Supplementary Table 1: EFFICACY OF STEM CELL THERAPIES IN PRECLINICAL STUDIES

Year	Reference	Mechanism	Animal model (Species/Strain)	Stem Cells used	Culture of SC cells	Nr. of SC	Brain tumor cells used	SC Admin Route	Timing of SC administration	Endpoint	Efficacy	Other outcomes
2000	Herrlinger et al., 2000	Oncolytic virus	nude mice (nu/nu)	C17.2 immortalized (v-myc) mouse NPCs transduced with replication conditional HSV-1 vectors	DMEM +10% FCS	1x10^5/mouse (NPC/Glioma cell: 1:5-10)	Rat CNS1 glioma	Intracranially into the tumor.	5 days after intracranial injection of 200,000 CNS1 cells	3 and 6 days after virus-NPCs injections	not assessed	HSV-1 RR- transduced NPCs migrate along invasive streams of CNS-1 tumors
2000	Aboody et al., 2000	Enzyme-prodrug (CD/5-FC)	nude mice (nu/nu), Fisher rats	C17.2 immortalized (v-myc) mouse NSCs transduced with CD (CD-NSC)	not described	4x10^4-2x10^6	Rat CNS1 glioma cells (3x10^4-1x10^5), HGL21 human glioma cell line, D72 (RG2) rat glioma cell line	Directly into the tumor, behind the tumor, intraventricular, contralateral hemisphere or tail vein injection	4-6 days after tumor implant	6–9, 10–12, 14-16 and 21 days after tumor implant	Exemplified in one animal treated with 5-Fluoro-Cytosine and CD-NPC, indicating reduced tumor mass in CD-NPC+5-FC	NPCs migrated towards the tumor in all routes of administration, much less effective after iv administration
2000	Benedetti et al., 2000	Cytokine (IL-4)	C57BL/6 mice	NPCs were isolated from the cortex of postnatal day 1 C57BL/6 mice. ST14A cells were generated from the striatal primordia of embryonic day 14 rats.	Initially in serum free medium, cultured with serum for BrdU incorporation and transduction	Mice: 2x10^4-2x10^6 NPC-IL-4; Rats: 4x10^5-1.2^10^6 ST14A-IL-4	mouse GL261 and rat C6 cells	Intracranially into the tumor	At the same time with tumor cells or 5-7 days after tumor implantation.	2 days, 19 days, one month, 51 days, 70 days after tumor implantation and survival analysis.	Increased survival at 90 days of tumor bearing mice injected with NPCs (survival of 86% vs 0% when injected at the same time with tumor cells or 71% vs. 0% when NPCs were injected 5 days later). In rats there was a 50% long term survival when NPCs were administered at the same time with tumor cells and 65% when administered 7 days later.	Increased IL-4 production. Control NPCs induced an antitumor effect in the absence of transduced IL-4, in vitro and in vivo, indicating that NPCs may produce antitumor factors. Development of immune memory by rejection of rechallenge implants.
2002	Ehtesham et al., 2002a	Cytokine (IL-12)	C57BL/6 mice	NSCs derived from the brains of embryonic (E15) mice and adeovirally transduced with IL-12	DMEM/F12 supplemented with B-27 and 20 ng/ml EGF and bFGF	2x10^5	GL26 (10^4 cells)	Intracranially into the tumor.-	2 or 7 days after injection of GL26 cells	Survival	Long term survival (>60 days) in 30% NSC-IL-12-treated mice.	Long term survivors rejected the tumors upon rechallenge, demonstrating antitumor immune memory. NSC-IL-12 migrated towards contralateral tumor hemispheres. Animals treated with NSC-IL12 had increased numbers of CD4 and CD8 in the tumors.
2002	Ehtesham et al., 2002b	Propapoptotic agent (TRAIL)	nude mice (nu/nu)	NSC-TRAIL: primary NSCs derived from fronto-parietal regions of E15 mouse brains, transduced with Ad-TRAIL.	DMEM/F12 with B27 supplement and 20 ng/ml of EGF and bFGF	2x10^5	human U343 MG cell line (1x10^6 cells)	Intracranially into the tumor	7 days after tumor cell implantation	7 days after NSC-TRAIL injection	Induction of apoptosis in tumor cells, in the tumor core and in invading tumor cells; significant decrease in tumor size 7 days after inoculation of NSC-TRAIL.	Recombinant TRAIL or NSC-TRAIL did not induce apoptosis in primary mouse NSCs (as opposed to U343 MG cells).
2004	Yang et al., 2004	Cytokine (IL-12)	Sprague-Dawley rats	hNSCs.IL-12: human fetal (3-5 months) hippocampus derived NSCs transduced to express IL-12: (these cells have not been characterized or described before)	DMEM with 10% FBS	3x10^5 simultaneoous with tumors or 1.2 x10^6 when administered 5 days later	C6 rat glioma cells (4 x10^4)	Intracranially into the tumor at the same time or 5 days after tumor implantation.	At the same time as tumor cells or 5 days later	Survival	hNSCs.IL-12 induced significant increase in MS from 17 days in control animals to 73 days when injected into established tumors and 87 days when injected at the same time with tumor cells.	Increased infiltration with CD8+ and CD4+ T cells was observed in the tumor.

2005	Li et al., 2005	Enzyme/Prodrug (HSV-tk/GSV)	nude mice	NSCtk: fetal rat forebrain derived NSCs infected with HSV-tk retrovirus	DMEM/F12 supplemented with N2, EGF and bFGF	2x10^4 NSCtk in mice and 2x10^6 in rats with established tumors with or without GCV	C6 rat glioma cell line (2x10^4 in mice and 1x10^5 in rats)	Intracranially, into the tumor	At the same time as tumor cell implantation	21 days after tumor/NSCtk implantation and survival analysis.	long term survival in mice and rats treated with NSC-tk and GCV	
2006	Kim et al., 2006	Enzyme/Prodrug (CD/5-FC))	Swiss athymic nude mice	HB1.F3-CD: Human HB1.F3 retrovirally transduced with CD.	DMEM with 10% FBs	4.8x10^5 of HB1.F3-CD with 5-FC.	Daoy medulloblastoma cell line injected into the forebrain (1.2x10^5 cells),	Intracranially, into established tumors.	Two weeks after implantation of Daoy cells	6 weeks after tumor inoculation, 3 weeks after the end of 5-FC treatment.	76% reduction of tumor volume in animals treated with of HB1.F3-CD and 5-FC.	HB1.F3-CD cells migrated towards medulloblastoma cells as they did towards malignant glioma cells. Possible chemoattractic cues: SCF, CXCL12, VEGF.
2006	Yuan et al, 2006	Cytokine (IL-23)	C57BL/6 mice, athymic nude mice, and CD4 T-cell knockout mice	BM-NSC-IL-23: mouse BM–derived neural stem-like cells (BM-NSC) transduced with IL-23.	DMEM/F-12 supplemented with B27, EGF and bFGF on polylysine coated plates	2x10^5	GL26 mouse glioma cells (1x10^4)	Intracranially, into the tumor	3 days after tumor inoculation	survival, tumor size and immune profile at 4 weeks	Long term survival of 60% of mice treated with BM-NSC-IL23. MS of control animals: 30-35 days.	Antibody depletion of either CD8+ cytotoxic cells (CTLS), CD4+ or NK cells reduced the survival benefit of tumor bearing mice. Upon rechallenge long term survivors rejected the tumors, showing increased levels of IFNg.
2007	(Corsten et al., 2007)	Proapoptotic agent (TRAIL) in combination with mir21 knockdown in glioma cells	nude mice (nu/nu)	NPC-S-TRAIL: Mouse C17.2 NPCs (mouse postnatal cerebellar neural progenitor cells immortalized with avian myc oncogene (Ryder et al, 1989)) transduced with S-TRAIL.	DMEM with 5%FBS and 2.5%HS	1x10^5	Human U87, U87-mir21KD, (2x10^5 cells)	Intracranially, into the tumor	At the same time as tumor cell implantation	6 days post inoculation	Synergistic effect of miR21 KD and NPC-S TRAIL, inducing marked decrease in bioluminescent signaling after 6 days. No survival data is shown.	Increase in Caspase3/Caspase7 activity in vitro, decreased viability in A172 and U87, synergistic effect with knockdown of miR-21.
2007	Lin et al, 2007	NSC distribution study	nude mice (nu/nu)	HB1.F3-C1	DMEM with 10% FBS	2×105	U251.eGFP	Adjacent to the tumor, posterolateral to the site of tumor implantation	7 and 14 days after tumor cell implantation	5 days following implantation of NSCs	Not assessed, this is a study of NSC distribution within the tumor.	Confocal analysis showed high coverage of the tumor by NSCs, with increased number of NSCs at the center. NSCs were also found in tumor satellites, away from the primary tumor.
2008	Sonabend et al., 2008	Oncolytic Virus	nude mice (nu/nu)	hMSCs (commercial) infected with CRAd-CXCR4-RGD	MesenPro RS medium supplemented with 20% FBS.	2x10^4 hMSC infected with 100vp/cell of CRAd-CXCR4-RGD	U87MG (1x10^5)	Intracranially, into the tumor	7 days after tumor cell implantation.	14 days after tumor cell implantation, 7 days after administration of hMSC CRAd-CXCR4-RGD.	hMSC CRAd-CXCR4-RGD migrated into the tumor and deliverd a higher load of viral particles (46 fold higher) than when virus was injected alone.	CRAd-CXCR4-RGD was more toxic to U87MG glioma cells than to hMSCs.
2008	Sasportas et al., 2008	Propapoptotic agent (TRAIL)	SCID mice	hMSC: human BM-derived MSCs (David Prockop) modified to express s-TRAIL	Alpha-MEM with 16.5% FBS	5x10^5	Gli36-EGFRvIII (1x10^5) or GBM8 patient derived CD133+ cells	Intracranially, into the tumor	At the same time as tumor cell implantation	Survival	Increased MS of mice with GBM8 intracranial tumors treated with MSC-TRAIL from 54.5 days to 72 days.	
2009	Hong et al 2009	Cytokine (IL-12)	C57Bl/6 mice	mMSC-IL12: mouse BM-derived MSCs retrovirally transduced to express IL-12	Alpha MEM with 10% FBS	not mentioned	Ast11.9-2 glioma cells	Intracranially, into the tumor	Seven days after tumor implantation	Survival	Increased survival in MSC control and MSC-IL-12 injected animals.	Increased infiltration of tumors with T cells and immune cells.

2009	Tyler et al., 2009	Oncolytic Virus	nude mice (nu/nu)	hNSCs (ReNCell) immortalized with c-myc (Millipore) infected with CRAd-S-pk7	Laminin coated plates with ReNCell NSC medium (Millipore) supplemented with EGF and bFGF	Intracranial injections: 5x10^5 hNSC infected with 100 vp/cell compared to 10^8 loose viral particles (vp), flank injections: 1x10^6 hNSCs infected with 1000 vp/cell compared to 10^7 vp	U87MG and U373MG human glioma cells (ATCC); 1x10^6 cells/ intracranial or flank injections	Intracranial injections: intratumoral or directly anterior to the tumor, flank injections: directly into the tumor	Intracranial injections: 14 days after tumor implantation, flank injections, 7 days after tumor implantation	intracranial injections: 4, 8, 12 days post injection, flank tumors: 10 days after NSC-CRAd injection	hNSC-CRAd-S-pk7 injected into flank tumors reduced tumor volume to about 50% when compared to intratumoral injection of loose viral particles administration.	hNSC-CRAd-S-pk7 infected both hNSCs and glioma cells, migrated towards glioma tumors, conditioned medium and delivered higher titers of viral particles into the tumor.
2009	Xu et al., 2009	Cytokine (IL-18)	Spague Dawley rats	rMSCs-IL18: rat BM-derived MSCs transduced with adenovirus to express IL-18	DMEM, 15% FBS	1x10^6	C6 rat glioma cells (1x10^5)	intracranially into the tumor	3 days after tumor cell inoculation	Survival and 2 weeks after implantation of MSCs for cytokine and immune cell analysis	40% of rats treated wuth rMSCs-IL18 survived long term; all control animals died after about 3 weeks; upon rechallenge all long term survivors rejected the C6 tumors.	Tumors treated with rMSCs-IL18 had increased infiltration with CD8 and CD4 T cells.
2010	Balyasnikova et al., 2010	Antibody (scFvEGFRvIII)	nude mice (nu/nu)	hMSC-scFvEGFRvIII: hMSC transfected to express single chain antibody against EGFRvIII	MEM alpha with 10% FBS	2x10^6 hMSCs for flank tumors and 1x10^5 with or without additional 3x10^5 cells in intracranial tumors	U87-EGFRvIII (2x10^6 in flank tumors and 1x10^5 in intracranial tumors)	Into the tumor, intracranial or flank tumor	At the same time with tumor cells; additional administration 2 weeks later. hMSCs were also tested in established flank tumors.	Survival analysis for intracranial tumors, tumor volume for flank tumors (10-15 days)	Delay in growth in flank tumors, dependent on initial tumor size; modest increase in MS with intracranial administration of hMSCs, slight increase in survival with repeated administration of hMSCs.	Downregulation of pAKt with hMSC-sc FvEGFRvIII.
2010	Josiah et al, 2010	Oncolytic virus (myxoma virus: vMyxgfp)	nude mice (nu/nu)	hAD-MSC-OV: Human adipose derived MSCs (ZenBio) infected with myxoma virus (vMyxgfp)	α-MEM with 10% FBS	1:1 ratio with implanted tumor cells (1x10^5)	U87MG (1x10^5)	intracranially, together with tumor cells or adjacent to the tumor	at the same time as tumor inoculation or at 7 days intervals (up to 6 injections)	Survival, longitudinal MRI assesment of tumor volume	Long term disease free progression when administered at the same time with tumor cells; increased MS with one administration, long term survival with repeated administrations.	Decreased tumor volume when analyzed with MRI.
2010	Chang et al, 2010	Enzyme/Prodrug (CD/5-FC)	Sprague Dawley rats	hMSC-CD: human BM-derived MSCs retrovirally transduced to express CD	DMEM with 10% FBS	3x10^5, in one experiment repeated 3 times at one week interval	C6/LacZ7 rat glioma cells (3x10^5)	intracranially into the tumor	At the same time with tumor cells or 3 days later	14 days after tumor cell implantation for tumor measurement	When implanted into the rat brain three days later after tumor cells, one administration of MSC-CD had no significant effect on tumor volume compared to control animals. Three administrations of MSC-CD at 1 week interval combined with 5-FC inhibited growth of tumors to ~10% of control animals. No survival data is shown.	
2010	Gunnarsson et al., 2010	Cytokine (IL-7, with IFNg tumor cells)	Fisher 344 rats	rMSC-IL7: rat BM-derived MSCs, retrovirally transduced to express IL-7	not described	On days 8 and 12, 2.5×10^5 MSCs with or without IL-7. On days 5 and 15, 3×10^6 irradiated IFNγ-producing tumor cells were injected i.p. to glioma-bearing animals.	N32 rat glioma cells generated from ENU induced mutagenesis in Fisher rat embryos (3x10^3)	Intracranially into the tumor	Days 8 and 12 after tumor inoculation	25 days after tumor cell inoculation	Tumor size was reduced in MSC-IL-7 treated animals and increased reduction was observed when combined with intraperiotoneal injection of irradiated tumor cells expressing IFNg.	Increased infiltration of T cells in combined cytokine treatment.

2011	Li et al., 2011	Nanoparticles	Balb/c nude mice	SN-DOX-MSCs: human BM derived MSC loaded with DOX-NP conjugated with anti CD73 and anti CD90 antibodies (silica nanorattle time bomb).	DMEM with 10% FBS	10^7 SN-DOX loaded MSCs	10^7 U251 cells implanted subcutaneously	administered into the flank tumor	After tumor size reached to about 200 mm^3	1, 3 and 7 days SN-DOX MSC administration	Mice treated with MSC-SNAb(CD90)-DOX had the largest number of apoptotic tumor cells, when compared to DOX alone or SN-DOX administration.	hMSCs derived from BM express CD90, CD73, CD105, and CD44. Coating the SN with antibodies against CD73 and CD90 allowed for efficient uptake by hMSCs; DOX release from the SN was pH-sensitive and sustained up to 3 days, with a more rapid drug release rate at pH 4 (close to pH in lysosomes) than at pH 7.4 . hMSCs are not sensitive to DOX induced apoptosis due to low proliferation and possible ABC transporters.
2011	Ryu et al, 2011	Cytokine (IL-12)	C57Bl/6 mice	hUCB-MSC-IL12M: human MSCs derived from umbilical cord blood, adenovirally transduced to express IL-12	aMEM with 10% FBS	1x10^5	GL26 (1x10^5)	Intracranially into the tumor	14 days after tumor implantation	Survival and 7 days after MSC administration for FACS analysis and IHC analysis	Long term survival in 70% of animals injected with UCB-MSC-IL12M. Induction of tumor specific log term memory.	Increased infiltration with CD4 and CD8 T cells, reduced intratumoral vasularization.
2011	Yin et al, 2011	Enzyme/Prodrug (CE/CPT-11)	nude mice (nu/nu)	AF-MSC-Endo-sCE: human amniotic fluid derived MSCs transduced to express endostatin and a secreted form of CE	DMEM with 10% FBs	5×10^4 intracranially or 2.5×10^5 subcutaneously	U87MG-EGFRvIII (2.5 × 10^5) injected intracranial or 2 × 10^6 subcutaneously	Intracranially, together with tumor cells or into the tumor site after resection	At the same time as tumor cells implanted intracranially or after 90% of the subcutanous tumor was removed	In vivo bioluminescence monitoring over 17 days, subcutanous tumor growth over 14 days	No survival data presented. Decreased tumor size intracranially and following recurrence.	Decreased vessel density in the tumor, decreased proliferation index and increased apoptosis.
2011	Altanerova et al., 2011	Enzyme/Prodrug CDy::UPRT/5-FC	Adult male Sprague Dawley rats	CDy-AT-MSCs: Adipose tissue derived MSCs transduced to express the yeast CD:: uracil phosphoribosyltransferase (Cdy::UPRT).	DMEM supplemented with 5% human platelet extract	5x10^5 (1:1), 2.5x10^5(1:0.5), 5x10^4 (1:0.1), 2.5x10^4 (1:0.05)	C6 rat glioblastoma (5x10^5)	Intracranially, together with tumor cells	At the same time with tumor implantation and then repeated administration of 4x more CDy-AT-MSCs.	survival	Administration of CDy-AT-MSCs at a 1:1 ratio of Tumor: Stem Cells induced 63% long term survival, 1:0.5 37% , 1:0.1 25% and 1:0.05 12.5% long term survivors. Repeated administration of 4x more SC coupled with intraventricular administration of 5-FC increased the percent of long term survivors to 88%.	CDy-AT-MSCs migrated towards gliomas at a distance when injected into the contralateral hemisphere.
2011	Balyasnikova et al., 2011	Proapoptotic agent (TRAIL) with or without Bortezomib	nude mice (nu/nu)	NSCs (unspecified source, assumed ReNCells) transduced with lentiviral particles encoding human TRAIL	Laminin-coated plates, ReNCell medium supplemented with EGF and bFGF	0.5x10^5 or 1x10^5 NSC-TRAIL	Human U87MG-EGFRvIII glioma (10^5 cells)	Intracranially, at the time of tumor inoculation	Simultaneous with tumor cells, or 7 days later. Bortezomib was administered twice a week i.v., weeks 3-7.	Survival	Increased survival of animals injected with NSC-TRAIL (1:1 ratio). Combined treatement of NSC-TRAIL with Bortezomib lead to long term survival of tumor bearing animals (5 of 5 survived more than 100 days) compared to NSC-TRAIL treatment alone (4 of 5) when NSCs were administered simultaneous with tumor cells. NSC-TRAIL were less effective in established tumors or when the ratio NSC:Tumor cells was 0.5:1.	In vitro, Bortezomib increased expression of DR5 (TRAIL-R2), that could account for TRAIL sensitization of U87MG-EGFRvIII cells. This was not found in vivo, putting into question penetration of Bortezomib into the tumor following systemic delivery.
2011	Ahmed et al., 2011 a	Oncolytic Virus	nude mice (nu/nu)	hNSCs immortalized with c-myc (ReNCells) infected with CRAd-S-pk7.	Laminin coated plates with ReNCell NSC medium (Millipore) supplemented with EGF and bFGF	5×10^5 NSC loaded with 50 I.U./NSC and other doses of vp	U87MG (2.5×10^5)	Intracranially, into the tumor site	5 days after implantation of tumor cells	Survival	Increased median survival of hNSC-CRAd-S-pk7 injected animals from 63 to 91 days, when compared to animals injected with CRAd-S-pk7. Control animals had a median survival of 56 days.	Reduced neuronal toxicity, reactive GFAP and MHC-II expression when compared to viral particle administration.

2011	Ahmed et al., 2011 b	Oncolytic Virus	nude mice (nu/nu)	hNSCs (ReNCell) immortalized with c-myc (Millipore) infected with CRAd-S-pk7 or hMSC cells (Cambrex and Lonza) infected with **50 IU/cell** of CRAd-S-pk7	hNSCs: laminin coated plates, ReNCell (Millipore) with 20ng/ml EGF and bFGF; hMSCs: MesenPro RS medium with 20% FBS and 4ng/ml bFGF	5×10^5 hMSC-CRAd-S-pk7 or hNSC-CRAd-S-pk7	U87MG (3 × 10^5)	Intracranially, into the tumor	5 days after implantation of tumor cells	Survival	ReNCells laden with CRAd-S-pk7 were more effective in killing the glioma cells, improving the MS of mice, from 44 to 68.5 days, when compared to hMSCs. Control animals had a MS of 41.4 days.	
2012	Choi et al., 2012	Enzyme/Prodrug (CE/CPT-11)	Fischer 344 rats	hAT-MSC.rCE: human Adipose Tissue derived MSCs transduced with rabbit CE	MSC expansion medium supplemented with 10% FBS	2x10^5 administered twice, at 2 week intervals	F98 rat glioblatoma cells implanted into the brainstem (5x10^4)	intratumorally, into the brainstem .	2 days and 16 days after tumor cell implantation	Survival	Administration of hAT-MSC.rCE in combination with CPT-11 increased MS of rat bearing brainstem gliomas from 19 to 24 days, when compared to CPT-11 administration alone.	hAT-MSC, expressed CD73, CD90 and CD105 (MSC markers) but not CD14, CD34, CD45 (hematopoietic markers). hAT-MSCs differentiated into adipogenic, chondrogenic, osteogenic and neural lineages and migrated towards glioma cells in vitro.
2012	(Hingtgen et al., 2012)	Cytokine (MDA-7/IL-24) with proapoptotic agent (TRAIL)	SCID mice	Mouse NSCs transduced to express MDA-7/IL-24 (SML7) alone or in combination with S-TRAIL	Neurocult NSC Basal media supplemented with proliferation supplements EGF and bFGF.	1x10^5	human U87MG cells (2x10^5)	Intracranially, into the tumor	At the same time as tumor cells	Longitudinal bioluminescence monitoring	Significant inhibition of tumor growth at day 14-35 in mice treated with mNSC-SM7L. Co-administration of sTRAIL by NSCs, further improved this beneficial effect.	Significant reduction in Ki-67-positive cells in mNSC-SML7 treated animals. Increased number of cleaved Caspase 3 positive cells in the brains of animals treated with NSC-SML7/sTRAIL.
2012	Li et al., 2012	Enzyme/Prodrug (HSV-tk/GSV)	nude mice	BMSC-tk: human and rat BM derived MSC, retrovirally transduced to express thymidine kinase.	BMSC growth medium	2×10^4 human BMSCtk	A-172 (human glioma), T98G (human glioma), or C6 (rat glioma) (2×10^4)	Intracranially, at the same time as tumor cell inoculation	At the same time as tumor cell inoculation; GSV was administered at 50 mg/kg of GCV twice daily (100 mg/kg/day) from day 0 for 10 days	21 days after tumor implantation for tumor size analysis and when animals became moribund, for survival analysis	Treatment with BMSC-tk/GCV induced long term survival (>100 days) of all animals bearing A-172 and T98G tumors; control animals died after 3 weeks. 40% of mice bearing tumors with rat C6 glioma cells and treated with BMSC-tk/GCV showed long term survival, whereas all control animals died before 3 weeks.	
2012	Thaci et al., 2012	Oncolytic Virus	nu/nu mice, hamsters, cotton rat	HB1.F3-CD infected with 50 IU/cell of CRAd-S-pk7	HB1.F3-CD: DMEM with 10% FBS	5 x 10^5 HB1.F3-CD loaded with infected with CRAd-S-pk7 OV (**50 I.U./cell**)	U87MG (5 × 10^5) (only in mice)	intracranial, into the tumor site	21 days after implantation of tumor cells	mice: 5,12,17, hamsters: 1,7,30 and cotton rat: 4,7,14 days after injection with HB1.F3-CD CRAd-S-pk7	No efficiency data. This study analyzed the safety and distribution and persistance of viral titers from HB1.F3-CD infected with 50 IU/cell of CRAd-S-pk7 in immunocompromized mice and immunocompetent semi-permissive hosts, cotton rat and hamster.	Oncolytic effect of loading of HB1.F3-CD infected with 50 IU/cell of CRAd-S-pk7 was tested in vitro on U251, U87, U118, N10 and A548 tumor cells, Adenovirus replication in cells reached a maximum at 5-7 days and in the brain decreased to barely detectable levels over 30 days. Outisde the brain, viral particles were only detectable up to 24h in the serum and in the liver up to 7 days post injection. Intracranial injection of HB1.F3-CD was rendered safe in all three animal models tested.
2012	Hingtgen et al., 2012	Cytokine (MDA-7/IL-24) with sTRAIL	SCID mice	mNSC-SM7L; primary mouse NSCs lentivirally transduced to express SML7, a modified form of MDA7/IL24	Neurocult NSC Basal media supplemented with proliferation supplements (Stem Cell Technologies) and EGF 20 ng/ml	1x10^5 mNSC-SML7, mNSC-S-TRAIL, or mNSC-SML7/S-TRAIL	U87-Fluc (2x10^5)	intracranial, into the tumor site	At the same time as tumor cells	Luminescence monitoring up to 35 days	Administration of mNSC-SML7 induced significant inhibition of GBM growth by day 14, and this reduction in tumor progression persisted through 35 days (bilouminescence imaging). No survival data is presented. Combined administration of SML7 and sTRAIL was more effective in reducing tumor size	Postmortem IHC revealed reduced KI67 staining. In vitro studies showed that coadministration of SML7 and sTRAIL increased radiosensitivity of glioma cells and increased caspase 3 activity and cleavage of PARP.

2013	Gutova et al., 2013	Enzyme/Prodrug (CE/CPT-11)	nude mice (nu/nu)	HB1.F3.CD.rCE: human NSCs transduced to express CD and rabbit CE	DMEM with 10% FBS	1x10^5 in two administrations, a week apart	Transgenic murine medulloblastoma model induced with viruses expressing Shh and Mycn injected in the cerebellum of mice at postnatal day 3. Tumor formation was monitored by MRI.	Intracerebellar injection, one week later a second round of NSCs was administered.	When animals developed tumors detectable by MRI (~1.5 months after tumor inoculation)	71 days, tumor growth was monitored by MRI and analyzed post euthanasia	Tumor growth rate was slower in animals treated with HB1.F3.CD.rCE and CPT-11 between days 50-71. Tumor volume, analyzed at postnatal day 71, when animals were euthanized, was smaller when compared to CPT-11 treatment alone.	HB1.F3.CD.rCE cells, labeled with superparamagnetic iron oxide migrated towards established cerebellar tumors and were trackable with MRI.
2013	Aboody et al., 2013	Enzyme/Prodrug (CD/5-FC)	nude mice (nu/nu)	human HB1.F3.CD	DMEM +10% FCS	1x10^4, 5x10^4, 1x10^5	U251 glioma cell line (2x10^5/mouse)	intracranial, ipsilateral	NPCs were injected 7 days after tumor cells	Tumor size 30 days post injection, survival	Decreased tumor volume in NPC+5FC treated mice (from ~16.5 cubic microns to ~15.5 cubic microns), increased event-free probability in mice injected with the highest 2 doses of NPCs.	HB1.F3.CD cells had a stable, normal karyotype, included just one copy of v-myc and CD, expressed the HLA-I antigens but not (or very low levels of) HLA-II.
2013	Cheng et al., 2013	Nanoparticles	nude mice (nu/nu)	DOX-NP-NPCs: human HB1.F3.CD loaded with doxorubicin (DOX) pH-sensitive NPs (DOX-NPs)	DMEM +10% FCS	2.5×10^5 MSN-Dox loaded HB1.F3.CD cells	U87 glioma cell line (2.5×10^5)	Intracranial, intratumoral and contralateral hemisphere	NPCs were injected 3 days after tumor cells	Suvival and 3 days and 10 days after injection of DOX-NP-NPC for visualizing NPC and Dox distribution	Increased MS from 36.5 days with intratumoral DOX-NP administration to 41days or 42 days when NPCs loaded with DOX-NPs were injected either intratumorally or in the contralateral hemisphere, 5mm away.	DOX-NP-NPCs were distributed extensively throughout the tumor. Apoptosis of U87 cells (cleaved caspase 3 IHC) 3 days after NPC delivery.
2013	Ahmed et al., 2013	Oncolytic virus	nude mice (nu/nu)	Human NSCs immortalized with c-myc (ReNCell, Millipore) infected with CRAd-S-pk7 or HB1.F3-CD	hNSCs (ReNCell): laminin coated plates, ReNCell (Millipore) with 20ng/ml EGF and bFGF; HB1.F3-CD: DMEM with 10% FBS	5 x 10^5 ReNCell or HB1.F3-CD infected with CRAd-S-pk7 OV (50 I.U./cell)	U87MG (5 × 10^5)	Intracranially, into the tumor site	5 days after implantation of tumor cells	Survival	HB1.F3.CD loaded with CRAd-S-pk7 improved MS in mice bearing U87MG tumors from 79.5 to 108.5 days. Control animals had a MS of 64 days.	HB1.F3.CD also increased survival of mice implanted with patient derived GBM43FL and GBM12FL cells from 13 to 19.5 days and 32.5 to 43.5 days respectively. HB1.F3.CD cells were loaded with iron oxide microparticles and were shown to migrate towards the tumor when injected into the contralateral hemisphere of mice. CRAd-S-pk7–loaded HB1.F3.CD cells were more efficient than ReNCells in supporting viral replication and killing glioma cells in vitro.
2013	Tobias et al., 2013	Oncolytic virus in combination with SOC	nude mice (nu/nu)	HB1.F3-CD infected with 50 IU/cell of CRAd-S-pk7	DMEM +10% FCS	5x10^5 or 3x10^6 administered either 5 days after tumor implantation and followed by TMZ and XRT for 5 days or administered 11 days after tumor implantation, after TMZ and XRT treatment	patient derived GBM43 glioma cells serially passaged subcutaneously as xenografts in athymic mice (3.5x10^5)	Intracranially, into the tumor site	5 days or 11 days after tumor implantation, before or after XRT and TMZ treatment	Survival	Administration of HB1.F3-CD-CRAd-S-pk7 5 days after tumor implantation and before XRT+TMZ increased MS compared to XRT and TMZ alone from 24 to 31 days (5x10^5 NSCs) and 35 days (3x10^6 NSCs). Controls had MS of 15 days. Administration of NSCs (5x10^5) after TMZ+XRT on day 12 resulted in a MS of 30 days, compared to 39 days before XRT and TMZ. Controls had MS of 17 days.	CRAd-S-pk7 increased radiosensitivity or glioma cells by imparing the DNA damage response. Upon CRAd-S-pk7 infection of glioma cell lines (U251, U87), levels of Mre11 and Rad50 (that make up the Mre-11-Rad50-NBS1 (MRN) DNA complex) decreased. The number of gH2AX foci in GBM43 cells increased over a 3 day timecourse when cells were treated with CRAd-S-pk7 prior to XRT, but not when treated with XRT prior to CRAd-S-pk7.

2014	Duebgen et al., 2014	Oncolytic Virus with TRAIL	SCID mice	hMSC-G47Δ: Human bone marrow–derived MSC (David Prockop) infected with G47Δ or G47Δ-TRAIL	Alpha-MEM with 16.5% FBS	MSC-G47Δ (2x10^5)	Gli36vIII (5x10^4), LN229 (5x10^5)	Intracranially, into the tumor	At the time of tumor implantation or at the time of tumor debulking, 7 days (for Gli36vIII) or 21 days for LN229 after tumor implantation	Survival	Increased MS of animals with Gli36vIII tumors treated with sECM encapsulated MSC-G47Δ from 20 days (viral particles alone) to 32 days. Arming the virus to express TRAIL, further enhanced efficacy of the treatment and increased MS of animals bearing LN229 tumors that were surgically removed after 21 days and treated with MSC-G47Δ-TRAIL from about 29 days (for MSC-G47Δ) to 41 days.	MSC-G47Δ-TRAIL induced apoptosis in TRAIL resistant LN229 cells.
2014	Li et al, 2014	Cytokine (BMP4)	NOD/SCID mice	hAMSC-BMP4: human adipose–derived MSCs (invitrogen), retrovirally tranduced to express BMP4	MesenPRO complete media with MesenPRO RS growth supplement	0.5x10^6 hAMSC-BMP4	Human BTIC cultures: 276 (mesenchymal)(1x10^6) and 612 (proneural) obtained from intraoperative tissue with stem cell medium, U87 cells 0.5x10^6 for survival study	Systemically into the left cardiac ventricle	Two weeks after tumor implantation; 10 days after tumor implanation for survival studies	Two weeks after SC injection for interim analysis, 125 days for survival	hAMSCs-BMP4 administered into the left cardiac ventricle induced long term survival (>125 days) in more than 75% of animals. Long term survivors; control mice had a MS of 52 days and hAMSCs treated animals of 76 days.	hAMSC-BMP4 decreased viability of primary glioma stem cells (BTIC) in vitro; BMP4 induced differentiation of BTIC.
2014	Lopez-Ornelas et al., 2014	Secreted growth inhibiting protein (Gas1)	athymic mice (nu/nu)	ReNcell-GFP/tGas1/TR: immortalized hNSCs (ReNCells, Millipore) modified to conditionally express a soluble form of tGas1.	ReNcell NSC Maintenance Medium, (Millipore) supplemented with bFGF and EGF 20 ng/mL	5x10^05	C6 rat glioma cells (1 x10^6)	Intracranially, into the tumor or in the contralateral hemisphere	7 days after tumor implantation	Survival	Administration of ReNcell-GFP/tGas1/TR cells (in the presence of tetracycline) increased the MS of tumor bearing animals from 24 days to 42 days (75%).	Expression of Gas1 was detected and dependent on administration of tetracycline. tGas1 decreased viability of both glioma and NSC cells.
2015	Xu et al;, 2015	Cytokine (IL-18 and IFNβ)	Fisher 344 rats	BMSCs-IL-18-IFNβ: rat BM derived MSCs lentivirally transduced to express IL18 and IFNβ.	Not described	BMSCs-IL-18-IFNβ (1x10^6)	Rat 9L glioma cells (1x10^6)	Intracranially, into the tumor	3 days after C6 tumor cell implantation	Survival	Combined delivery by MSCs of both IL-18 and IFN-β increased the percentage of long term survivors in tumor animals, when compared to delivery of each cytokine alone. Delivery of IFN-β or IL-18 by MSCs each resulted in about 40% of long term survivors, when control animals succombed after about 20 days.	BMSCs-IL-18, BMSCs-IFN-β and BMSCs-IL-18-IFN-β had a direct cytotoxic effect on C6 cells in vitro.
2015	Morshed et al., 2015	Oncolytic Virus (NSC distribution study)	nude mice (nu/nu)	HB1.F3-CD infected with 50 IU/cell of CRAd-S-pk7	DMEM +10% FCS	5x10^4 HB1.F3-CD infected or not with 50 IU/cell of CRAd-S-pk7	Patient derived GBM43 glioma cells serially passaged subcutaneously as xenografts in athymic mice (5x10^4)	Adjacent to the tumor site or in the contralateral hemisphere	6 days after tumor implantation	Distribution analysis MRI analysis days 0, 1, 4, 7 after NSC implantation, post mortem analysis at day 4 and day 7	Not assessed, NSC distribution study	MRI analysis of ferumoxytol labeled NSCs and NSC-CRAd-S-pk7 indicated NSC localization primarily at the tumor border. A single administration of NSC-CRAd-Spk7 resulted in up to 31% intracranial tumor distribution, assuming a therapeutic diameter for each NSC of 100 microns.

2015	Martinez-Quintanilla et al., 2015	Oncolytic virus	nude mice (nu/nu)	hMSCs-O ICOVIR17: human adipose-derived MSC (Celleng-tech) infected with ICOVIR17 (CRAd replicating in pRB defective cells, encoding the PH20 hyaluronidase gene that promotes ECM degradation and virus distribution)	DMEM +20% FCS	hMSC-ICOVIR17 (2 × 10^5 cells) infected with 70 PFU/cell embedded or not in a synthetic ECM matrix	U87-Fmc (1.5x10^5) or patient derived GBM4-Fmc cells (3 × 10^5), for post-resection studies U87-FmC (1.5 × 10*5) were injected and the tumor was debulked 7 days later	Intracranially, into the tumor	4 days after administration of tumor cells or tumors were debulked 7 days after implantation and MSC-ICOVIR17 (2 × 10^5) encapsulated or not in sECM were placed into the tumor cavity	Survival analysis and 3, 7, 11, 24 days post hMSC implantation	Treatment with MSC-ICOVIR17 increased MS of animals with U87 gliomas from 24 days to 77 days and of animals with GBM4 gliomas from 53 to 63 days. Following tumor debulking sECM encapsulated MSC-ICOVIR17 increased MS from 34.5 to 45 days.	Glioma tumors express high levels of hyaluronic acid. Expression of hyaluronidase by OV increases their tumor killing efficacy, MS in U87 tumor bearing animals treated with OV increased from 30 to 58 when hyaluronidase was expressed.
2015	Stuckey et al., 2015	Antibody mediated toxin	SCID mice	hNSC-IL-13-PE: hNSCs immortalized with v-Myc, expressing a toxin resistant form of EF-2 and transduced with IL-13-PE	DMEM: F-12 supplemented with N2, 1% BSA, EGF and bFGF	2x10^6 cells	U87 (0.5x10^6)	Intracranially into the tumor resection site, encapsulated in synthetic extracellular matrix (sECM)	6 days after tumor implantation, surgical tumor resection was performed and hNSC-IL-13-PE encapsulated itn sECM were placed in the resection cavity	Survival and 85 days after tumor implantation	Treatment with hNSC-IL13-PE increased MS in tumor animals from 48 days (IL13-PE infusion) to 79 days. Control animals had a MS of 26 days.	
2016	Chung et al., 2016	Enzyme/Prodrug (CD/5-FC)	male BALB/c nude mice	MSC-CD: primary BM derived human MSCs transduced to express CD	DMEM with 10% FBS	3x10^5	U87MG cells (3x10^5), DPD (dihydropyrimidine dehydrogenase) deficient	Intracranially, into the tumor site	4 days after intracranial tumor inoculation.	Survival and longitudinal monitoring of tumor growth with bioluminescence, MRI, and PET imaging	Increase in MS in animals treated with MSC-CD/5-FC from about 26 days to about 33 days. Decreased tumor progression in MSC-CD/5-FC treated animals evidenced by imaging analysis.	Sensitivity to CD/5-FC was found to be dependent on the levels of expression of DPD (dihydropyrimidine dehydrogenase), an enzyme that metabolizes 5-FU into β-alanine.
2016	Jiang et al., 2016	Proapoptotic agent (TRAIL)	NCr nude mice	hADMSC-TRAIL: human adipose derived MSCs: hADMSC transduced to express human TRAIL by means of polymeric nanoparticles loaded with TRAIL plasmid DNA.	DMEM with 10% FBS supplemented with 10ng/ml FGF	3x10^5	Patient-derived D-270MG GBM (7x10^5 cells)	Intracranially into the tumor, in the contralateral hemisphere or systemic (tail vein) (3x10^5 cells)	5 days after tumor innoculation or two administrations: 5 and 15 days after tumor implantation (3x10^5 cells)	Survival and 15 days after tumor innoculation	Increased MS of tumor bearing animals treated with hADMSCs-TRAIL from 22 days to 27 days (one administration) and 45 days (two administrations).	Increased levels of cleaved caspase-8, cleaved caspase-3 and cleaved PARP in GBM cells co-cultured with hADMSC-TRAIL.
2016	Bagó et al., 2016	Proapoptotic agent (TRAIL)	nude mice	iNSC-TRAIL: Mouse Embryonic Fibroblasts (MEFs) were transdifferentiated with via lentiviral induced expression of Brn2, Sox2 and FoxG1into iNSCs and then lentivirally transduced to express a secreted form of TRAIL.	N3 medium supplemented with FGF and EGF	7.5x10^5	human GBM8 or 7063 GBM cells (5x10^5 cells)	Intracranially, into the tumor	3 days after tumor inoculation	Survival and longitudinal monitoring of tumor growth with bioluminescence	Increased MS in GBM8 tumor bearing animals treated with iNSC-TRAIL (from 37 to 59 days). Decreased tumor size evidenced by bioluminescence. Decreased tumor size and proliferation in 7063 GBM tumor bearing animals treated with iNSC-TRAIL. No survival data provided for this patient derived GBM line.	
2016	Mangraviti et al., 2016	Cytokine (BMP4)	athymic rats	hAMSCs-BMP4: hAMSCs StemPro® Human Adipose-Derived Stem Cells (Life Technologies) transfected witih NP to produce BMP4	Complete Mesenpro RS medium supplemented with 2% serum	2x10^6	1x10^6 U87 cells or 5x10^5 BTICs (GBM1a)	Intranasal (IN) administration or systemic injection (IV)	Two doses were administered intranasally, one at day 7 after tumor implantation and the other at day 14.	Survival	Repeated (2x) intranasal administration of 2x10^6 hAMSCs-BMP4 significantly increased MS of athymic rats implanted with patient derived BTIC from about 14 days to about 17 days.	hAMSCs-BMP4 migrated with similar efficiency into the tumor of athymic rats following intranasal or intravenous administration.

2016	Dey et al., 2016	Oncolytic Virus	nude mice (nu/nu)	NSC-OV: HB1.F3.CD cells were transduced with lentivirus encoding CXCR4 generating CXCR4-HB1.F3.CD that were subsequently infected with CRAd-S-pk7	DMEM +10% FBS	5x10^5 delivered intranasally (IN) at one week interval, three times	Patient-derived GBM43 (2x10^4) and GBM6 (1x10^5) glioma cells, maintained as mouse flank tumors, subsequently cultured in DMEM with 10% FBS or in serum free Neurobasal medium supplemented with B27, N2, EGF and bFGF at 20ng/ml.	Intranasally (IN)	8 days after tumor implantation animals received XRT of 2Gy/day for 5 days (days 8-12). On day 14, 21 and 28 after tumor implantation animals received IN administration of NSC-OV.	Survival	Treatement with hypoxia preconditioned NSC-OV increased MS from 32.5 to 37 days in GBM43 mouse xenografts pretreated with XRT. Treatment with CXCR4-NSC-OV also increased MS following XRT from 39 days (vector transduced NSC) to 48 days. Control animals had MS of 21 days (w/o XRT) and 31 days with XRT.	Hypoxic preconditioning of NSCs led to decreased expression of SOX2, MUSASHI and b-TUBULIN and increased expression of NESTIN.
2017	(Bagó et al., 2017)	Proapoptotic agent (TRAIL) and Enzyme/Prodrug (TK/GCV)	SCID mice	h-iNSC-TRAIL and h-iNSC–TK: human iNSCs were generated by transdifferentiating fibroblasts with lentiviral vectors encoding hTERT and SOX2. hiNSCs were then transduced with lentiviruses encoding sTRAIL or thymidine kinase.	Not specified	5x10^5 and 7.5x10^5 cells	Human U87 cell line, and human GBM4 cells	Directly into the tumor, also into the tumor cavity postsurgically	At the same time with tumor cells (h-iNSCTE) or 3 days after tumor implantation or in the postsurgical resection cavity of a 10 day-old tumor (h-iNSCTE–TK).	Survival and longitudinal monitoring of tumor size with bioluminescence	h-iNSC-TRAIL extended the survival of mice bearing U87 tumors from 25 to 51 days; h-iNSC–TK and GCV increased MS from 37 to 67 days; post-surgical treatment with h-iNSC–TK and GCV resulted in an increased MS of animals from 46 to 60 days.	
2017	Choi et al., 2017	Cytokine (IFN-β)	Female C57/B6 or female SCID	MSC-mIFNβ: mouse MSCs transduced to express IFNβ	Not mentioned	Not mentioned	CT2A or Gl261 cells (1x10^5) in B6 mice or GBM4 cells in SCID mice	Intratumorally in established tumors or in the resection cavity in sECM following debulking	Into estalished tumors or in the resection cavity following debulking. Timing was determined by bioluminescence.	Survival	In SCID mice there was a small increase in MS in animals with established tumors treated with MSC-mIFNb (18 days vs. 15 days). In C57/B6 MSC-mIFNβ significantly prolonged MS (46 days vs. 31 days), 1/5 of mice showing long-term survival exceeding 80 days. When MSC-mIFNb were placed in the post-resection cavity, in a sECM matrix, the survival benefit was greater, half of the mice surviving beyond 80 days vs. 23 days MS of controls. Survival benefit was also observed in SCID mice with human primary GBM4 cells treated with mouse MSC-mIFNb.	Tumor resection enhanced recruitment of both CD4 and CD8 effector T cells into the resected area (5d post resection); IFNβ increased CD8 but not CD4 T cell infiltration. Tumor resection increased the ratio of M1(CD38+)/M2(Egr2+) ratio and IFNβ treatment enhanced this effect and increased the number of IFNγ producing CD4+ cells. IFNβ has direct cytostatic effect on tumors inhibiting S phace entry.
2019	Spencer et al., 2019	Oncolytic Virus	nude mice (nu/nu)	NSC-OV: HB1.F3.CD overexpressing CXCR4, labelled with micron-size paramagnetic iron oxides (SPIOs) at 20 particles/cell, and infected with CRAd-S-pK7 at 10 or 50 viral particles (vp) per cell	DMEM +10% FBS	5x10^5 cells, 3 separate intranasal (IN) inoculations of 4 µL aliquots at 5 min intervals	U87MG and patient-derived GBM43 glioma xenograft line, subcultured in DMEM with 10% FBS	Intranasally (IN) with nasal epithelium modification with either 3 µL of fibrin glue via IN injection immediately following NSCs administration or i.p. injections of 50 µg/g Methimazole, 48 h prior to NSC-OV administration.	For migration studies: at least 7 days after intracranial implantation, for survival studies, NSC-OV were administered IN 7,14, and 21 days (3 doses) after tumor implantation - (GBM43).	For migration studies, 2 days after IN administration of NSCs	Pretreatment of animals with methimazole improved NSC-OV migration into the tumor and the MS of mice with GBM43 intracranial tumors from 23.5 to 28 days, when compared to administration of NSC-OV without methimazole. MS in control animals was 23 days.	Pretreatment of mice with either intranasal (IN) fibrin glue or intraperitoneal methimazole, delayed clearance of IN inoculated NSCs from the nasal cavity. Pretreatment of mice with methimazole, improved migration of NSCS through the cribriform plate.