Supplementary Table 1A **Clinical information on Glioblastoma Patient 1**

Age of patient at the time of surgery & study (years)	Tumor type	Tumor stage	Tumor location in brain	Brain surgery for GBM	Drugs and/or other treatments for GBM	Diseases in past & present except GBM	Drugs and/or other treatments for other diseases	Significant health events before the onset of GBM (injury or other)	Immune tests and/or treatments before the onset of GBM	Prognosis	Other info. of any kind
Adult Patient	Glioblastoma IDH wild-type	4	Left frontal	August 17th, 2022	1. WBTR 2. Temozolomide 3. Avastin	1. Diabetes Melitus type 2 2. Gastritis 3. Psychiatric disorder	1. Insulin Aspart 2. Escitalopram 3. Esomeprazole	None	None		

Adult patient, presented with behavioral changes and headaches on August 2022. A left frontal mass lesion was diagnosed based on CT and MRI scans.

On August 17, 2022, the patient underwent an image-guided left frontal craniotomy. A 5-Aminolevulinic Acid-guided resection with electrophysiological monitoring was performed, resulting in a gross total resection.Pathological findings confirmed Glioblastoma IDH wild type. The patient recovered quickly with no residual neurological deficits and was discharged home. Adjuvant therapy, including external beam radiotherapy and concomitant Temozolomide, was initiated.

Follow-up MRI on December 26, 2022, showed a small nodular recurrence at the lateral aspect of the resection bed. Following a tumor board discussion, the patient was scheduled for re-craniotomy and safe resection of the nodular recurrence. During anesthesia induction for this surgery, peripheral blood was drained for the present immunotherapy study. Second-line therapy included Avastin after the second surgery. The patient remained clinically well until March 2024, when the patient was hospitalized in the Department of Neurology with a generalized seizure and acute confusional state, likely secondary to disease progression in the cerebellum with suspected leptomeningeal dissemination. The patient expired in hospice due to aspiration pneumonia on April 15, 2024, at 19 months since the initial diagnosis.

Supplementary Table 1B **Summary of the results obtained in this study on the T cells of Glioblastoma Patient 1**

SUMMAYRY OF ALL THE FINDINGS RELATED TO THE T CELLS OF GLIOBLASTOMA PATIENT 1	
Decreased expression of exhaustion-related checkpoint inhibitors in T cells of Glioblastoma Patient 1	
PD-1	**YES !!!** **Glutamate** (50% decrease) ; **Dopamine** (43% decrease); **GnRH-II** (28% decrease; **Glutamate**+**Neuropeptide Y** (31% decrease) ; **Dopamine**+**GnRH-II** (25% decrease) ; **Dopamine**+**Neuropeptide Y** (3% decrease); **Neuropeptide Y**+**GnRH-II** – No decrease
LAG-3	**YES !!!** **GnRH-II** (90% decrease) ; **Glutamate**+**Neuropeptide Y** (88% decrease) ; **Neuropeptide Y** (85% decrease, BEST) ; **Dopamine**+**GnRH-II** (82% decrease) **Dopamine** +**Neuropeptide Y** (85% decrease) ; **Glutamate** (76% decrease) ; **Neuropeptide Y** (52% decrease) ; **Dopamine** (47% decrease) ; **Neuropeptide Y**+**GnRH-II** (18% decrease)
Tim-3	**YES !!!** **GnRH-II** (87% decrease) ; **Glutamate**+**Neuropeptide Y** (83% decrease) ; **Dopamine**+**GnRH-II** (80% decrease) ; **Dopamine**+**Neuropeptide Y** (80 % decrease) ; **Neuropeptide Y** (52% decrease) ; **Glutamate** (41% decrease) ; **Dopamine** (27% decrease) ; **Neuropeptide Y**+**GnRH-II** (7% decrease)
TIGIT	**YES !!!** **Glutamate**+**Neuropeptide Y** (94% decrease) ; **Dopamine**+**Neuropeptide Y** (92 % decrease) ; **Neuropeptide Y**+**GnRH-II** (87% decrease) ; **Glutamate** (45% decrease) ; **Neuropeptide Y** (52% decrease) ; **Dopamine** (31% decrease) ; **GnRH-II** (30% decrease) ; **Dopamine**+**GnRH-II** (16% decrease)
CD160	**YES !!!** **Dopamine**+**Neuropeptide Y** (70% v) ; **Glutamate**+**Neuropeptide Y** (65% less) ;**GnRH-II** (60% less) ; **Dopamine**+**GnRH-II** (52% less) ; **Glutamate** (30% decrease); **Neuropeptide Y** (27% decrease) ; **Neuropeptide Y**+**GnRH-II** (60% decrease) ; **Dopamine** - No decrease
Increased expression of the CD3zeta in T cells of Glioblastoma Patient 1	
YES !!! **Dopamine**+**GnRH-II** (45% increase) ; **Glutamate**+**Neuropeptide Y** (34% increase) ; **Neuropeptide Y**+**GnRH-II** (31% increase) ; **Neuropeptide Y** (20% increase) ; **Glutamate** (9% increase) ; **Dopamine** (9% increase) ; **GnRH-II** (no increase)	
Increased number of big alive T cells of Glioblastoma Patient 1	
	Blood sample 1 - during brain surgery / **Blood sample 2 - 10 days after brain surgery**
Increased no. of big & not granular alive T cells	**YES !!!** Averages (n=3)**: Glutamate** (73% increase) ; **Dopamine** (52% increase) ; **GnRH-II** (52% increase) ; **Neuropeptide Y** (51% increase) ; **Neuropeptide Y**+**GnRH-II** (32% increase) ; **Dopamine**+**GnRH-II** (30% increase) ; **Dopamine**+**Neuropeptide Y** (27% increase) ; **Glutamate**+**Neuropeptide Y** (18% increase) / **YES, DRAMATICALLY !!!!!** **Glutamate** (11-fold increase) ; **Dopamine**+**GnRH-II** (8-fold increase) ; **Neuropeptide Y**+**GnRH-II** (8-fold increase) ; **GnRH-II** (7-fold increase) ; **Neuropeptide Y** (7-fold increase) ; **Dopamine** (5-fold increase) ; **Glutamate**+**Neuropeptide Y** (6-fold increase) **Dopamine**+**Neuropeptide Y** (4-fold increase)
Increased arrest of human Glioblastoma cells by T cells of Glioblastoma Patient 1 (in co-cultures for 1 week)	
Fewer Glioblastoma cells grew in co-cultures with T cells of Glioblastoma Patient 1, when the patient's T cells are pre-treated with Neurotransmitters and/or Neuropeptides	**YES !!!** **Glutamate**+**Neuropeptide Y** (26.3% decease in number of cancer cells) ; **Dopamine**+**Neuropeptide Y** (24.7% decrease) ; **Dopamine**+**GnRH-II** (21.6% decrease) ; **Neuropeptide Y**+**GnRH-II** (21% decrease) ; **Neuropeptide Y** (16.5% decrease)

Supplementary Table 2A **Clinical information on Glioblastoma Patient 2**

Age of patient at the time of surgery & study (years)	Tumor type	Tumor stage	Tumor location in brain	Brain surgery for GBM	Drugs and/or other treatments for GBM	Diseases in past & present except GBM	Drugs and/or other treatments for other diseases	Significant health events before the onset of GBM (injury or other)	Immune tests and/or treatments before the onset of GBM	Prognosis	Other info. of any kind
Adult	Glioblastoma-IDH Wild-type	4	Left frontotemporal	January 31st, 2023	WBTR Temozolomide, Avastin Tumor Treating Fields (TTF)	1. Diabetes type I 2.Hypothyroidism 3. Overweight	Cardiloc 5 mg per day	None	None	Stable disease after 15 months	

Adult patient, presented with a frontal headache followed by a sudden onset of incontinence. Neurological examination revealed right hemiparesis, motor dysphasia, and drowsiness. MRI data sets showed a 70mm mass lesion in the left fronto-temporal region with associated mass effect and severe perilesional vasogenic edema, indicative of a high-grade glioma. On January 31st, 2023, the patient underwent an image-guided left fronto-temporal craniotomy. A 5-Aminolevulinic Acid-guided resection with electrophysiological monitoring was performed, resulting in a gross total resection. The postoperative course was uneventful, with improvements in hemiparesis and speech functions. Pathological findings confirmed Glioblastoma IDH wild type. Adjuvant therapy, including external beam radiotherapy and concomitant Temozolomide, was initiated. Treatment continued with Avastin and TTF until her last clinical follow-up on April 16, 2024

Supplementary Table 2B **Summary of the results obtained in this study on the T cells of Glioblastoma patient 2**

SUMMAYRY OF ALL THE FINDINGS RELATED TO THE T CELLS OF GLIOBLASTOMA PATIENT 2	
Decreased expression of exhaustion-related checkpoint inhibitors in T cells of Glioblastoma Patient 2	
PD-1	**YES !!!** **Dopamine** (50% decrease) ; **Neuropeptide Y** (24% decrease) ; **GnRH-II** (12% decrease) ;
LAG-3	**YES !!!** **Neuropeptide Y** (53% decrease) ; **GnRH-II** (43% decrease) ; **Dopamine** (12% decrease);
Tim-3	**YES !** **Neuropeptide Y** (10% decrease) ; **GnRH-II** (9% decrease)
TIGIT	**YES !!!** **Neuropeptide Y** (52% decrease) ; **Dopamine** (decrease) ; **GnRH-II** (7% decrease) ;
CD160	**YES !!!** **Neuropeptide Y** (56% decrease) ; **Dopamine** (8% decrease) ; **GnRH-II** (4% decrease) ;
Increased expression of the CD3zeta in T cells of Glioblastoma Patient 2	
YES !!! **Neuropeptide Y** (2.8-fold Increase) ; **Dopamine** (2.2-fold Increase) ; **Dopamine+GnRH-II** (2.3-fold Increase) ; **Dopamine+Neuropeptide Y** (2.2-fold Increase) ; **Glutamate+Neuropeptide Y** (1.9-fold Increase) ; **Glutamate** (1.6-fold Increase) ; **GnRH-II** (1.6-fold Increase)	
Increased number of big alive T cells, and decreased number of small granular T cells of Glioblastoma Patient 2	
Increased no. of big not granular alive T cells	**YES !!!** **Dopamine** (84% increase) ; **Glutamate** (82% increase) ; **Dopamine+Neuropeptide Y** (61% increase) ; **Neuropeptide** Y (54% increase) ; **Dopamine+GnRH-II** (53% increase) ; **GnRH-II** (51% increase) ; **Glutamate+Neuropeptide Y** (50% increase) ; **Glutamate+GnRH-II** (45% increase) ; **Neuropeptide Y+GnRH-II** (34% increase)
Decreased no. of small & granular T cells	**YES !!!** **Neuropeptide Y+GnRH-II** (BEST, 38% less) ; **Dopamine+Neuropeptide Y** (27% less) ; **Glutamate+GnRH-II** (23% less) ; **Dopamine+GnRH-II** (22% less) ; **Dopamine** (19% less); **GnRH-II** (17% less) ; **Neuropeptide Y** (15% less) ; **Glutamate** (11% less)
Increased arrest of human Glioblastoma cells by T cells of Glioblastoma Patient 2 (in co-cultures for 1 week)	
Fewer Glioblastoma cells grew in co-cultures with T cells of Glioblastoma Patient 2 pre-treated with Neurotransmitters and/or Neuropeptides	**YES !!!** **Dopamine+Neuropeptide Y** (BEST, 95% less) ; **Neuropeptide Y+GnRH-II** (79% less) ; **Dopamine+GnRH-II** (79% less) ; **Glutamate+Neuropeptide Y** (79% less) ; **Neuropeptide Y** (42% less) ; **GnRH-II** (27% less) ; **Dopamine** (22% less)

Supplementary Table 3A **Clinical information on Glioblastoma Patient 3**

Age of patient at the time of surgery & study (years)	Tumor type	Tumor stage	Tumor location in brain	Brain surgery for GBM	Drugs and/or other treatments for GBM	Diseases in past & present except GBM	Drugs and/or other treatment for other diseases	Significant health events before the onset of GBM (injury or other)	Immune tests and/or treatments before the onset of GBM	Prognosis	More info. of any kind
Adult	Glioblastoma IDH wild type	4	Right temporal lobe	May 17th, 2023	1. WBTR 2. Temozolomide	1. Diabetes Miletus type 2, 2. Ischemic heart disease, 3. Dyslipidemia, 4. Corneal implantation	1. Aspirin, 2. Plavix 3. Amlodipine 4. Cardiloc 5. Crestor 6. Eucreas 7. Ramipril	None	None	Dismal	The patient is living now in Russia

Adult patient who presented in May 2023 with confusion, anxiety, aggressive behavior, and headaches. Neurological examination revealed a gentleman with some minor cognitive loss.

A right temporal mass lesion was diagnosed based on CT and MRI scans. On May 17th, 2023, he underwent an image-guided left frontal craniotomy.

A 5-Aminolevulinic Acid-guided resection with electrophysiological monitoring was performed, resulting in a gross total resection.

Pathological findings confirmed Glioblastoma IDH wild type. The patient recovered quickly with no residual neurological deficits and was discharged home.

Adjuvant therapy, including external beam radiotherapy and concomitant Temozolomide, was initiated. Follow-up MRI on July 29th, 2023, one month following completion of irradiation, showed a suspected tumor recurrence around the resection cavity with involvement of the right hippocampus. Tumor board discussion advised re-operation, however, the patient declined surgical options and preferred to continue medical therapy with oral Temozolomide.

As of April 29th, 2024, the patient is still under neuro-oncological surveillance and therapy, with a poor functional status.

Supplementary Table 3B

Summary of the results obtained in this study on the T cells of Glioblastoma Patient 3

SUMMARY OF ALL THE FINDINGS RELATED TO THE CELLS OF GLIOBLASTOMA PATIENT 3	
Increased arrest of human Glioblastoma cells by T cells of Glioblastoma Patient 3 (in co-cultures for 1 week)	
Fewer human Glioblastoma cells grew in co-cultures with T cells of Glioblastoma Patient 3, when the T cells pre-treated with Neurotransmitters and/or Neuropeptides	**YES !!** **Glutamate**+**Neuropeptide Y** (35% decease in no. of cancer cells) **;** **Dopamine**+**Neuropeptide Y** (30% decease) ; **Neuropeptide Y** (20% decease) ; **Glutamate** (7% decrease) ; **GnRH-II** (7% decrease) ; **GnRH-II** +**Neuropeptide Y** (7% decrease)

Supplementary Table 4A **Clinical information on Glioblastoma Patient 4**

Age at the time of surgery & study (years)		Tumor type	Tumor stage	Tumor location in brain	Brain surgery for GBM	Drugs and/or other treatments for GBM	Diseases in past & present except GBM	Drugs and/or other treatments for other diseases	Significant health events before the onset of GBM (injury or other)	Immune tests and/or treatments before the onset of GBM	Prognosis	Other info. of any kind
Adult		Glioblastoma IDH wildtype	4	Left Temporal lobe	1st surgery: May 5th, 2021 2nd op: May 31st, 2023	1. WBTR 2. Temozolomide 3. TTF 4. 'Personalized tumor neoantigen-specific vaccine treatment' in a private clinic in Germany. (This treatment was remote, independent and prior to the current study)	1. Asthma 2. ADHD	1.Methylphenidate 2. Montelukast 3. Fluticasone – nasal spray	None	None	Dismal	

Adult patient who presented back in April 2021 with word-finding difficulties. CT and MRI scans revealed an oval lesion at the base of the left temporal lobe measuring 23 by 21 mm with a moderate amount of surrounding edema. A radiological diagnosis of suspected high-grade glioma was made, leading to the patient undergoing an image-guided left temporal craniotomy, assisted by A 5-Aminolevulinic Acid-guided resection. Postoperative MRI showed gross total resection, and the postoperative course was uneventful. Pathological findings confirmed Glioblastoma IDH wild type. Adjuvant therapy, including external beam radiotherapy and concomitant Temozolomide, was initiated.

Treatment continued with Temozolomide and TTF. Additionally, the patient received– 'Personalized tumor neoantigen-specific vaccine treatment' in a private clinic in Germany (treatment was remote, independent and prior to the current study). In May 2023, the patient experienced reading difficulties, prompting an urgent MRI on May 28, 2023, which revealed recurrent tumor at the surgical bed with similar size and shape. After a detailed discussion with the patient, we proceeded with a recraniotomy on May 31, 2023.

During anesthesia induction for this surgery, peripheral blood was drained for the present immunotherapy study. Once again, a careful A 5-Aminolevulinic Acid-guided resection of the tumor was conducted, resulting in gross total resection. The patient opted to continue the investigational immunotherapy protocol in Germany. Since then, the patient was lost to our clinical and radiological follow-up. The patient died in 2025.

Supplementary Table 4B **Summary of the results obtained in this study on the T cells of Glioblastoma Patient 4**

SUMMAYRY OF ALL THE FINDINGS RELATED TO THE CELLS OF GLIOBLASTOMA PATIENT 4	
Decreased expression of exhaustion-related checkpoint inhibitors in T cells of Glioblastoma Patient 4	
PD-1	**YES !!** Neuropeptide Y (33% decrease)
LAG-3	**YES !!!** Neuropeptide Y (59% decrease) ; Glutamate+Neuropeptide Y (40% decrease) ; Dopamine (15% decrease)
Tim-3	**No**
TIGIT	**YES !** Glutamate+Neuropeptide Y (17% decrease)
CD160	**YES !!!!!!!!** Dopamine+Neuropeptide Y (99% decrease) ; Glutamate+Neuropeptide Y (82% decrease) ; Neuropeptide Y (26% decrease)
Increased number of big alive T cells of Glioblastoma Patient 4	
Increased no. of big not granular alive T cells	**YES !!** Dopamine+Neuropeptide Y (21% increase); Glutamate+Neuropeptide Y (15% increase) ; Dopamine (15% increase) ; Glutamate (13% increase) ; GnRH-II (13% increase) ; Neuropeptide Y (13% increase)
Increased arrest of human Glioblastoma cells by T cells of Glioblastoma patient 4 (in co-cultures for 1 week)	
Fewer Glioblastoma cells grew in co-cultures with T cells of Glioblastoma Patient 4 pre-treated with Neurotransmitters and/or Neuropeptides	**YES !!** Dopamine (23% decrease) ; Glutamate (15% decrease) ; Glutamate+Neuropeptide Y (15% decrease) ; Dopamine+Neuropeptide Y (15% decrease)
Increased migration In Vitro of T cells of Glioblastoma patient 4, towards the growth medium and secreted factors of human Glioblastoma cells	
Increased in vitro migration Glioblastoma patient's big and alive T cells towards human Glioblastoma's cells medium and secreted factors	**YES !!** Neuropeptide Y (28% increase) ; Dopamine (23% increase); ; Glutamate+Neuropeptide Y (23% increase)