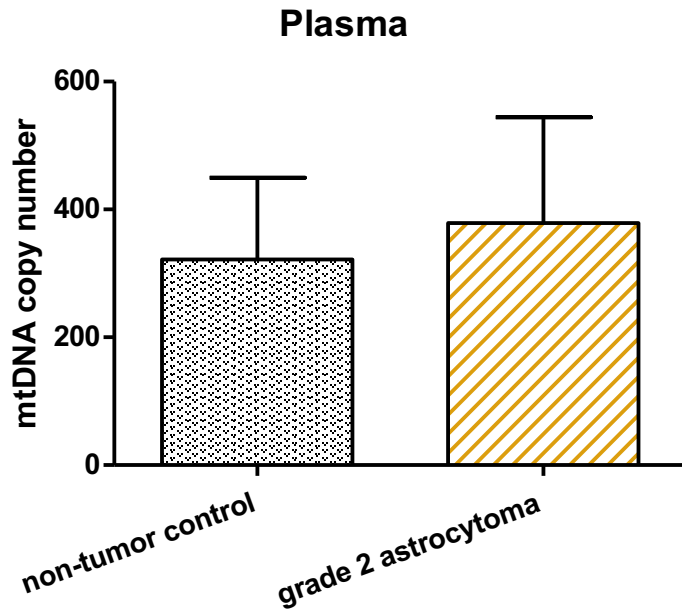
** p < 0.01

Results V.



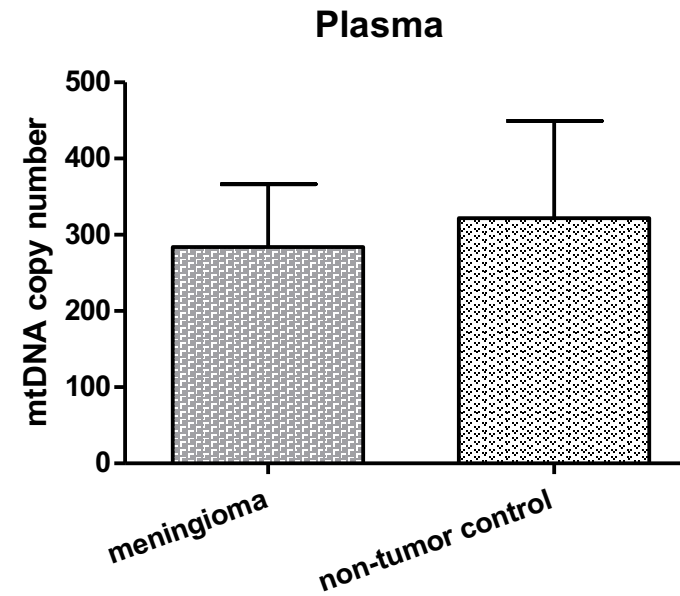
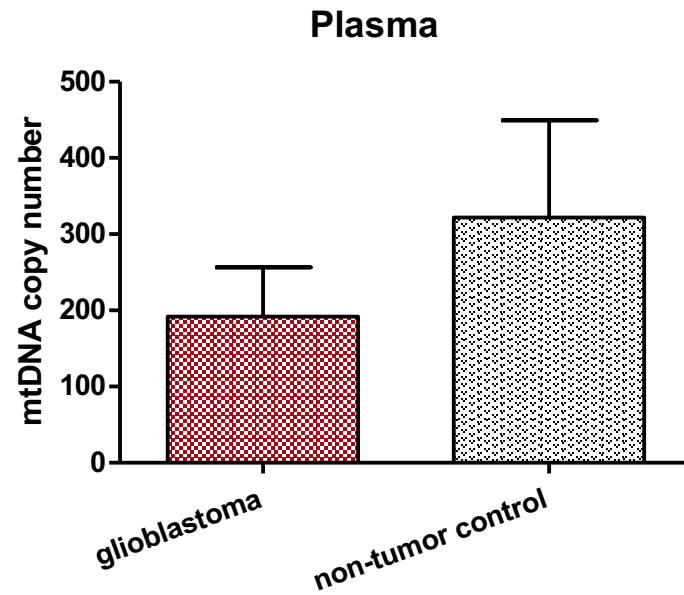
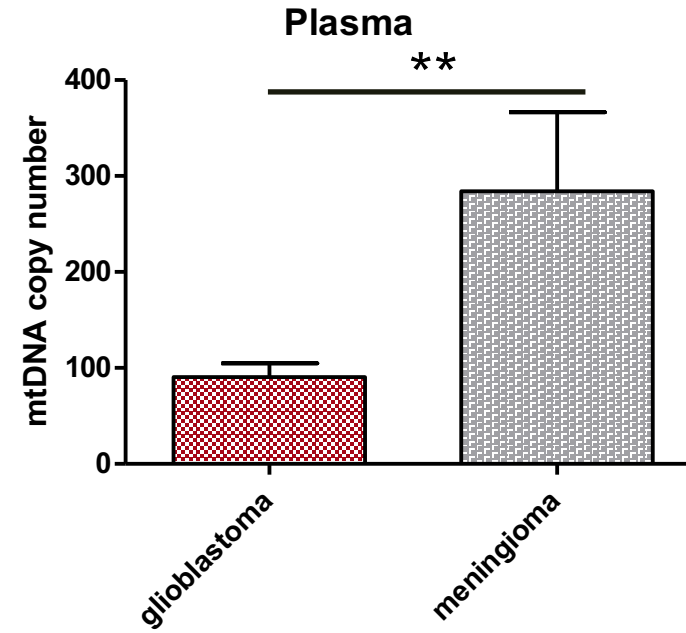
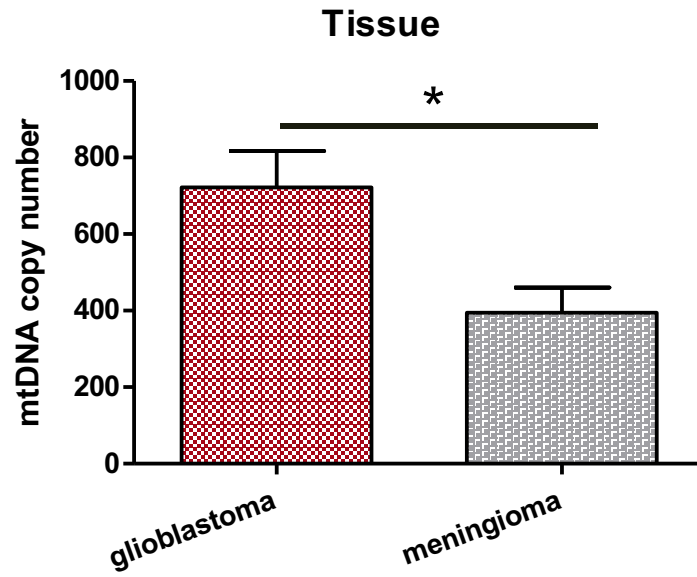
* p < 0.05
** p < 0.01

Results VI.



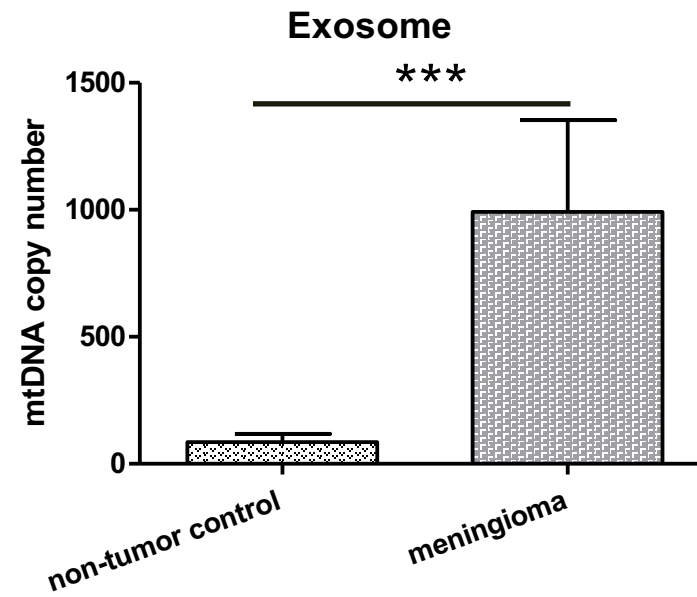
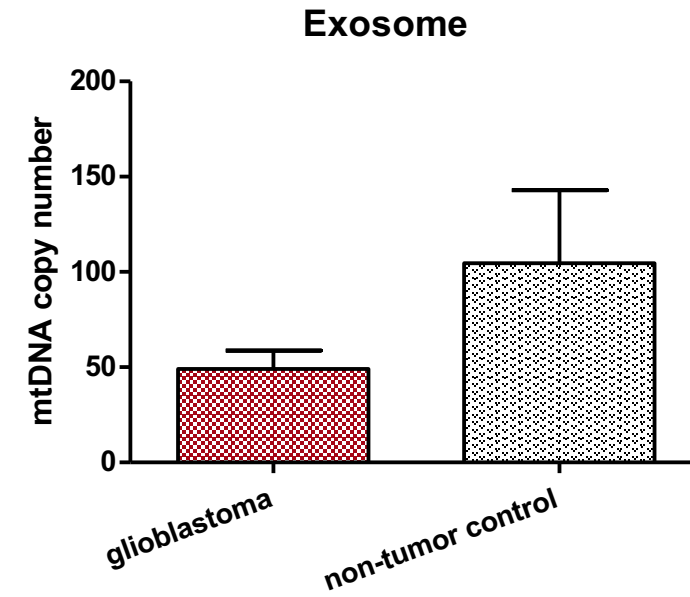
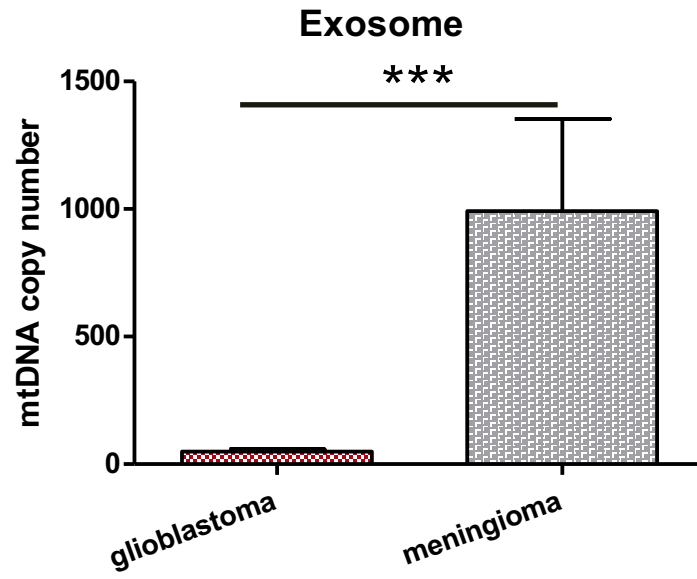
* p < 0.05

Results VII.



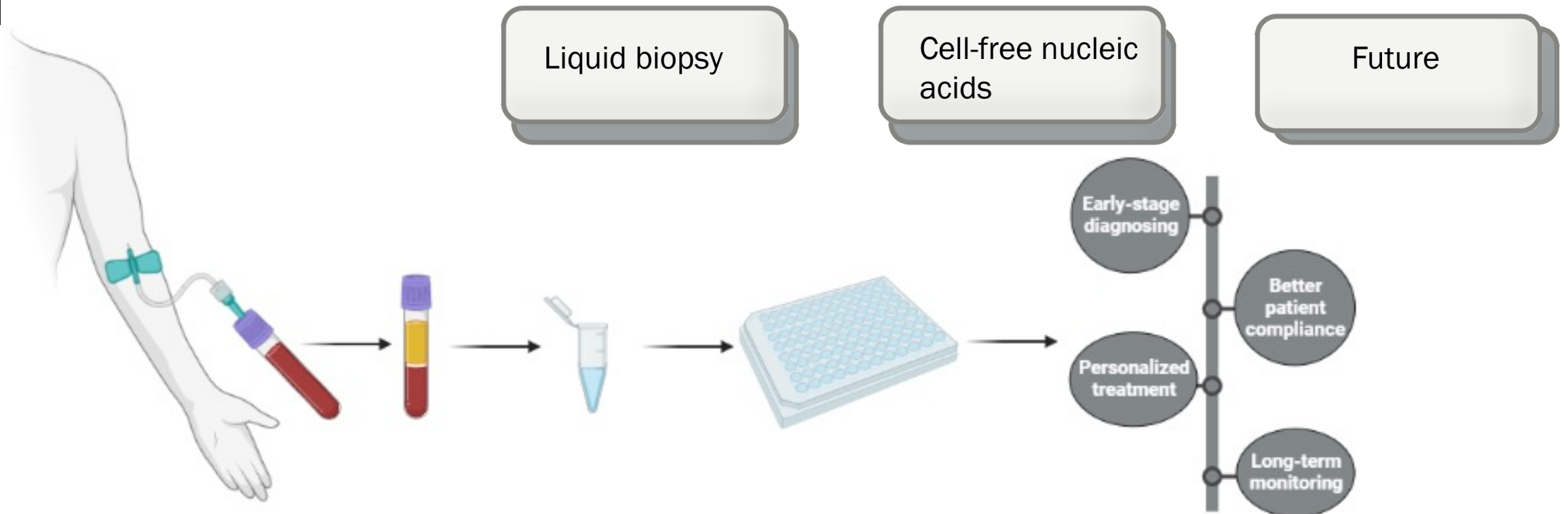
* p < 0.05
** p < 0.01

Results VIII.



Conclusions

- 1 . Mitochondrial DNA copy number could influence the patomechanism of gliomas
2. The mtDNA copy number can be different in the tissue and plasma sample of the given glioma suggesting there is a mechanism that alters the release of certain nucleic acids



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THANK YOU FOR YOUR KIND
ATTENTION!

