**Table S1. List of studies using genetically engineered MSCs for cancer treatment**

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| --- | --- | --- | --- | --- | --- | --- | --- |
| **Reference** | **Disease/disease models** | **Species/number of subject** | **MSC source and passage, treatments** | **Vector/****gene insertion /expressed proteins/drug** | **Outcome** | **Adverse event** | **Mechanism of action** |
| (Segaliny et al., 2019) | Breast Cancer- bone metastasis | BALB/c JmiceC= 22T= 18 | Hu BM-MSC, Pa: NR.C= PBS/MSC+5FC/ 5FUT= MSC-gene +5FC 1x, 3x | mRNA-lipofectamine/ PSGL-1/ SLEX,CD, OPG | Best Survival: T 3x | Minimal toxicity >< chemo (5FU) | Homing factor 🡪tumor blood vesselsConversion: 5-FC🡪 5-FUOsteolysis inhibition |
| (Fritz et al., 2008) | Bone (tibia) metastasis of prostate cancer | Male SCID/Bg mice C= 7T1= T2= T3= 15 | C3-MSC, Pa= NRCo-injection PC3 with:C= C3-MSC= 1:3T= C3-MSC-ATF= 1:3/1:1/3:1 | Adeno virus/ hATF | tumor growth-d-14, d-21,tumor vascular network d-21,New bone formation-d-14: T(1:3) the best | NR | hATF:anti- invasion, anti-migration, anti-angiogenesisMSC: new bone formation |
| (Sasportas et al., 2009) | Glioma (GBM8) mouse model: | SCID MiceC= 9T= 9 | Hu BM-MSC, Pa: NRImplantation/co-injection GBMB IC with:C= MSCT= MSC-s-TRAIL | Lentiviral vector/ s-TRAIL | Glioma cell T<CSurvival T>CAct-Cas3:T1> C | NR | s-TRAIL🡪 apoptosis |
| (Altanerova et al., 2012) | Glioblastoma (C6) rat model | Male SD ratC=8T= 21 | Hu AT-MSC, Pa: NRCo-injection C6 IC-with:C= 5FC-IP/MSC+5FC-IVeT= MSC-CD (1:2) CL+ 5FC-IP/ MSC-CD (1:0.2) CL + 5FC-IP/MSC-CD (1:4) + 5FC-IVe/MSC-CD (1:4)+5FC–Ive (2xT) | Retrovirus/ CD-UPRT | Survival:Best: MSC-CD (1:4) + 5FC -Ive (2xT) | (-) | Conversion: 5-FC🡪 5-FU |
| (Altaner et al., 2014) | Glioblastoma (C6) rat model | Adult male CD® IGS rats C1= 37T= 64 | hu BM-MSC/hu AT-MSC, Pa: NRC= (-)/ d-13-R/ d-13R + BM IC+ 5FC –IVeP/ d-10 RT= d-5 -AT-CD-IC+ 5FC IVeP/ d-5, d-14 AT-CD-IC +5FC-IVeP/ d-5- AT-CD-P + 5FC –IveP/ d-5 -d-14-AT-CD-P + 5FC –IVeP/ **d-13-R -d13, d-21+ BM-CD -IC+ 5FC –IveP**/ d-10 R, d-10, d-17 AT-CD-IC - 5FC –IveP/ d11-R, d-11, d-24 + AT-CD-IC+ 5FC -IVeP | Retrovirus/ CD-UPRT | Best 150 day survival: d-13-R -d13, d-21+ BM-CD -IC+ 5FC –IveP | (-) | Conversion of pro drug 5-FC🡪 5-FU |
| (Fei et al., 2012) | Glioma (C6)rat model | SD rats C= 8T= 14 | Rat BM-MSC, Pa= P3Co-injection d-0-C6-IC with:C= 5FC-IC (d7-14)T= MSC-CD (1:1)+ 5FC-IC (d7-14) / MSC-CD (1:2)+ 5FC-IC (d7-14) | Lentiviral vector/ CD | Smallest tumor size, longest survival, highest apoptosis: MSC-CD (1:2) + 5FC | NR | Conversion: 5-FC🡪 5-FU |
| (Kosaka et al., 2012) | Glioma (9L)rat model | (balb/c- nu/nu mice (SC)C= 8T= 4Fischer-344 rats (IC)C= NRT= NR | Rat BM-MSC, Pa= NR**Co-injection 9L SC with:**C= MSC+PBS/MSC+ 5FC-IPd2-14T= MSC-CD+5FC IP d2-14**Tumor injection:**C= PBS/MSC IT+PBS/ MSC IT + 5FC IP d2-14/ MSC-CD IT+PBST= MSC-CD IT+ 5-FC-IP-d2-14 | Adenovirus vector/ CD | Co-injection: smallest tumor size d-21, d-28, d-36:MSC-CD + 5-FCTumor: longest survival: MSC-CD + 5-FC | 5FC systemic toxicity (-) | Conversion: 5-FC🡪 5-FU |
| (Chung et al., 2016) | Glioma(U87MG)Mouse model | BALB/c nude miceC= 10T= 10 | Hu BM-MSC, Pa= NRC= 5-FC-IP 5x/wkT= MSC-CD-IC+ 5-FC –IP- 5x/wk | Retroviral vector/ CD | Tumor size:T < C (T↓, C↑)Survival: T > CKi67: T < CApoptosis: T > C | NR | Conversion: 5-FC🡪 5-FU |
| (Chang et al., 2010a) | Glioblastoma (C6) rat model | Adult male SD albino ratsC= 32T= 24 | Hu BM-MSC, Pa= NRCo-injection C6 IC with:C= PBS IC/PBS IC+d-2-5FC50-IP/ PBS IC+d-2-5FC500–IP/ MSC-CD (H)-IC**T**= MSC-CD-IC+d-2-5FC50-IP/ **MSC-CD IC+d-2-5FC500 IP**/ MSC-CD- IC+d-25FC500–IP repeat d-7, d-14/ d-3 MSC-CD-IC +d-4 5FC500 IP, repeat d-10, d-17 | Retrovirus/ CD | Smallest tumor size: MSC-CD IC+d-2-5FC 500 IP | NR | Conversion: 5-FC🡪 5-FU |
| (Bak et al., 2011) | Glioma (U87MG) mouse model | Balb/c athymic, nude miceATS:C= 16T= 8ACLS:C= 20T= 10 | Hu ESC derived MSCPa= P13-P20**Bacvec:** ATSC= PBS+ GCV/ MSC+GCVT= MSC-TK+ GCV**d-5-Lenvec**: ACLSC= PBS+GCV/ MSC+ GCVT= MSC-TK+ GCV | Rec Baculo virus or Rec Lentivirus/ HSV-TK | ATS: Tumor sized11, d-25: T< CACLS: Tumor necrosis: T> CATS, ACLS: Survival:T>>C | NR | HSV-TK: GCV phosphorylated🡪 toxicMSC: HomingLentiviral broadened expression window vs baculovirus vector |
| (Martinez-Quintanilla et al., 2013) | Glioblastoma multiforme(Gli36vIII) mouse model | Scid/nude mice C= 14T= 12 | Mouse MSCSource, Pa: NRC= PBS IC/ PBS IC+ GCV-IP – 10dT= MSC-TRAIL-IC +GCV IP 10d/ MSC-TRAIL-TK -IC +GCV IP- 10d | Lentiviral and retroviral vector/ HSV-TK,s-TRAIL | Tumor growth: T< CMedian survival:MSC-TRAIL +GCV (39d)> MSC-TRAIL -TK +GCV (31.5d)> C (17 d) | NR | HSV-TK 🡪 GCV– phosphorylated🡪 toxics-TRAIL 🡪apoptosis |
| (Suryaprakash et al., 2019) | Solid tumorGlioblastoma multiforme (U87MG) mouse model | Nu/J nude mouse C= 6T= 3 | Hu MSC spheroidMSC source: NRPa= P3-P6C= PBS/MSC+MTX NC-ETT= MSC hybrid spheroids –TRAIL - MTX –NC-ET | PEGylated DNA-templated NC system / TRAIL, PL against IL13Rα2, MTX | Tumor size:d-21: T< CT= 14% C (PBS) (0.053 g vs 0.360 g ) | Histology: No significant organ toxicity | TRAIL🡪apoptosisMSC-PL against IL13Rα2 🡪 homingMTX🡪anticancer drug |
| (NguyenThai et al., 2015) | Solid tumorOsteosarcoma (Cal 72) mouse model | Nude miceC= 5T= 5 | Hu BM-MSCPa: P2-P3Co-injection Cal72 SC with:C= 5FC IP d2-4-6T= MSC-CD+5FC IP-d2-4-6 | pEGFP- vector/Yeast CD-UPRT | Tumor size:C= 118.43 ± 23 mm3T= 69.7 ± 21 mm3 (p< 0.05).Metastasis (lung):C=4, T= (-) | (-) | Conversion: 5-FC🡪 5-FU |
| (Kucerova et al., 2007) | Solid tumorColon adenocarcinoma (HT-29) mouse model | Athymic nude mice(BALB/c-nu/nu)Co-injC= 21T= 12Tumor TC= 12T= 6 | AT-MSC, Pa= P5**Co injection HT-29 SC with:**C= 5FC-IP-10x/ MSC 1:1+5FC-Ip-10x/ MSC 10:1+5FC-IP-10xT= MSC-CD 1:1+5FC-IP 10x/ MSC-CD 1:0.1+5FC-IP 10x**Tumor** **treatment**C= PBS IV+ 5FC-IP-10x/ MSC IV+5FC-IP-10xT= MSC-CD1:4 IV + 5FC-IP-10x | pST2 retrovirus + protamine sulfate/ CD-UPRT | **Co-injection:**Tumor size d-5, d-7, d-10, d-12: T-HD= T-LD <Ctumor weight d-18: T-HD < T-LD < C**Tumor injection -**Tumor size d-10, d-14, d-18: T < C | (-) | Conversion: 5-FC🡪 5-FU |
| (Schug et al., 2018) | Solid tumorHepatocellular carcinoma (HuH7) mouse model | CD1 nu/nu mice (Charles River) C= 4T= 8 | Primary Hu BM-MSCPa= NRTumor Irradiation:C= 0 GyT= 2 Gy/5 Gyd-2: MSC-NIS tail veind-4: 0.5 mCi 123I IP | CMV-NIS-pcDNA3/ NIS | MSC-NIS engraftment 5Gy> 2Gy > CRadioiodide accumulation in tumor: 5Gy> 2Gy> C | Radioiodide accumulation in salivary gland, thyroid, stomach and bladder | NIS🡺uptake radioiodide by MSCExternal beam radiation 🡪homing of MSC to tumor |
| (Nouri et al., 2015) | Solid tumorOvarian cancer (SKOV3) mouse model | nude miceC= 35T= 15 | Hu BM-MSC, Pa= NR.C= PBS-IT/ MSC-TK- IT/ MSC-CD- IT/ MSC-NTR-IT/GCV-IT/ 5-FC –IT/ CB1954-ITT= MSC-TK- IT + GCV/ **MSC-CD- IT+ 5-FC/** MSC-NTR- IT+ CB1954 | pBudCE4.1 (dual promoter mammalian expression vector)/ HSV-TK-SR39Yeast CD-UPRTNTR | Tumor size:d-18: smallest in **MSC-CD- IT+ 5-FC=** 5-FC –ITd-36:smallest in**MSC-CD- IT+ 5-FC**< MSC-NTR- IT+ CB1954= CB1954-IT | NR | HSV-TK-SR39: GCV phosphorylated🡪 toxicCD-UPRT: 5-FC🡪 5-FUNTR: CB 1954 🡪 cytotoxic form |
| (Amara et al., 2016) | Solid tumorLung epithelial tumor (TC1) mouse model | C57BL/6mice Co-Inj:C= 22T= 24Tumor injC= 21T= 15-3 | Murine BM MSC from C57BL/6 mice, Pa= NR**Co-injection TC1 with:**C= PBS-IP/ CPA-45 IP/ CPA- 90 IP/ CPA-140 IPT= TC1-Cyp +PBS-IP/ TC1-Cyp + CPA- 45 IP/ TC1-Cyp + CPA- 90 IP/ TC1-Cyp + CPA- 140 IP**Tumor injection:**C= (-)/ CPA-90 IP/ MSC-IT/ MSC-IT + CPA-90 IPT= MSC-Cyp-IT/ MSC-Cyp-IT + CPA –90 IP | pHIV-EF1L-thy1/GFP-W lentiviral vector/ CYP2B6TM | Co=injection:Tumor size d-20, d-40, d-70: TCI-Cyp + CPA- 90 IP = TCI-Cyp + CPA- 140 IP < CTumor injection:Tumor size d-42, d80: MSC-Cyp-IT + CPA –90 IP (n=3) << (n=6) = MSC-IT + CPA-90 IP | 3/12 MSC-Cyp dead (anaphylactic shock ??) due to residual FCS in MSC-Cyp | Cyp: CPA 🡪 toxic form |
| (Krassikova et al., 2016) | Solid tumor(LLC) lung carcinoma mouse model | C57BL/6 miceC= 8 -10T= 32-40 | Syngeneic ATMSCPa= NRC= PBS-IT/ d-7-AT-MSC-IT/ d-14 Lysomustine IPT= d-7- AT-MSCs-CD –UPRT-IT+ 5FC –IP (d8-14)/ d-7- AT-MSCs-CD-UPRT-VP22-IT+5FC-IP (d-8-14)/ d-7-AT-MSCs-CD-UPRT -IT+ 5FC –IP (d-8-14)+ d-14-Lysomustine IP | pCpGfree-mcs + electroporation/ CD-UPRT, VP22 | Tumor growth inhibition: d-7-AT-MSCs-CD- UPRT + 5FC (d-8-14) + d-14 Lysomustine IP (86%) > d-7- AT-MSCs-CD-UPRT + 5FC (d-8-14)= d-7- AT-MSCs-CD-UPRT-VP22 + 5FC (d-8-4)= 56% > CIncrease life span:Best AT-MSCs- CD- UPRT + 5FC (d-8-14) + d-14 Lyso-mustine IP= 60% | NR | Conversion: 5-FC🡪 5-FU5FU-lysomustine synergyVP22: facilitate secretion and re-uptake offusion proteins to neighboring cells, |
| (Toro et al., 2016) | Solid tumourand metastatic ovarian cancer(SKOV-3, A2780) mouse model | Athymic nude mice (Balb/cnu/nu)C= 19-28T= 19-28 | Hu AT-MSC, Pa= NR**Co-inj SKOV-3 (SC) with:**C=(-)T= MSC-CD 1:0.1 + 5-FC –IP (d-3-14)**Co-inj A2780 cells (SC) with:**C= (-)/ MSC 1:0.2T= MSC-CD 1:0.2 + 5-FC –IP (d-0-14)**Metastasis SKOV-3 -IP:**C= (-)T= MSC-CD 1:0.4 IP (d-7,d-14,d-21)+ 5-FC IP (d-7-21)**Metastasis A2780 - IP:**C= (-)T= MSC-CD 1:0.4 IP (d-7,d-14,d-21) +5-FC -IP(d-7-21) | pST2 retrovirus/ Yeast CD-UPRT | Tumor size:Co-inj SKOV-3 -d-0: T< CCo-inj A2780 cells: T< CMetastasis SKOV-3 cells: T= CMetastasis A2780 cells: T< C120d disease free survival:Metastasis A2780 :T= 33%. | NR | CD::UPRT: 5-FC🡪 5-FU |
| (Zou et al., 2012) | Solid tumormurine breast tumor(TUBOcell line) mouse model | BALB/c micePreventionC= 16T= 8Tumor injC= 16T= 8CD4/CD8 T deletion =3Blocking LIGHT =3 | BALB/c BM-MSC, Pa= NR**Prevention:**C=d-0 PBS/ d-0 MSC SC+d-13 TUBO 2.5:1 ACLS SCT= d-0 MSC-L SC + d-13 TUBO 2.5:1 ACLS SC**Tumor inj:**C= d-0 TUBO SC + d-7 PBS/ d-7 MSC 1:2.5 ACLS SCT= d-0TUBO SC+ d-7 MSC-L 1:2.5 ACLS SC**CD4/CD8 T cell deletion:**anti-CD8 SCanti-CD4 SC**Blocking LIGHT**:**LTβR-Ig** 100 mg IP | Retrovirus/LIGHT | **Prevention:**Tumor size-d-15-30: T= (-) << d-20-C=100-200mm3, d-30-C=1400 mm3d-50 survival: T=100% >> C= 0%**Tumor inj:**Tumor size T<<Cd-60 survival:T =90% >> C= 0%.**CD4/CD8 deletion:**Abolished MSC-L. effect**Blocking LIGHT**3d- before/after, 1 wk, and 3wk MSC-L abolished MSC-L prevention effect | NR | LIGHT.🡪 primes potent immune reaction vs tumour |
| (Abrate et al., 2014) | Solid tumorProstate cancer (TRAMPC1/ TRAMPC2) mouse model andProstate cancer (TRAMP) mouse model | C57BL/6 andTRAMPmice**Solid tumor:**C= 8T= 36**TRAMP**C= 12T=13 | C57BL/6 mouse AT-MSC, BM-MSC, Pa= NR**Solid tumor mouse model:**C= AT-MSC-IVT= AT-MSC-CD-IV/ AT-MSC-CD-IV+ 5FC-IP/ BM-MSC-CD-IV+ 5FC-IP/ AT-MSC-CD-IV (2x) + 5FC-IP (1x)/ AT-MSC-CD-IV (2x)+ TAC-IM (2x) + 5FC-IP (1x)**TRAMP mouse :**C= (-)/5FC-IPT= -AT-MSC-CD or BM-MSC-CD -IV+ 5-FC-IP (1 cycle)/ AT-MSC-CD or BM-MSC-CD -IV+ 5-FC-IP (2 cycles) | Retrovirus/ yeast CD-UPRT | **Solid tumor:**Tumor size:AT-MSC-CD + TAC (2x) + 5 FC (1x)=AT-MSC-CD+ 5FC = BM-MSC-CD+ 5FC< AT-MSC-CD = C**Prostate Cancer:**Tumor size:AT-MSC-CD or BM-MSC-CD +5-FC << CAT-MSC-CD or BM-MSC-CD + 5-FC (2 cycles) << C | NR | Conversion: 5-FC🡪 5-FU. |
| (Cavarretta et al., 2010) | Solid tumorProstate cancer (PC3) mouse model | Nude mouse**Co-inj PC3 4x106:**C= 8T= 20**Co-inj PC3 3x106**:C=10T= 19 | Hu AT-MSC, Pa= NR**Co-inj PC3 4×106 with:**C= (-)/ MSC-CDy 40%T= MSC-CDy 40%+5FC-IP/ MSC-CDy 30%+5FC-IP/ MSC-CDy 20%+5FC-IP/ MSC-CDy 10%+5FC-IP/ MSC-CDy 5%+5FC-IP**Co-inj PC3 3×106 with:**C= (-)T= MSC-CDy 50%+5FC-IP/ MSC-CDy 40%+5FC-IP/ MSC-CDy 10%+5FC- IP/ MSC-CDy 67% IV+5FC-IP/ MSC-CDy 67% IV+5FC-IP/ MSC-CDy 67% IV (2x) + 5FC-IP | Retrovirus/ CD-UPRT | **Co-inj pc3 4X!06**C: (-)/MSC-CDy 40%: 100% tumour, died d-18/d-12T: MSC-CDy (20%, 30%, 40%) +5FC: d-16, d-12, d10 - 25% tumour, d-20 regressedT: MSC-CDy (40%-30%, 10%, 5%) +5-FC - d-40: 100% tumour free**Co-inj PC3 3× 106:**100% tumour free: MSC-CDy 50% +5FCTumour regression (50%) MSC-CDy 67% IV (2x) + 5FC | NR | Conversion: 5-FC🡪 5-FU. |
| (Zolochevska et al., 2012) | Solid tumorProstate cancer (PC3, TC2Ras) mouse model | Balb/c nu/nuand C57/BL6 mice**Co-inj PC3:**C= 9T= 6**Co-inj TC2Ras**:C= 6T= 6 | Hu AT-MSC, Pa= NRC57/BL6 AT-MSC, Pa= NR**Co-inj PC3 106 –SC with:**C= (-)/ hu MSC/ hu MSC-GFP 1:0.2T= hu MSC-MDA7 1:0.2/ hu MSC- PEDF 1:0.2**Co-inj TC2Ras – SC with:**C= (-) /mMSCT= mMSC- PEDF/ mMSC- MDA-7 | Lentivirus/ MDA-7, PEDF | **Tumour size –co-inj PC3:**T: hu MSC- PEDF << hu MSC-MDA7, Cd-0-53: hu MSC- PEDF 1:0.2 – no tumour**tumour size – co-inj TC2Ras:**mMSC- PEDF << mMSC- MDA7< Cd-0-27: mMSC- PEDF – no tumor | NR | MDA-7= tumour suppressor🡪 induce differentiation, apoptosis, and reduce proliferation. PEDF= inhibitor of angiogenesis, stimulate differentiation and promote apoptosis |
| (Yan et al., 2017) | Solid tumorProstate cancer (22Rv1) mouse model | Nude miceC=10T= 10 | MSC, Pa= NRC= PBS IV/MSC.EGFP 1:0.1-IVT= MSC.scFv-tBid 1: 0.1-IV/ MSC.scFv-Fdt-Bid.1:0.1-IV | Lentivirus/scFv-Fdt-tBid | Tumor size: d-9 - MSC.scFv-Fdt-tBid.- tumor growth inhibitionTumor weights: d-30T MSC.scFv-Fdt-tBid << C < MSC.scFv-tBidApoptosis TUNEL: MSC.scFv-Fdt-tBid | NR | scFv-Fdt-tBid= antitumor immuno-pro-apoptotic moleculeFdt 🡪 cleaved by furin proteases --> transfers from endosome to cytosol 🡪induces cell apoptosis |
| (Lee et al., 2013) | Solid tumorProstate cancer (DU145, PC3) mouse model | Nude mice DU145 tumour:C= 7T= 14PC3 tumour:C=5T=10 | Hu fetal limbMSC, Pa= NR.**DU145 tumor:**C= GCV IP 5xT= MSC-TK-IV+ GCV- IP 5x/ Dox -IP**PC3 tumor:**C= GCV-IP 5xT= MSC-TK-IV+GCV-IP5x/ Dox-IP | Lentivirus/ SV40-TK | DU145 and PC3 tumor:Tumor size:MSC-TK+ GCV, Dox << CApoptosis: MSC-TK+ GCVDU145 tumor:4/5 - MSC-TK + GCV-🡪 no tumor | NR | SV40-TK 🡪 GCV– phosphorylated🡪 toxic |
| (Zhang et al., 2011) | Solid tumorProstate Cancer (PC3) mouse model | Balb/c nu/nu miceC= 9T= 3 | Wistar rats BM-MSCPa= NRC= PBS IT/ MSC IT – 3x/ MSC-EGFP-IT – 3xT= MSC-TT- IT – 3x | Lentivirus/TNF-α-Tumstatin 45–132 (TT) | d-30 Tumor size:MSC-TT <<Cproliferating tumor cells : MSC-TT <<CTUNEL assay:MSC-TT >>C | NR | TNF-α- 🡪cancer cell apoptosis, inhibited endothelialcell proliferationTumstatin reduce TNF-α systemic toxicity |
| (Wang et al., 2012) | Solid tumorProstate cancer (PC3) mouse model | C.B-17/Icr,(SCID) miceC= 30T= 12 | Human BM-MSC, Pa= P4C= (-)/ MSC AD5 3: 20-IV/MSC 3:20-IV/AD5-IFN-β 3:2x104 viral particles-IV/rec IFN-β (105 IU).-SCT= MSC IFN-β 3:20-IV/MSC IFN-β 3:2-IV | Adenovirus (AD5)/ IFN-β | Tumor weight:T= MSC IFN-β 3:20/ MSC IFN-β 3:2<<CSurvival analysis:80d: MSC IFN-β 3:20= MSC IFN-β 3:2, C= all dead80-90d: MSC IFN-β 3:20 < MSC IFN-β 3:2 | NR | IFN-β 🡪inhibited malignant cell growth |
| (Chen et al., 2008) | Solid tumormetastasis melanoma (B16), breast tumor (4T1), and hepatoma (Hca) mouse model | IC57BL/6mice (B16) / BALB/ c mice (4T1) or(Hca)Melanoma/breast tumor/ hepatoma:C=36 x 3T= 24 x3 | BALB/c mouse BM-MSC,Pa= PD7-PD10Melanoma/breast tumor/ hepatoma:C=PBS-IV/ MSC-LacZ-IV/MSC-IVT=free Ad-IL-12-IV, MSC-IL-12 -IVAll injection: 5x every 5d | Adenovirus/ IL-12 | MSC-IL-12 migrated to:Tumor periphery and capsule after 1 wkInto tumor after 5 wkSerous or IT IL-12: MSC-IL-12 > free Ad IL-12C = no elevated IL-12.d-20 tumor size:MSC-IL-12T3 << free Ad-IL-12, CLN metastases: MSC-IL-12 suppressed and reversed (para-iliac LN 78.8%, axilla LN 100%}, free Ad-IL-12 partly retard, but do not reverse.Metastasis-lung, liver: MSC-IL-12 (-), free Ad-IL-12, C (+)d-20-LVD: MSC-IL-12-↓, free Ad-IL-12, C↑ | (-) | IL-12 🡪 rapid destruction of tumor-associatedendothelial cells 🡪 metastasis regressionMSCs homing to tumor or metastatic sites |
| (Kucerova et al., 2008) | Solid tumorMelanoma(A375) mouse model | Balb/c nude miceCo-inj1: C= 11T= 5Co-inj2:C= 20T= 14Tumor inj:C= 16T= 12 | Hu AT-MSCPa=P15-20**Co-injection A375 SC-1:**C= (-)/10% MSC-SC+ 5FC-IPT= 10% MSC-CD-SC + 5FC-IP**Co-injection A375 SC-2**C= (-)/ 10% MSC-SC+ 5FC -IP/ 20% MSC-SC+ 5FC-IPT= 10%MSC-CD-SC + 5FC -IP/ 20%MSC-CD-SC + 5FC -IP**Tumor- injection**T= 5FU-IP/ MSC-CD-IV + 5FC-IPC= MSC-IV/ MSC-CD-IP + 5FC-IP/ Fib-CD-IV+ 5FC-IP | pST2 retrovirus protamine sulfate / Yeast CD-UPRT | **Co-injection-1:**Tumor size:Up to d-10: T<< Cd-21: T= C**co-injection-2:**Tumor weight d-24:20% MSC-CD-SC + 5FC-IP <<10% MSC-CD-SC + 5FC-IP< CTumor size:d-3-7-10-14:20%MSC-CD-SC + 5FC-IP< 10%MSC-CD-SC + 5FC-IP< CTumor free > d14:20%MSC-CD-SC + 5FC-IP= 89%20% MSC-SC+ 5FC-IP= 0%**Tumor injection**:Tumor size d-23:MSC-CD-IV + 5FC-IP < 5FU-IP < C | (-) | Conversion: 5-FC🡪 5-FU |
| (Kucerova et al., 2014) | Solid tumorMelanoma(A375)Mouse model | Balb/c-nu/nu**Co-inj HD**C=8T=9**Co-inj LD**C= 0T= 42**Co-inj AMD-Avastin**C= 8T= 16**Co-inj SU11274**C= 8T= 16 | HuAT-MSC, Pa=NR**Co-injection HD A375 1.5 x106-SC with:**C= MSC-CD 1:0.2T= MSC-CD 1:0.2+ 5FC-IP**Co-injection LD A375/ A375-rel1/A375-rel2 0.5x106-SC with:**T=A375 + MSC-CD 1:1+5FC-IP/ A375/Rel1 + MSC-CD 1:1+5FC-IP/ A375/Rel2 + MSC-CD 1:1+5FC-IP**Co-injection A375-rel3 5:1 –AMD-Avastin:**C= MSC-CD SC+5FC-IPT= MSC-CD SC+5FC -IP+ AMD SC/ MSC-CD SC+5FC-IP + Avastin-IP**Co-injection A375-rel3-SU11274:**C= MSC-CD+5FC-IPT= MSC-CD+SU11274-IP/ MSC-CD + 5FC-IP+ SU11274-IP | pST2 retrovirus/ CD | **Co-injection HD:**d-60 tumor free T>C**co-injection LD:**d-90 tumor free:A375> A375-rel1> A375-rel2**Co-injection A375-rel3- AMD-Avastin:**Tumor size:C= T-AMD < T- avastinTime to >100mm3 tumor:T-AMD < C < T-Avastin**Co-injection A375-rel3 – SU11274:**d-60 tumor freeMSC-CD+ 5FC+ SU11274 > MSC-CD+SU11274 | NR | Conversion: 5-FC🡪 5-FU |
| (Tyciakova et al., 2015) | Solid tumorMelanoma(A375) mouse model | Balb/c nude mice C=10T= 8 | HuAT-MSCPa= NRCo-injection A375 SC with:C=(-)/MSC (9:1)/MSC (4:1)T=MSC- hTNFα (9:1)/MSC- hTNFα (4:1) | pST40 retrovirus+ protamine sulfate/ hTNFα | d-28 tumor size:MSC- hTNFα (4:1) < Cd-26 tumor weight:MSC- hTNFα (9:1)=MSC- hTNFα (4:1) < C | NR | hTNFα 🡪 apoptosis |
| (Krasikova et al., 2015) | Solid tumorMelanoma(B16F10)Mouse model | C57/BL6 miceC= 8-10T= 16-20 | Mouse AT-MSCPa=P2 -P 4B16F10-tumor-injection:C=(-)T=MSC-CD-UPRT IT1x + 5FC–IP-7x/ MSC-CD-UPRT-VP22-IT-1x+5FC-IP–7x | Recombinant plasmid+ electroporation/ CD-UPRT-VP22 | d-20 tumor size :C >> TTGI: d-6- d-9: T (>50%) >Cd13: CD-UPRT-VP22 (46%) > CD-UPRT (40%) > CSurvival T> C | NR | Conversion: 5-FC🡪 5-FUVP22 enhances CD effect on cells |
| (Ahn et al., 2013) | Solid tumormelanoma(LMeC) mouse model | Balb/c nude miceC= 13T= 8 | Canine AT-MSCPa= P4-P6LMec-tumour injection:C= PBS-CT-3x/ cis-IP -3x/ MSC- CT-3xT= MSC-IFN-β CT-3x/ MSC-IFN-β CT+ Cis-IP-3x | Lentiviral vector/ IFN-β | d-30 tumor size:MSC-IFN-β CT+ Cis < MSC-IFN-β CT <Cd-12- apoptosis:MSC-IFN-β CT+ Cis > MSC-IFN-β CT > C | NR | IFN-β 🡪 apoptosis, anti-angiogenic |
| (Seo et al., 2011) | Solid tumorMelanoma(B16F10)MouseModel | C57BL/6 miceC=18T= 6 | Canine AT-MSCPa= P5-P8B16F10-tumor injection:C=PBS-3x/ Cis IT/ Cis IT+MSC SC 3xT= Cis IT+ MSC-IFN-β SC 3x | Lentiviral vector/ IFN-β | D17-26-tumor size:T= Cis-MSC < Cis = PBSSurvival:T> Cis-MSC > Cis > PBS | (-) | IFN-β 🡪 apoptosis, anti-angiogenic |
| (Grisendi et al., 2015) | Solid tumorEwing’s sarcoma(RD-ES) mouse model | NOD mice (Charles River) C= 14T=7 | Hu AT-MSCPa= up to P12C= (-)/MSC- ITT= MSC-TRAIL- IT | Retroviral vector/ TRAIL | Tumor size:T< MSC= CApoptosis:C< MSC- < TAngiogenesis:C= MSC> T | NR | TRAIL 🡪 apoptosis, anti-angiogenesis |
| (You et al., 2009) | Solid tumorGastric cancer(MKN45) mouse model | nude miceC=14T=21 | Hu BM-MSC, Pa= P6C= (-)/ MSC IV + 5FC IVT= MSC-CD IV + 5-FU IV/ MSC-CD IV + 5-FC IV/ MSC-CD IV + 5-FC) IV x2 | Plasmid + lipofectamine/ CD | Tumor sized-7, d-9, d-11:MSC-CD+5FU< MSC-CD+5FC2x < MSC-CD+5FC< C | Reduced BW: MSC-CD- 5FU | Conversion: 5-FC🡪 5-FU |
| (Luetzkendorf et al., 2010) | Solid tumorColorectal cancer (CRC: DLD-1, HCT-8, HCT-15, SW480) mouse model | nude mice (Harlan Winkelmann) Co-injC=7T=27Tumor IV injC=3T=3 | MSC, Pa= up to P12**Co-injection mixed CRC cells with**:C=(-)/ MSC SCT= 20% MSC-TRAIL SC/ 10% MSC-TRAIL SC/ 3% MSC-TRAIL SC/ 1% MSC-TRAIL SC**DLD-1 tumor IV injection: d-2-4-7-15:**C=PBS/20% MSC IVT= 20% MSC-TRAIL IV | Lentiviral vector/ TRAIL | **Co-injection**:d-17 tumor size:20% MSC-TRAIL << 10% MSC-TRAIL < C= 3% MSC-TRAIL = 1% MSC-TRAIL**Tumor IV injection**d-18 tumour size:T= C | (-) | TRAIL 🡪 apoptosis |
| (Gao et al., 2010) | Solid tumorRenal cancer(786-0 RCC) mouse model | nude miceC= 40T= 40 | Hu BM-MSCPa=P3 or P4C=(-)/MSC (1:0.1)IVT= MSC-IL12 (1:0.1) IV/ MSC-IL12 (1:0.05) IV | Adenovirus/ IL-12 | d-32 tumor size:T- HD < T- LD < CSurvivalT- HD > T- LD >CIT, serum IL12, IFN-γ: T > C | NR | IL-12 activate T cells, NK cells 🡪 IFN-γ |
| (Yan et al., 2013) | Solid tumorNon-Hodgkin’s Lymphoma(BJAB) mouse model | NOD/SCID miceC= 20T= 10 | Hu UC-MSCPa=P3-P5C= PBS/MSC IV/ MSC Con IV/ MSC-scFvCD20 IVT= MSC.ISZ-sTRAIL IV/ MSC-scFvCD20-sTRAIL IV | Lentivirus/ scFvCD20-sTRAIL | d-24 tumor size:MSC-scFvCD20-sTRAIL = MSC.ISZ-sTRAIL < Cd-24 tumor weightC >> MSC.ISZ-sTRAIL > MSC-scFvCD20-sTRAIL | NR | TRAIL 🡪 apoptosisscFvCD20 🡪 antibody against CD20BJAB cells are CD20 (+) |
| (Yao et al., 2017) | Metastatic lung cancer(4T1) mouse model | babl-c miceC= 22T= 33 | SD Rat BM-MSCPa= P2-P8**IV:** d- 6-9-12-15-18:C= saline/ MSCT=free dox/ BPCD/ MSC-BPCD | Biotinilated MSCs/ avidin-BPCD | 24-h bio-distributionMSC-BPCD vs MSC: lung: 93 vs 85.5%, liver: 6.3 vs 7%,Spleen: 0.7 vs 7.5%.MSC - lung - 2 wk.ILS: MSC-BPCD (+26.6%) > BPCD (+58.5%) > free dox Apoptosis: MSC-BPCD> BPCD > free dox> saline> MSC | NR | MSCs as vehicle for dox delivery |
| (Matuskova et al., 2015) | Metastatic lung cancer(MDA-MB-321) mouse model | SCID/bg miceC= 26T= 22 | Human AT-MSCPa= NRC: (-)/ MSC-IVT: MSC-CD-IV+ 5FC-IP-14d/ MSC-TK IV+ GCV-IP-14d/ MSC-CD+ MSC-TK 1:1 -IV+ 5FC+ GCV-IP-14d(all 5FC, GCV- 2 cycles) | pST2, pAPtk retrovirus / Yeast CD-UPRT, HSV-TK | d-40 MDA-MB-321 –in lungs:(-)=11/15MSC =9/11MSC-CD+ 5FC =4/4MSC-TK+ GCV =3/6MSC-CD+ MSC-TK 1:1+5FC+GCV =0/12 | NR | Synergistic cytotoxicity from Conversion: 5-FC🡪 5-FU and HSV-TK |
| (Hu et al., 2014) | Solid tumor and metastatic lung tumor(B16BL6) mouse model | C57BL6 miceMetastasisC=12T=36Solid tumorC= 12T=54Survival:C= 20T= 60 | SD Rat BM-MSCPa= P2-P6Metastasis -IV injectionC=(-)/PBST=MSC(102)/ MSC (104)/ MSC (106)/ SP-IL12/ MSC IL12 (106)Solid tumor –injection🡪 tumor size, survivalC2= (-)/ PBS-IVT=MSC (104) IV/ MSC (105) IV/ MSC (106) IV/ SP-IL12 IV/MSC-IL12 (106) IV/ MSC (106) IT/ SP-IL12 IT/ MSC-IL12 (106) IT | Spermin-Pullulan-DNA nanoparticles/ IL-12 gene | **Metastasis:**d14-metastasis no:MSC (106) > (104)= (102)= C(-)D21-metastasis no:MSC IL12 < SP-IL12 << PBS**Solid tumor:**IV-tumor size: C(-)> MSC 106=105>104 (IV-tumor size: PBS> MSC-IL12> SP-IL12 (NS)IT tumor size: MSC-IL12= SP-IL12<< PBS= MSC(106)d-30: Survival IV- IT:MSC-IL12> SP-IL12 > PBS> MSC (106) | NR | IL-12 🡪 cytotoxic NK activity↑cytolytic T cell↑interferon-γ ↑.MSC-IL12 >< MSC tumor growth effect |
| (Xin et al., 2009) | Multiple lung metastasis(C26, LLC)Mouse model | BALB/c, C57BL/6 miceC=48T= 32 | BALB/c, C57BL/6 mouse BM-MSC, Pa= P3-P5BALB/c–C26, C57BL/6-LLCC= PBS- ITr/ MSC-LacZ-ITr/ Fib-FKN -ITrT= MSC-FKN- ITr/ Ad-FKN -ITr | Adenovirus vector/ CX3CL1 (Fractalkine) | d12-metastasis no:BALB/c –C26: MSC-FKN < Ad-FKN << CC57BL/6-LLC: MSC-FKN << Ad-FKN = Csurvival:BALB/c –C26:MSC-FKN (33d) >> Ad-FKN, C (23-19d)C57BL/6-LLC:MSC-FKN (17d) >> Ad-FKN, C (15-10d) | Ad-FKN🡪 Immune reaction | MSC- homingCX3CL1 🡪 antitumoreffect through NK cells and T lymphocytes. |
| (Ren et al., 2008) | Lung metastasis(TRAMPC2)Mouse model. | C57BL/6 mice C=30T= 20 | C57BL/6 mice BM-MSCPa= P4-P8C= (-)/ MSC-IV 2x/ MSC- GFP-IV -2xT= MSC p IFN-IV-2x/ MSC-rAAV IFN-IV-2x | rAAV/ IFN-β | d75- metastasis/ weight: MSC-rAAV-IFN< MSC p-IFN = Cd-75-blood vessels:MSC-rAAV-IFN<< Cd-75 apoptosis:MSC-rAAV-IFN>> C | NR | IFN-β suppresses tumor cell growthby induction of differentiation, S-phase accumulation and apoptosis. |
| (Conrad et al., 2011) | Orthotopic pancreatic carcinoma (panc02), and mammary adenocamouse model | C57BL/6 mice,Balb-neuT (*neuT*+*/neuT*-) **Panc02:**C= 27T= 7**Breast Ca**C= NRT= NR | C57BL/6 homozygous*p53-* mouse BM-MSCPA= NR**C57BL/6-Panc02**:C= PBS-IV/GCV-IV d-5-6-7/ p53−MSC-RFP-IV/ week 3xT= (*p53*−MSC-TK - IV+GCV IV d-5-6-7 ASC)/week -3x**Breast ca :**C= PBS-IV/ *p53*−MSC-*RFP-*IV/week 3xT= (*p53*−MSC-TK IV+ GCV IV d-5-6-7-8 ASC)/week -3x | CMV vector/ *Tie2-RFP-HSV-TK* gene | **Pancreatic cancer**Tumor weight:MSC-TK-GCV<< MSC-RFP< PBS< GCVTumor size:T<< PBS**Breasr cancer:**Tumor weight~body weight: T<< Cd-6-survival:T>> PBS > MSC-RFP | NR | HSV-TK 🡪 GCV– phosphorylated🡪 toxicTie🡪 homing to tumor blood vessels |
| (Mirzaei et al., 2018) | Lung metastasis (B16F10) mouse model | C57BL/6 miceC= 80T= 20 | Hu AT-MSC, Pa=P3C= (-)/PBS IV/MSC IV/ MSC-mock IVT= MSC-CXCL10 IV | Plasmid-lipofectamine/ CXCL10 | Median survival time:T (50d) >> MSC (26d) = PBS (26d) > MSC mock (24d)> C(-) (23d)Apoptosis, activated T cell no: T>> CMean vessel density, T reg cell no: T<< C | (-) | CXCL10 🡪 apoptosis, anti-angiogenic on various cancer cells |
| (Kim et al., 2013) | Lung metastasis(Renca) mouse model | Balb/mice**Tr d1-d**7C=22T= 66Survival= 5 x 9**Multiple inj**C= 6T=38Lung nodule= 3 x 3 | Rat BM-MSC, Pa= P5-P6**Tr d1, d7 after Renca IV:**C= PBS IV+d2-GCV-IP 7d/ 5x105 MSC-GFP IV + d2-GCV-IP 7dT= 5x105 MSC-TK IV + d2 GCV-IP 7d/ 5x105 MSC-dTRAIL IV + d2 GCV-IP 7d/ 5x105 MSC-TRAIL-TK- IV + d2 GCV-IP 7d**d7- various dose- multiple inj + d2 GCV-IP-7d:**C= 5x105 MSC-GFP IVT= 5x105 MSC-TRAIL-TK IV-1x/ 106 MSC-TRAIL-TK IV-1x/ 1.5x106 MSC-TRAIL-TK IV-1x/ 5x105 MSC-TRAIL-TK IV -2x/ 5x105 MSC-TRAIL-TK IV -2x | Adenovirus/ TRAIL-TK | Tr d1, d7: d14 lung nodule no: MSC-TRAIL-TK < MSC-TRAIL= MSC-TK << MSCTr d7: d100 survival: MSC -TRAIL-TK > MSC-TK > MSC-TRAIL > C**d7- various dose multiple injection:**d120-survival rate:T-LD-3x (=100%) >> T-LD-2x >T-HD=T-MD> T-LD>> Cd-60 lung nodules no: T-LD 1x >> T-LD 2x > T-LD 3x (=0) | NR | TRAIL 🡪 apoptosisTK 🡪 conversion of nontoxic GCV into toxic form |
| (Harati et al., 2015) | Liver metastasis(SW48)mouse model | C57BL/6 mice Non Me C= 12C= 18T= 6 | huBM-MSCPa=NRNon Me C=PBS IV/ MSC IVC= PBS IV/ MSC IV/ MSC-GFP IVT= MSC-Lcn2 IV | pEGFPN1 plasmid + FuGENE transfection/ Lipocalin-2 | Liver metastasisNon Me C (0/6, 0/5)< T(1/5) << C (3/4-4/5)VEGF expressionNon Me C< T< C | NR | Lipocalin-2🡪Inhibit HIF-1a, FA-kinase phosphorylation, VEGF synthesis |
| (Lakota et al., 2015) | Lung metastasis- tongue squamous caT2N0M0Surgery 2x | Human, male 41 y- case reportT= 1 | AT-MSC, NRd-1-7: 2.5 g 5FC/250 ml solution –IV-2x/dd-2: 60x106MSC-IV | pST2 retrovirus + protamine sulfate/ CD-UPRT | d-6: CT scan- no difference – lung metastasisd-40: CT scan: progression of metastases | Fever, resolved after antipyretic, thrombocytopenia, neutropenia | Conversion: 5-FC🡪 5-FU |

MSC= mesenchymal stem cell, C= control, T= treatment, hu= h= human, BM-MSC= human bone marrow mesenchymal cells, Pa= passage, NR= not reported, PBS= Phosphate buffered saline, 5FC= 5fluorocytosine, 5FU=5fluorouracil, PSGL-1= P-selectin glycoprotein ligand-1, SLEX= Sialyl-Lewis X= homing factors, CD= cytosine deaminase, OPG= osteoprotegerin (therapeutic factors), c3-MSC= Murine C3H10T1/2 MSC line, PC3= androgen-independent hu prostate ca cell line from a bone metastasis, ATF= urokinase-type plasminogen antagonist amino-terminal fragment, d- =day-, GBM8= glioblastoma multiforme cells, IC= Intra cerebral, s-TRAIL= secreted TRAIL, TRAIL= TNF related apoptosis-inducing ligand, TNF= tumor necrosis factor, Act-Cas3= Activated caspase-3(+) cells, AT-MSC= Adipose tissue derived MSC, IP= Intraperitoneal, Ive= Intra ventricular, CL= contralateral, C6= rat glio(blasto)ma cell line, CD-UPRT= cytosine deaminase::uracil Phospho-Ribosyl-Transferase, R= tumour resection, IVeP= Intraventricular Pump, AT-CD-IC= AT-MSC-CD intracerebral, AT-CD-P= AT-MSC-CD intracerebral pump, 9L= rat glioma cells, SC= subcutaneous, SD= Spraque Dawley, U87MG= human glioma cell line, Ki67= proliferation marker, ATS= at tumor site, ACLS= at contra lateral site, ESC= embryonic stem cells, rec= recombinant, Bacvec= insect baculovirus vector (plasmid pFastBac1) , Lenvec= lentiviral vector/HSV-TK, GCV= Ganciclovir, HSV-TK= herpes simplex virus thymidine kinase, Gli36vIII= human glioblastoma mutiforme cells expressing a constitutively active variant of Epidermal growth factor receptor (EGFR), MTX= methotrexate, PEG= poly ethylene glycol, NC= nanocomposite, ET= edge of tumor, PL=peptide ligand, IL13Ra2=Interleukin13 Receptora2, g= gram, Cal72= hu osteosarcoma cell line, HT-29= Human colon adenocarcinoma cell line, inj= injection, T-LD= Treatment low dose, T-HD= treatment high dose, huH7= Human hepato cellular carcinoma cell line, CMV= cytomegalovirus, NIS= sodium Iodide transporter, SKOV3= ovarian ca cells, NTR= nitroreductase, IT= Intra tumour, TC1 cells= murine lung epithelial-cell line, LLC= Lewis lung carcinoma cells, VP22= Herpes Simplex VirusType1 tegument protein, A2780= Human ovarian adenocarcinoma cell line, TUBO= murine breast tumor cell line, LIGHT= homologous to lymphotoxin, LTßR-Ig= lymphotoxin ß receptor Imunnoglobulin, TRAMP= transgenic adenocarcinoma of the mouse prostate, TRAMPC1/TRAMPC2= murine prostate tumour cells, TAC= Tacrolimus (immunosuppresant), TC2Ras= TRAMPC2-Ras, MDA-7= IL 24= Melanoma differentiation associated gene-7, PEDF= pigment epithelium-derived factor, 22Rv1= Human prostate cancer cell line, scFv-Fdt-tBid= single chain anti-g-SM antibody (scFv)-short furin cleavage sequence from diphtheria toxin (Fdt)-activated truncated Bid (tBid), DU145= human prostate cancer cell, dox= doxorubicin, TT= TNF-a-Tumstatin 45–132 fusion protein, EGFP= enhanced green fluorescent protein, SCID= severe combined immune deficiency, B16= melanoma cells, 4T1= breast tumor cells, Hca= Hepatoma cells, PD= population doubling, Ad= adenovirus, wk= week(s), LN= lymph node, A375= human melanoma cells, rel(1-3)= relapse 1-3x tumour cells, AMD= AMD3100= SDF-1a/CXCR4 signaling inhibitor, SU1127= small molecule tyrosine kinase inhibitor of c-Met signaling, B16F10= murine melanoma cells, TGI= tumor growth inhibition, LMeC= Canine melanoma cells, CT= circum-tumoral, Cis= Cisplatin, RD-ES= Ewing's sarcoma cell line, MKN45= human gastric cancer cells, CRC= colorectal cancer, DLD-1, HCT-8, HCT-15, SW-480= human colorectal cancer cell lines, 786-0 RCC= human renal cancer cell line, BJAB= CD 20 positive B-cell lymphoma line, scFv= single chain Fv antibody fragment, scFvCD20= CD20-specific scFv, Con= CopGFP (vector control), ISZ= isoleucine zipper, PPCD= PEG PAMAM-cis-aconityl-DOX, BPCD= Biotinylated PPCD, h= hour(s), ILS= increased life span, DA-MB231 cells= hu breast ductal adenocarcinoma cell line, B16BL6= melanoma cells, SP= spermin pululan, no= number, NS= not significant, C26= Murine colon adenocarcinoma cell line, ITr= Intra trachea, Fib= fibroblast, FKN= fractalkine (CX3CL1), IFN= interferon, p-IFN= plasmid-IFN, Panc02= mouse pancreatic cancer cells, adenoca= adenocarcinoma, Balb-neuT (neuT+/neuT-) mouse= transgenic mice with spontaneous focal mammary adenoca, RFP= red fluorescent protein, ASC= after stem cell, Tie2-RFP-HSV-TK gene= RFP + angiopoietin receptor tyrosine kinase, CXCL10= interferon-inducible protein (IP-10) that possesses various anti-cancer effects, Renca= murine renal carcinoma cell line, T-MD= treatment medium dose, SW48= human colon cancer cell line, non Me= non metastasis, Lcn2= lipocalin-2, HIF= hypoxia inducible factor, VEGF= vascular endothelial growth factor