Supplementary table 1. Tests of *Tdo2* induction in cultured cells

Murine mesenchymal stem cells (C3H/10T1/2 and MSC-BALB/c)	**Impact on *Tdo2* expression?**
Differentiation into a fibroblast/vSMC-like phenotype	
TGFβ	No
TGFβ + FGF	No
Pregnancy hormones	
Progesterone (alone / + TGFβ / + TGFβ + FGF)	No
Estradiol (alone / + TGFβ / + TGFβ + FGF)	No
hCG (alone / + TGFβ / + TGFβ + FGF)	No
Progesterone + estradiol (alone / + TGFβ / + TGFβ + FGF)	No
Progesterone + estradiol + hCG (alone / + TGFβ / + TGFβ + FGF)	No
Cytokine mix: IL-1β + IL-6 + IL-10 + TNFα	No
Murine freshly isolated endometrial cells	
From non-gravid females (*Tdo2*-negative undecidualized cells)	
Progesterone + estradiol	No
cAMP	No
Progesterone + estradiol + cAMP	No
Glucocorticoids (dexamethasone)	No
LPS + IFNγ	No
From gravid females (*Tdo2*-positive decidualized cells)	
Progesterone + estradiol	No
Glucocorticoids (dexamethasone)	No
LPS + IFNγ	Small increase

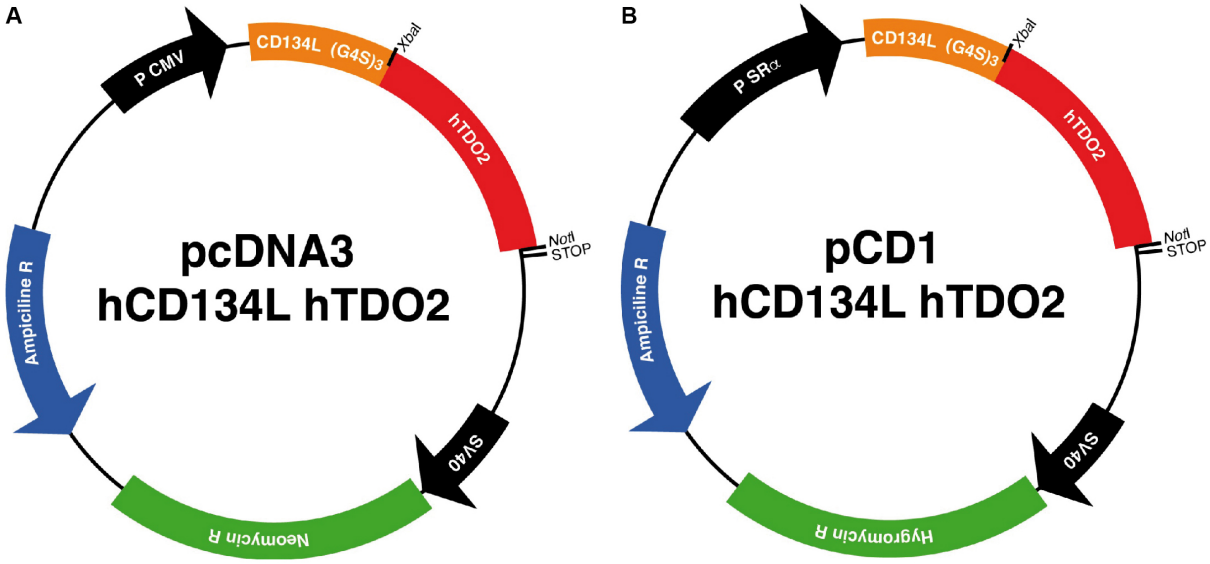
The induction of *Tdo2* was studied in murine mesenchymal stem cells (MSC), which are precursor cells of pericytes, and in cells freshly isolated from murine uteri.

Two different MSC lines were used. C3H/10T1/2 cell line (C57BL/6J background) was purchased from ATCC. MSC-BALB/c cells were established from the bone marrow of BALB/c mice. The bone marrow was collected, CD11b-positive cells were negatively selected and remaining adhering cells were cultured. The purity of MSCs was controlled by flow cytometry. They expressed PDGFRβ and CD44 and were negative for CD31, CD45 and CD11b.

Normal or decidualized endometrial cells were respectively collected from the uteri of non-gravid or gravid mice by dispase, collagenase I and collagenase II digestion.

The cells were cultured with the indicated hormones, growth factors or cytokines and *Tdo2* expression was analyzed by RT-qPCR.

Abbreviations: cAMP = cyclic adenosine monophosphate; FGF = fibroblast growth factor; hCG = human chorionic gonadotropin; IFNγ = interferon gamma; IL = interleukin; LPS = lipopolysaccharide; TGFβ = transforming growth factor beta; TNFα = tumor necrosis factor alpha, vSMC = vascular smooth muscle cell.

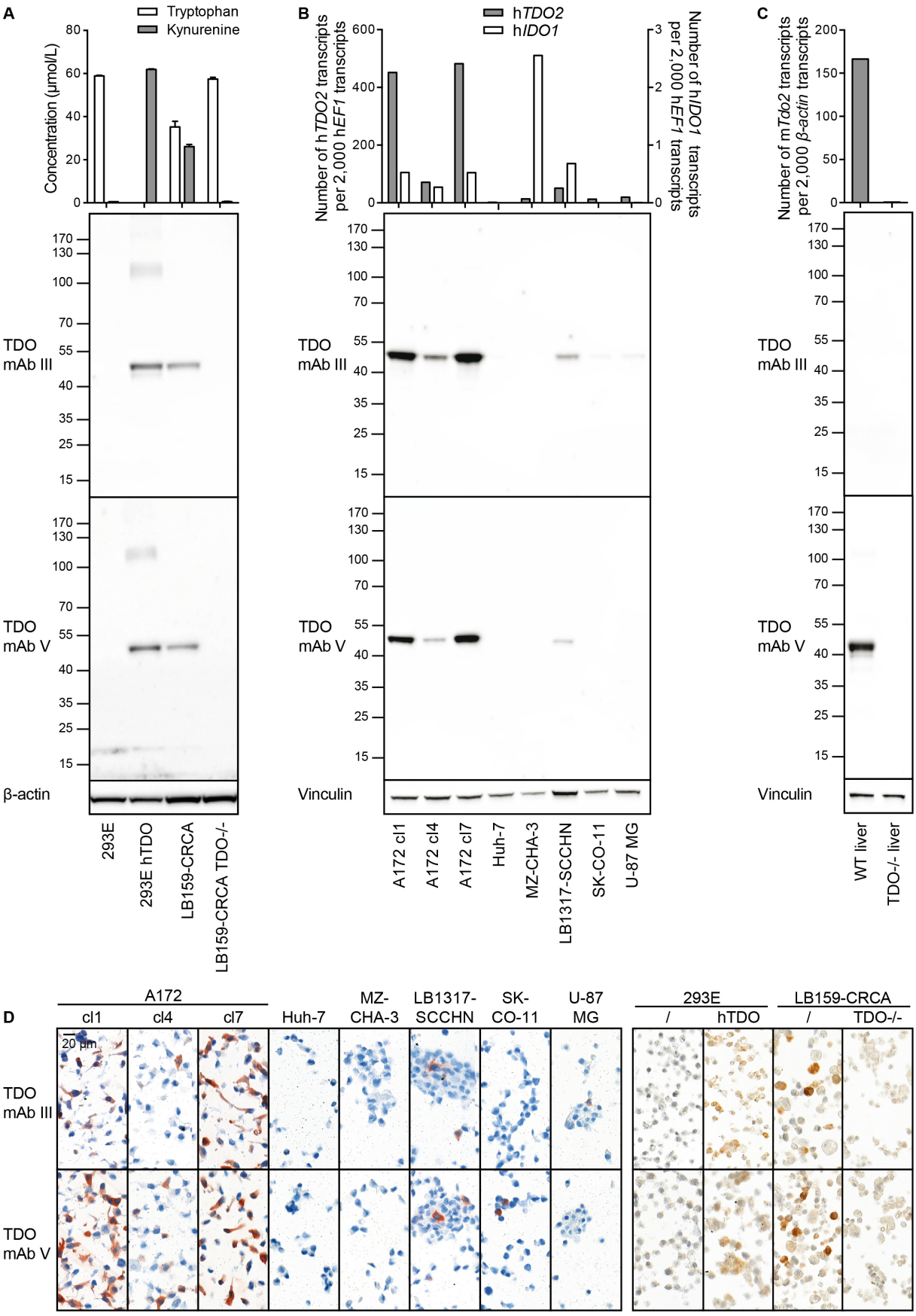


Supplementary figure 1. Plasmids used for mouse immunization

(**A**) In the pcDNA3 hCD134L vector, the human *CD134L* cDNA followed by a (G4S)3 coding linker, a XbaI/NotI cloning site and a stop codon were inserted downstream of the CMV promoter. The *hTDO2* insert was obtained by XbaI/NotI digestion of pCD1 hCD134L hTDO2 (described below in Fig. S1B) and cloned by XbaI/NotI digestion into the pcDNA3 hCD134L vector.

(**B**) In the pCD1-hCD134L vector, the human *CD134L* cDNA followed by a (G4S)3 coding linker, a XbaI/NotI cloning site and a stop codon were inserted downstream of the SRα promoter. The *hTDO2* open-reading frame was obtained by RT-PCR using a forward primer 5'-CAGTGCCTTTCTAGAATGAGTGGGTGC-3' containing a XbaI restriction site and a reverse primer 5'-GCAGAGCGGCCGCATCTGATTCATCAC-3' containing a NotI restriction site. The amplicon was then cloned by XbaI/NotI digestion into the vector resulting in pCD1 hCD134L hTDO2.

(Nizet Y, Gillet L, Schroeder H, Lecuivre C, Louahed J, Renauld JC, et al. Antibody production by injection of living cells expressing non self antigens as cell surface type II transmembrane fusion protein. J Immunol Methods 2011;367(1-2):70-7.)


A
Tryptophan
Kynurenine
Concentration (µmol/L)
TDO mAb III
TDO mAb V
β-actin
293E
293E hTDO
LB159-CRCA
LB159-CRCA TDO-/-
B
hTDO2
hIDO1
Number of hTDO2 transcripts per 2,000 hEF1 transcripts
Number of hIDO1 transcripts per 2,000 hEF1 transcripts
Vinculin
A172 cl1
A172 cl4
A172 cl7
Huh-7
MZ-CHA-3
LB1317-SCCHN
SK-CO-11
U-87 MG
C
Number of mTdo2 transcripts per 2,000 β-actin transcripts
WT liver
TDO-/- liver
D
A172
cl1
cl4
cl7
Huh-7
MZ-CHA-3
LB1317-SCCHN
SK-CO-11
U-87 MG
293E
/
hTDO
LB159-CRCA
/
TDO-/-
20 µm

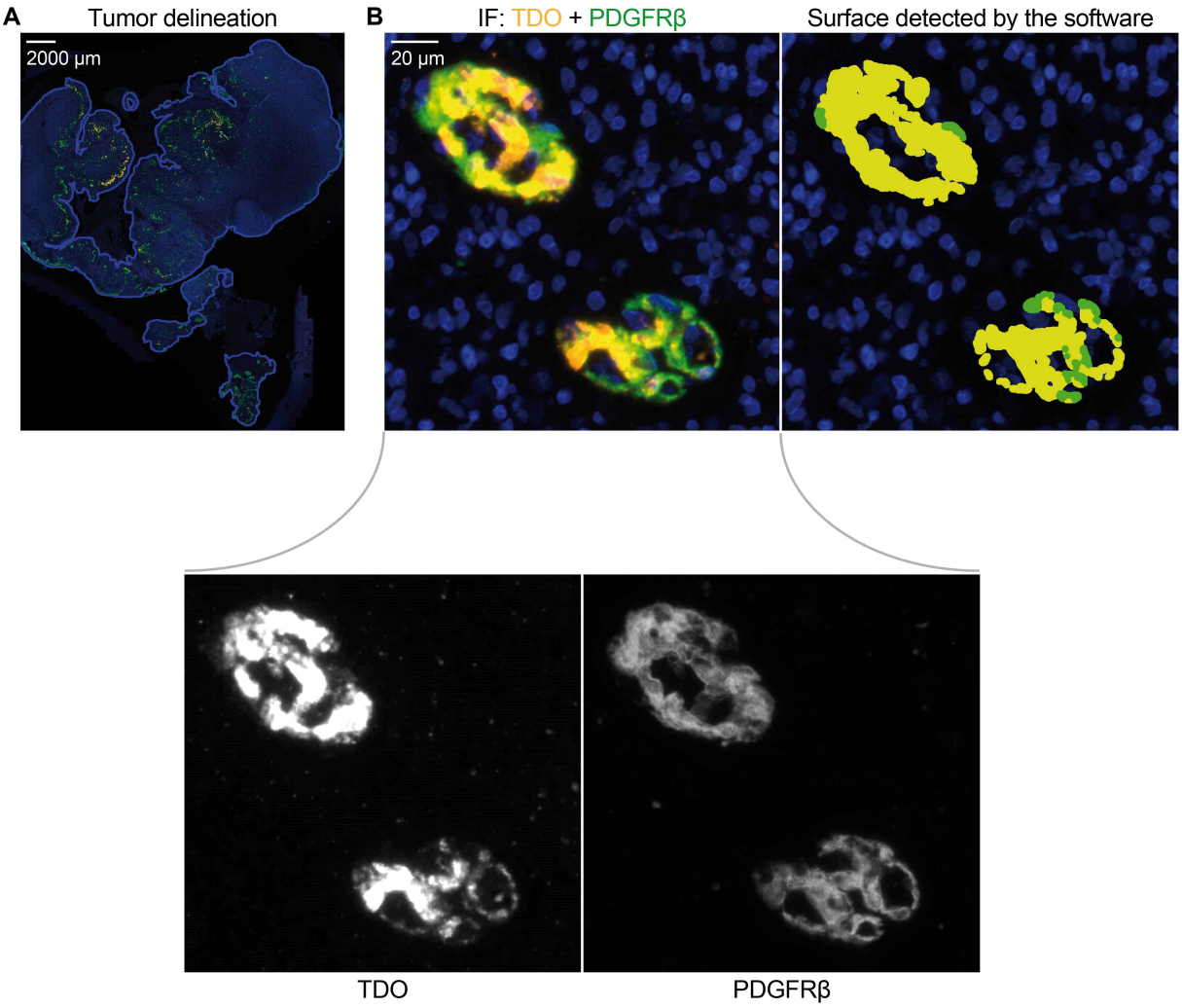
Supplementary figure 2. **Validation of the TDO mouse monoclonal antibodies mAb III and mAb V**

(**A**) Tryptophan and kynurenine were quantified by HPLC in cell culture supernatants of HEK-293 cells transfected or not with *TDO2* (mean±SD), or TDO-expressing colon carcinoma line LB159-CRCA and its derivative in which the *TDO2* gene had been inactivated by CRISPR-Cas9. TDO was revealed by western blot (WB) (protocol #1) with the mouse TDO mAb III and V. Beta-actin was used as loading control.

(**B**) Parallel analysis of the expression of *TDO2* mRNA by RT-qPCR and TDO protein by WB. Human tumor lines expressing different levels of *TDO2* mRNA were tested, including three clones of human glioblastoma line A172, an hepatocarcinoma line (Huh-7), a cholangiocarcinoma (MZ-CHA-3), a head and neck squamous cell carcinoma (LB1317-SCCHN), a colon carcinoma (SK-CO-11) and an astrocytoma line (U-87 MG). TDO protein was revealed by WB (protocol #2) with the mouse TDO mAbs III and V. Vinculin was stained as loading control. Thirty minutes before harvesting the cells for WB, 200 µmol/L of tryptophan were added to the culture medium to stabilize the TDO protein.

(**C**) Murine *Tdo2* was quantified by RT-qPCR on RNA extracted from WT and $TDO^{-/-}$ livers. TDO was revealed by WB (protocol #2) with the mouse TDO mAbs III and V. Vinculin was used as loading control.

(**D**) TDO was revealed by IHC on FFPE cell pellets from the validated cell lines indicated in (A and B), using mouse TDO mAbs III and V. Thirty minutes before harvesting the cells, 200 µmol/L of tryptophan were added to the culture medium to stabilize the TDO protein. Scale bar = 20 µm. Negative controls were performed with a mouse IgG2a isotype control and remained unstained.

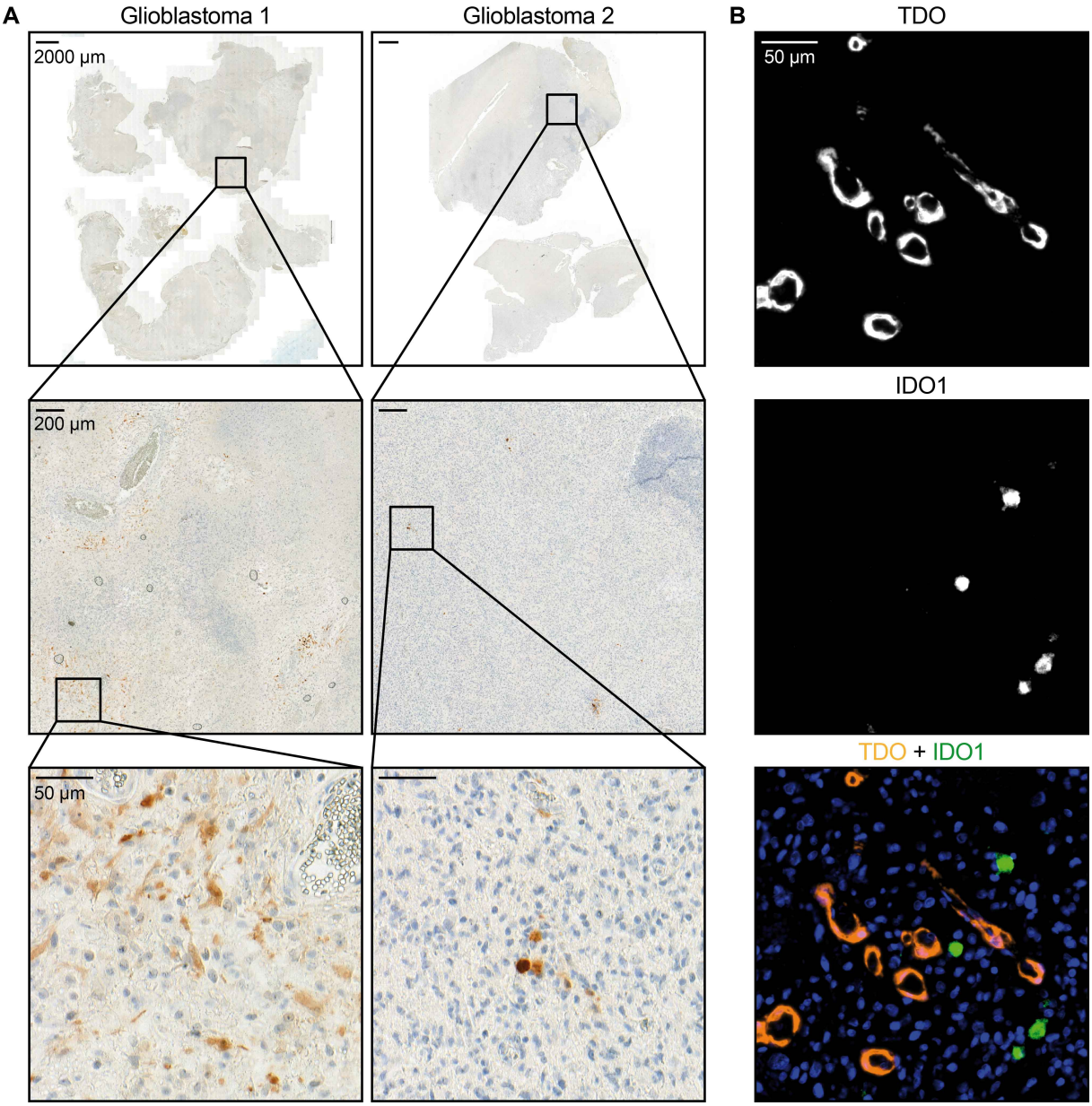


Supplementary figure 3. **Workflow for quantification of TDO-positive pericytes**

Immunofluorescence co-stainings were performed for TDO mAb V (orange) and PDGFRβ (green) on tissue sections from 34 glioblastomas multiforme. Negative controls were performed by omitting the primary antibody and remained unstained.

(**A**) The tumor was manually delineated (blue lines) on the fluorescent scan at a low digital magnification based on an adjacent section stained with HE.

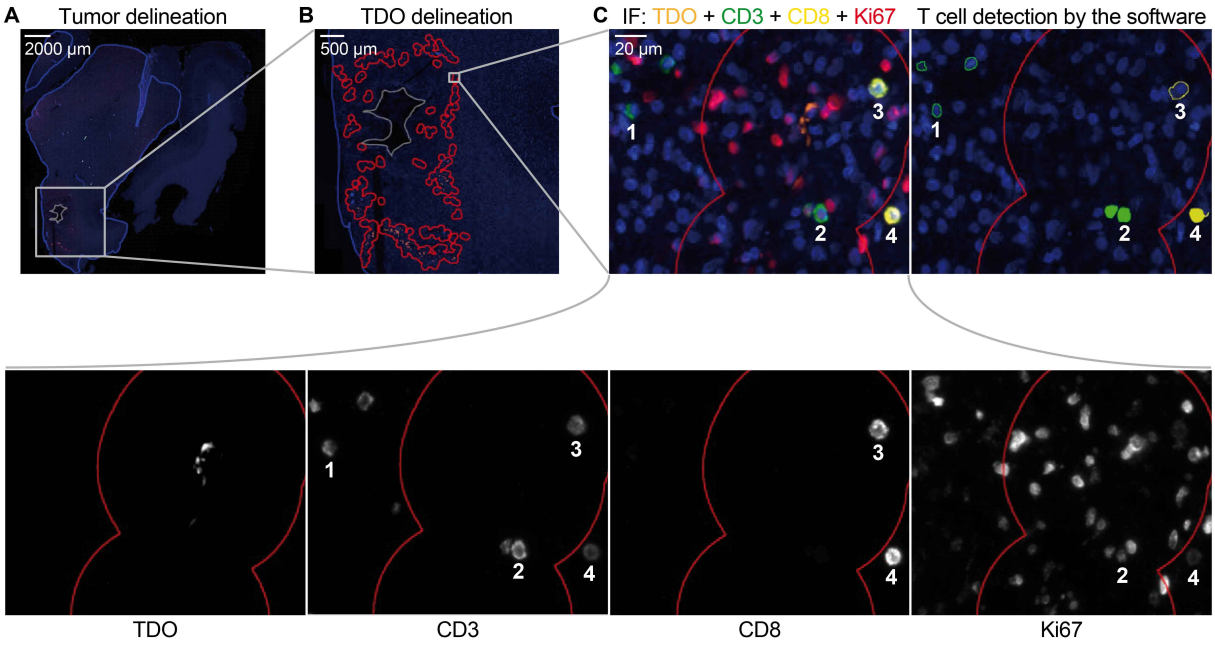
(**B**) TDO- and PDGFRβ-stained surface was detected. The left picture shows an example of the IF staining. The right picture shows the surface detection by the software in the same tissue region. Co-localization of both markers is represented in yellow whereas PDGFRβ-positive regions without TDO are stained in green. TDO- and PDGFRβ-stained pixels were detected at high resolution (x20) using a thresholding classification method on Cy5 (TDO) and Sp-Green (PDGFRβ) image features. Thresholds were adjusted on representative stained vs not stained regions. The same parameters were kept constant for all slides. Results are expressed as percentage of co-stained pixels among PDGFRβ-stained pixels.



Supplementary figure 4. **IDO1 expression in human glioblastomas**

(**A**) Representative pictures showing IDO1 IHC staining in glioblastomas with high (left column) and low (right column) IDO1 expression. Scale bars = 50-2,000 µm.

(**B**) Co-stainings were performed by immunofluorescence on FFPE glioblastoma sections, with TDO mAb V in orange and IDO1 in green. Scale bar = 50 µm.



Supplementary figure 5. **Workflow for lymphocyte quantification**

(**A**) The tumor was manually delineated by blue lines on the fluorescent scan at a low digital magnification based on an adjacent section stained with HE. Non-tumoral or necrotic regions that were located inside of tumor regions were eliminated by grey lines.

(**B**) TDO-stained clusters were automatically delineated (red lines) at a digital magnification of x10 using a thresholding method relying on the Cy5 (TDO) image feature. Clusters smaller than 4500 μm^2 were discarded. Delineations were dilated of 60 µm. TDO-negative tumor regions were all the remaining zones of the tumor area.

(**C**) Infiltrating lymphocytes were counted in TDO-positive and -negative tumor regions. The left picture shows an example of the IF staining. The right picture shows the lymphocyte detection by the software in the same tissue region. Ki67-negative (1 and 3) and -positive (2 and 4) lymphocytes are respectively shown as unfilled and filled circles. CD3+CD8- cells are stained in green (1 and 2), CD3+CD8+ cells are stained in yellow (3 and 4). Nuclei (expressing or not Ki67) were detected at high magnification (x20) with a cell classification relying on the DAPI (nuclei) and SP-Red (Ki67) image features enhanced by a polynomial blob filter. Following segmentation, post-processing steps were applied to separate CD3- and CD8-stained cells according to the detection of these antigens, based on SP-Green (CD3) and SP-Gold (CD8) features, around the detected nuclei. Detected cells (CD3+CD8+Ki67+/-, CD3+CD8-Ki67+/-) were finally quantified using a counting frame to avoid double cell counting. The same parameters were kept constant for all slides.