[0010] **Figure 6** presents data demonstrating that KMMP9 and KGw exhibit comparable cell entry and growth patterns. (A) Cells listed to the left of the panel were infected with virus at the multiplicities in gc/cell listed above the panels. After 6 hours cells were fixed and immunostained for ICP4. (B) GBM30 and (C) GBM169 cells were dissociated and infected with KMMP9 or KGw at 200gc/cell. Cell lysates were collected at 1, 2, 4, and 6 dpi and viral genome copy titers were determined by qPCR. No significant differences were observed between the two viruses in either host cell line (GBM30: P=0.20; GBM169: P=0.11).

[0011] **Figures 7A and 7B** present data demonstrating that KMMP9 shows similar or better tumor cell killing in comparison with KGw *in vitro*. U87, SNB19 or GBM30 cells were infected at 10 or 100 gc/cell for 3 days (FIG. 7A) or 7 days (FIG. 7B). Percentage cell survival relative to uninfected cells was determined by MTT assay (n=3; asterisk: P<0.05, unpaired student t-test).

[0012] **Figure 8** presents data demonstrating that MMP9 improves infectivity of oHSV in spheroids. GBM30 cells were grown in suspension and infected with $1x10^3$ pfu of either KMMP9 or KGw. Green fluorescence from the gC-T2a-eGFP cassette in both vectors was visualized daily at 2-6 dpi in whole-mount spheroids. (A) Representative images at 3 and 5 dpi. (B) Averaged quantification of eGFP signal in 6 spheroids per vector demonstrated an approximately 2-fold infectivity increase of KMMP9 over KGw (P=0.006). (C-E) Two groups of GBM30 spheroids were infected with KMMP9 or KGw at $4x10^7$ genome copies per spheroid. Spheroids were fixed, stained with DAPI, and Z section confocal images were recorded at intervals of 5 μm. Panel (C) shows 2 representative spheroids each from the KMMP9 and KGw groups after 3D reconstruction from 0 μm to 150□μm. Blue, DAPI; green, eGFP. Panel (D) shows Z-sections of 2 spheroids from each group at Z=100 μm. (E) Each spheroid was divided into 5 segments in terms of depth on the Z axis (from bottom up: 0-20μm, 25-50μm, 55-80μm, 85-100μm, 105-120μm, and 125-140μm). Relative signal intensity in each segment of the spheroid was calculated by averaging eGFP signal divided by DAPI signal. n=7; asterisk: P<0.05.

[0013] **Figure 9** presents data concerning KMMP9 treatment of a nude mouse model of GBM. GBM30 cells were implanted intracranially and KMMP9, KGw or PBS were injected 5 days later at the same coordinates (0.5mm anterior, 2mm lateral (right), 3mm deep to bregma). Animals were monitored daily and sacrificed when showing signs of morbidity. Data is presented as a Kaplan-Meier survival plot. Animals treated with KMMP9 or KGw survived