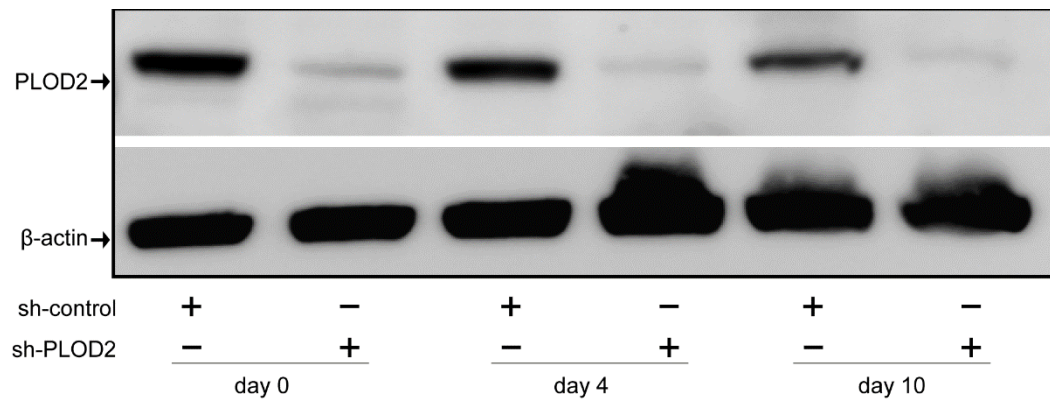
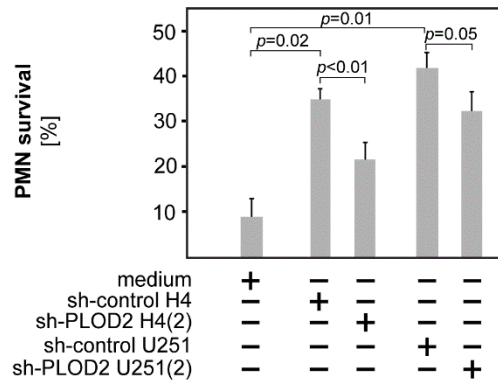
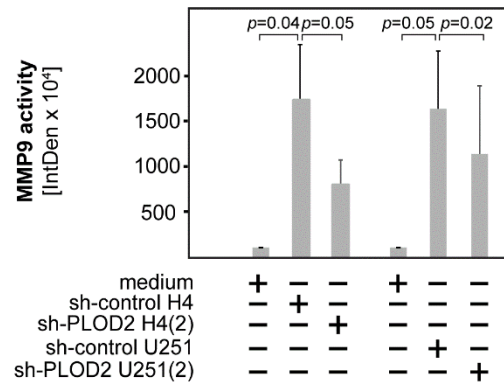


## Supplementary Figure S1



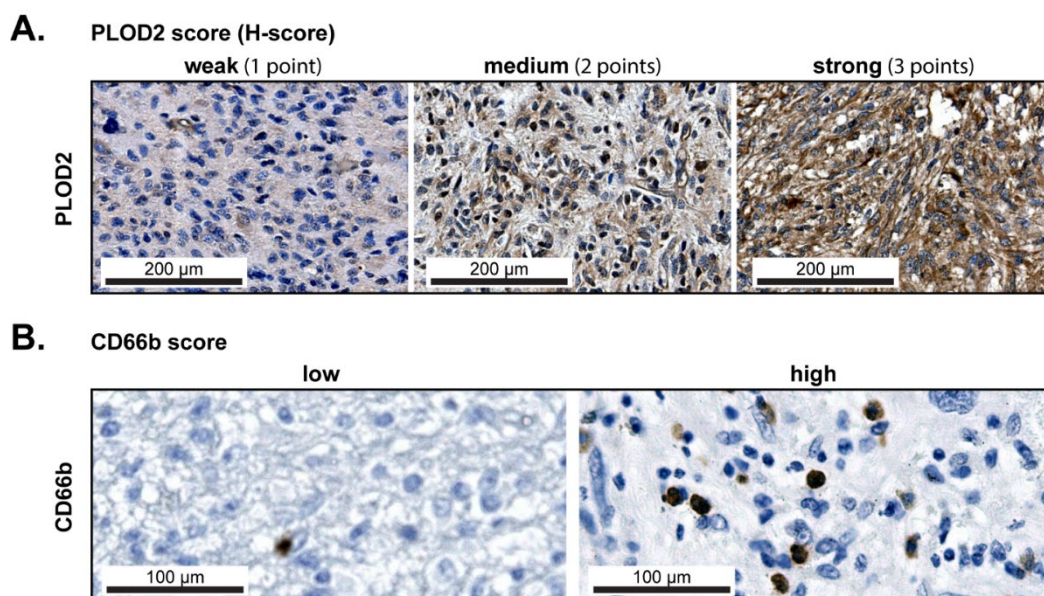
**Supplementary Figure S1. Stability of PLOD2 knock-down during functional assays.** Transfected H4 cells were cultured in medium without puromycin. The cells were lysed at day 0, day 4 and day 10 in culture and PLOD2 expression was analysed by western blot. Beta-actin was used as loading control.

## Supplementary Figure S2

**A.****B.****Supplementary Figure S2. PLOD2 and neutrophils in GBM – exclusion of clonal effects.**

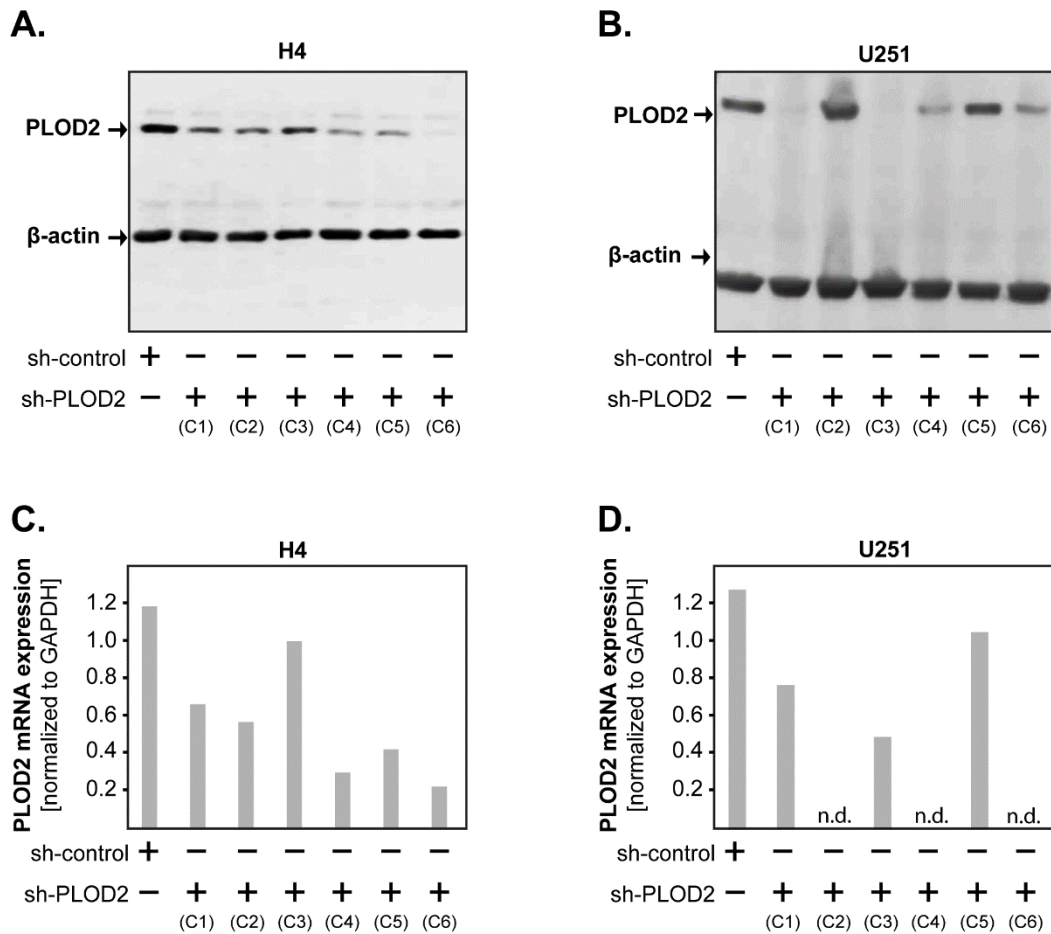
Neutrophils were incubated with supernatants (SN) derived from sh-control or a second clone (2) of sh-PLOD2 GBM cells. Culture medium was used as control. The survival of neutrophils was assessed at 24 h and the release of MMP9 at 1 h post-stimulation. **(A)** Sh-control SN prolonged the survival of neutrophils in both cell lines. This effect was significantly lower upon stimulation with PLOD2 knock-down SN **(B)** Neutrophils stimulated with sh-PLOD2 SN released significantly lower levels of MMP9 compared with their sh-control stimulated counterparts. For quantification, the integrated density of the bands was determined using the ImageJ software. The data are presented as percentage to medium only. Shown are the means + S.D. of three independent experiments. Statistical analysis was performed with the paired *t*-test.

# Supplementary Figure S3



**Supplementary Figure S3. PLOD2 and CD66b: expression and scoring in GBM tissues.** (A) Representative micrographs showing “weak” (1 point), “medium” (2 points) and “strong” (3 points) expression of PLOD2 in GBM tissues. The H-score was subsequently calculated according to the formula:  $(1 \times X) + (2 \times Y) + (3 \times Z)$ , where  $X + Y + Z = 100\%$  of the total tumor area. (B) Representative micrographs showing low and high CD66b expression in GBM tissues.

## Supplementary Figure S4



**Supplementary Figure S4. Stable knock-down of PLOD2 in H4 and U251 GBM cell lines.** H4 and U251 cells were transfected with PLOD2 shRNA (sh-PLOD2) or a control shRNA (sh-control). After antibiotic selection and limiting dilution, we tested 6 clones (C1-C6) for PLOD2 expression. Representative western blot showing PLOD2 expression in sh-control versus sh-PLOD2 C1-C6 in **(A)** H4 cells and **(B)** U251 cells. Beta-actin was used as loading control. PLOD2 mRNA levels in knock-down versus control **(C)** H4 cells and **(D)** U251 cells. GAPDH was used as a housekeeping gene to normalize the expression of PLOD2 in these cells. Clone C6 (H4 cells) and clone C3 (U251 cells) were used in all experiments. Clone C4 (H4 cells) and clone C1 (U251 cells) were used in selected experiments to exclude clonal effects.

Supplementary Table S1

|                           | Hannover cohort |      |        |      | Magdeburg cohort |      |        |      |
|---------------------------|-----------------|------|--------|------|------------------|------|--------|------|
|                           | all patients    |      | IDH WT |      | all patients     |      | IDH WT |      |
|                           | No.             | %    | No.    | %    | No.              | %    | No.    | %    |
| <b>All patients</b>       | 204             | 100  | 181    | 100  | 203              | 100  | 164    | 100  |
| <b>Sex</b>                |                 |      |        |      |                  |      |        |      |
| female                    | 87              | 42.6 | 76     | 42.0 | 95               | 46.8 | 78     | 47.6 |
| male                      | 117             | 57.4 | 105    | 58.0 | 108              | 53.2 | 86     | 52.4 |
| <b>KPS</b>                |                 |      |        |      |                  |      |        |      |
| 0                         | 0               | 0    | 0      | 0    | 3                | 1.5  | 3      | 1.8  |
| 10                        | 2               | 1.0  | 2      | 1.1  | 0                | 0    | 0      | 0    |
| 20                        | 1               | 0.5  | 1      | 0.6  | 2                | 1.0  | 2      | 1.2  |
| 30                        | 3               | 1.5  | 2      | 1.1  | 9                | 4.4  | 9      | 5.5  |
| 40                        | 10              | 4.9  | 9      | 5.0  | 10               | 4.9  | 8      | 4.9  |
| 50                        | 26              | 12.7 | 23     | 12.7 | 32               | 15.8 | 29     | 17.7 |
| 60                        | 43              | 21.1 | 39     | 21.5 | 38               | 18.7 | 27     | 16.5 |
| 70                        | 40              | 19.6 | 37     | 20.4 | 70               | 34.5 | 54     | 32.9 |
| 80                        | 41              | 20.1 | 36     | 19.9 | 19               | 9.4  | 16     | 9.8  |
| 90                        | 29              | 14.2 | 23     | 12.7 | 19               | 9.4  | 15     | 9.1  |
| 100                       | 1               | 0.5  | 1      | 0.6  | 0                | 0    | 0      | 0    |
| n.d.                      | 8               | 3.9  | 8      | 4.4  | 1                | 0.5  | 1      | 0.6  |
| <b>Therapy</b>            |                 |      |        |      |                  |      |        |      |
| surgery                   | 22              | 10.8 | 22     | 12.2 | 36               | 17.7 | 31     | 18.9 |
| surgery + RTX             | 26              | 12.7 | 25     | 13.8 | 21               | 10.3 | 18     | 11.0 |
| surgery + CTX             | 5               | 2.5  | 4      | 2.2  | 1                | 0.5  | 1      | 0.6  |
| surgery + RCTX            | 140             | 68.6 | 121    | 66.9 | 140              | 69.0 | 109    | 66.5 |
| n.d.                      | 11              | 5.4  | 9      | 5.0  | 5                | 2.5  | 5      | 3.0  |
| <b>Surgical resection</b> |                 |      |        |      |                  |      |        |      |
| total                     | 81              | 39.7 | 68     | 37.6 | 77               | 37.9 | 59     | 36.0 |
| subtotal/biopsy           | 110             | 53.9 | 101    | 55.8 | 115              | 56.7 | 96     | 58.5 |
| n.d.                      | 13              | 6.4  | 12     | 6.6  | 11               | 5.4  | 9      | 5.5  |
| <b>MGMT status</b>        |                 |      |        |      |                  |      |        |      |
| methyalted                | 90              | 44.1 | 79     | 43.6 | 118              | 58.1 | 100    | 61.0 |
| unmethyalted              | 99              | 48.5 | 87     | 48.1 | 78               | 38.4 | 64     | 39.0 |
| n.d.                      | 15              | 7.4  | 15     | 8.3  | 7                | 3.4  | 0      | 0    |
| <b>IDH mutation</b>       |                 |      |        |      |                  |      |        |      |
| wild-type                 | 181             | 88.7 | 181    | 100  | 164              | 80.8 | 164    | 100  |
| mutated                   | 9               | 4.4  | 0      | 0    | 10               | 4.9  | 0      | 0    |
| n.d.                      | 14              | 6.9  | 0      | 0    | 29               | 14.3 | 0      | 0    |

**Supplementary Table S1. Clinical characteristics of GBM patients.** WT: wild-type; KPS: Karfnofsky Performance Scale; RTX: radiotherapy; CTX: chemotherapy; RCTX: radio-chemotherapy; n.d.: not determinable.

Supplementary Table S2

|                        | H4 cells                                     |   | U251-MG cells              |  |
|------------------------|--|---|----------------------------|--|
|                        | Properties                                   | Source  | Properties                 | Source   |
| <b>Age</b>             | 37   | Expasy;<br>ATCC                                       | 75                         | Expasy;<br>DOI:10.1002/cam4.219                                |
| <b>Sex</b>             | male   |   | male                       |  |
| <b>Ethnicity</b>       | caucasian                                    |   | caucasian                  |  |
| <b>Morphology</b>      | epithelial                                   |   | epithelial                 |  |
| <b>Growth</b>          | adherent                                     |   | adherent                   |  |
| <b>Karyotype</b>       | hypertriploid<br>73, XXYY in<br>26% of cells |   | DNA index<br>1.75; 66, XXY |  |
| <b>PTEN</b>            | mutation<br>(missense)                       | DOI:<br>10.1023/a:1010680<br>920087; DepMap<br>portal | mutation<br>(frameshift)   | DOI:<br>10.1111/j.1750-<br>3639.1999.tb00536;<br>DepMap portal |
| <b>TP53</b>            | LOH<br>mutation                              | DOI:<br>10.1023/a:1010680<br>920087                   | mutation                   | DOI:<br>10.1111/j.1750-<br>3639.1999.tb00536                   |
| <b>CDK2NA/<br/>p16</b> | no mutation                                  | DOI: 10.1186/1756<br>-9966-30-76                      | deletion                   | DOI:<br>10.1111/j.1750-<br>3639.1999.tb00536                   |
| <b>EGFR</b>            | low<br>expression                            | DOI:10.1007/s110<br>60-018-2903-8                     | moderate<br>expression     | DOI:<br>10.1007/s11060-<br>018-2903-8                          |

Supplementary Table S2. Characteristics of the GBM cell lines used in this study.