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| **Supplementary Table 1. Preclinical testing of Pericyte-targeted antitumor therapy** |
| ***Direct pericyte-targeted antitumor therapy (via pericyte markers or pericyte-derived agents)*** |
| **Cancer type** | **Treatment** | **Targets** | **Impact on tumor PCs or vasculature** | **Impact on tumor growth** | **Reference** |
| RIP1-Tag2 transgenic mouse model of pancreatic neuroendocrine cancer | Imatinib; SU10944; CTX | PDGFR, c-Kit, and BCR-Abl; VEGFR | Imatinib reduced PC coverage in combination therapy with metronomic chemotherapy or VEGFR inhibition | No effect on the growth of tumors in imatinib monotherapy; enhanced anti-tumor efficacy in combination with metronomic chemotherapy or VEGFR inhibition | (Pietras and Hanahan, 2005) |
| CRC in subcutaneous mouse model | Imatinib; bevacizumab | PDGFR, c-Kit, and BCR-Abl; VEGFR | Combination of imatinib with low-dose bevacizumab increases PC coverage and promotes vascular normalization; monotherapies have no effect on PC coverage | Combination therapy inhibits tumor growth; tumor growth is not significantly affected after imatinib monotherapy | (Schiffmann et al., 2017) |
| Lewis lung carcinoma and fibrosarcoma implanted in murine models | PDGFR ectodomain (Ad sPDGFR); VEGFR2/Flk1 ectodomain (Ad Flk1-Fc)  | PDGFRβ; VEGFR | Ad sPDGFR blocks PC recruitment and reduces PC coverage; Ad Flk1-Fc decrease PC content | Addition of Ad sPDGFR produces additive antitumor effects on tumors vs. Ad sPDGFR or Ad Flk1-Fc monotherapies; Ad sPDGFR monotherapy was less efficacious than Ad Flk1-Fc | (Kuhnert et al., 2008) |
| RIP1-Tag2 transgenic mouse model of pancreatic islet cancer | SU6668; SU5416;STI571 | PDGFR; PDGFR, c-Kit, and BCR-Abl; VEGFR | Increased apoptosis and regressed BV in SU6668 and SU5416 combination therapy; reduced abundance and detachment of PC as well as decreased vascularity in SU5416 and STI571 combination therapy | Reduced tumor in SU6668 and SU5416 combination therapy; combination of STI571 with SU5416 causes late-stage tumor regression | (Bergers et al., 2003) |
| Ovarian carcinoma in orthotropic mouse model | STI571; AEE788; paclitaxel | PDGFR, c-Kit, and BCR-Abl;VEGFR | Reduced PC coverage in STI571 group;decreased PC coverage in the AEE788 plus STI571 group and in the triple combination group | STI571 alone is not effective; triple combination is more effective than all other treatments; greatest improvement in survival and regression of formed tumors in triple combination | (Lu et al., 2007) |
| Human thyroid cancer in subcutaneous mouse model | STI571; PTK/ZK; taxol | PDGFR, c-Kit, and BCR-Abl; VEGFR | Decreased PC coverage in monotherapies and combination therapy  | No significant effect on tumor growth alone or in combination but the inhibitors enhance the effect of taxol chemotherapy in triple combination | (Kłosowska-Wardega et al., 2009) |
| Human cervical carcinogenesis mouse model  | Imatinib | PDGFR, c-Kit, and BCR-Abl | Reduced lesional neovascularization and diminished blood vessel density in CIN3 lesions and SCC; decreased PC coverage | Decreased median tumor volume | (Pietras et al., 2008) |
| Pancreatic islet tumor in RIP-Tag2 transgenic mouse model | Imatinib; CTX | PDGFR | N/A  | No effect on tumor growth by imatinib; stopped tumor growth and reduced tumor burden in combination therapy | (Falcon et al., 2011) |
| Diffuse large B-cell lymphoma in human xenograft and EL4 lymphoma in murine allograft models | Imatinib | PDGFR, c-Kit, and BCR-Abl | Induced PC apoptosis and loss of perivascular integrity as well as microvascular density | Impaired lymphoma growth | (Ruan et al., 2013) |
| Melanoma in subcutaneous mouse model | Imatinib | PDGFR, c-Kit, and BCR-Abl | Inhibited vascular mimicry | Suppressed tumor growth | (Thijssen et al., 2018) |
| Pancreatic cancer in subcutaneous and orthotropic mouse models | TKI258 | PDGFR, VEGFR, FGFR | Impaired PC function and motility | Significant inhibition of tumor growth as well as reduced lymph node and liver metastases; delayed growth of established tumors and extended survival | (Taeger et al., 2011) |
| Ovarian carcinoma and NSCLC in subcutaneous mouse models | IMC-2C5a | PDGFRβ | N/A | Decreased tumor growth rate in IMC-2C5 monotherapy in two mouse models | (Shen et al., 2009) |
| Lewis lung carcinoma in subcutaneous mouse model | CP673451 (PDGFRβ inhibitor)  | PDGFRβ | Improved inhibition of PC was associated with increasing doses of CP673451 | CP673451 slowed the tumor growth without improving survival but enhanced metastasis in combined radiotherapy and Endostar therapy | (Yin et al., 2018) |
| Pancreatic cancer and CRC in subcutaneous and orthotropic mouse models | PDGF-BB (transfected); followed by imatinib mesylate  | PDGFR, c-Kit, and BCR-Abl | Increased the number of PC in PDGF-BB–overexpressing clones; imatinib mesylate treatment decreased the number of PC | Reduced tumor mass in PDGF-BB–overexpressing clones; imatinib mesylate treatment reversed the growth inhibition of tumor | (McCarty et al., 2007) |
| HaCaT skin carcinogenesis mouse model | hPDGF-B and mVEGF-164 (transfected); followed by imatinib  | PDGFR, c-Kit, and BCR-Abl | Combined hPDGF-B and mVEGF-164 expression results in mature functional tumor vasculatures and higher microvessel density; decreased tumor vasculatures and reduced association of αSMA+ PC with the BV following treatment with imatinib  | Coexpression of mVEGF-164 and hPDGF-B shows no significant effect on tumor growth as compared with mVEGF-164 transfectant tumors, but improves tumor organization; treatment with imatinib reverses the above effect | (Lederle et al., 2010) |
| Breast cancer in orthotropic PDGFRβ-TKb transgenic mouse model | N/A | PDGFRβ knockout | Reduced BV and increased permeability in PC-depleted tumors | PC depletion enhanced intra-tumoral hypoxia, decreased tumor growth, and increased lung metastasis in advanced-stage hypoxic tumors | (Keskin et al., 2015) |
| Human gastric cancer in orthotropic mouse model | Nilotinib; everolimus | PDGFR; mTOR  | Decreased stromal reactivity and PC coverage in nilotinib treatment alone; decreased microvessel density in everolimus monotherapy | Tumor growth and metastasis are not inhibited in nilotinib treatment alone but significantly decreased stromal reactivity; both of the growth rate and stromal reaction were reduced in combination treatment with everolimus | (Onoyama et al., 2013) |
| Lewis lung carcinoma in colonization mouse model and subcutaneous melanoma in human CD248 knock-in mouse model | MORAb-004c  | CD248 | Impaired tumor microvasculature maturation and dysfunctional tumor microvasculature | Reduced primary tumor growth and inhibited tumor metastasis | (Rybinski et al., 2015) |
| RENCA in subcutaneous mouse model | DLK1-based vaccine | DLK1 | Enhanced vascular normalization | Inhibited tumor growth and increased frequencies of CD8+ T cell tumor infiltrating lymphocytes | (Chi Sabins et al., 2013) |
| RENCA and melanoma in subcutaneous mouse models | DLK1- and DLK2-based vaccines (lvDLK1 and lvDLK2) | DLK1 and DLK2 | Decreased vascular pruning and increased PC coverage when vaccinated with lvDLK1 or with combined lvDLK1 and lvDLK2 | Combined vaccination leads to improved antitumor benefits as compare with single vaccine treatment; enhanced antitumor efficacy when further combined with PD-L1 blockade | (Fabian et al., 2017) |
| Infantile hemangioma in subcutaneous mouse model | NOTCH3 Decoy (NOTCH3 inhibitor) | NOTCH3 | Decreased blood flow, vessel caliber, and αSMA+ perivascular cell coverage | Disrupted IH development | (Edwards et al., 2017) |
| *Indirect PC-targeted antitumor therapy* |
| **Cancer type** | **Treatment** | **Targets** | **Impact on tumor PCs or vasculature** | **Impact on tumor growth** | **Reference** |
| Lewis lung carcinoma in subcutaneous mouse model | Anti-Olfml3 antibody | Olfml3 | Reduced angiogenesis and PC coverage of tumor vessels | Inhibited tumor growth | (Miljkovic-Licina et al., 2012) |
| Melanoma, Lewis lung carcinoma in subcutaneous mouse models | N/A | CCL2 knockout | No effect on PC coverage, blood vessel density and function | Reduced tumor cell growth | (Wong et al., 2020) |
| Orthotropic GBM xenograft model | Ibrutinib | BMX kinase | Disrupted glioma stem cell-derived PCs and blood-tumor barrier; increased vascular permeability  | Improved chemotherapy efficacy resulting in retarded tumor growth and extended survival | (Zhou et al., 2017) |
| Melanoma, Lewis lung carcinoma, fibrosarcoma in subcutaneous mouse models | G6-31d | PDGF-B knockout;VEGF-A | Reduced PC abundance in *pdgfbret/ret* mice | No improvement of VEGF-A inhibition in PC-deficient *pdgfbret/ret* mice tumor | (Nisancioglu et al., 2010) |
| Lewis lung carcinoma mouse model and pancreatic islet tumor in RIP-Tag2 transgenic mouse | AX102e | PDGF-B | Reduced PC and tumor vascularity | No decrease in tumor size in Lewis lung carcinoma; less prominent antitumor effect in pancreatic islet tumor. | (Sennino et al., 2007) |
| Lewis lung carcinoma mouse model and pancreatic islet tumor RIP-Tag2 mouse | AX102; CTX | PDGF-B | Decreased tumor vascularity in AX102 treatment in LLC tumors | Greater efficacy of CTX on tumors when combined with AX102 | (Falcon et al., 2011) |
| Highly metastatic human ovarian carcinoma in orthotropic mouse model | AX102; bevacizumab | PDGF-B; VEGF | Decreased PC coverage in the AX102 treatment group; reduced microvessel density in the bevacizumab treatment group | AX102 monotherapy is not effective; combination with bevacizumab treatment is highly efficacious | (Lu et al., 2010) |
| RCC, ovarian cancer and HCC subcutaneous mouse models; human melanoma xenograft | MEDI3617f; bevacizumab; paclitaxel | Ang-2; VEGF | Reduced vessel lumen area and decreased functional vessels | Inhibited tumor growth by blocking tumor angiogenesis; delayed tumor growth when combining with chemotherapy and bevacizumab | (Leow et al., 2012) |
| GBM multiforme in orthotropic mouse model | Trebananib; aflibercept | Ang-1/2; VEGF | Reduced vascular permeability and improved PC coverage (with depletion of tumor-associated macrophages and increased intratumoral T lymphocytes in combination therapy | Extended survival in combination therapy | (Scholz et al., 2016) |
| Human colon cancer in orthotropic mouse model | L1-7[N] (Ang-2 inhibitor);mL4-3 (Ang-1 inhibitor) | Ang-2; Ang-1 | Reduced tumor vessels and enhanced vascular normalization in Ang-2 inhibitor treatment including increased PC coverage and reduced EC sprouting | Little effect on the tumor vascularity with Ang-1 inhibitor treatment; suppressed tumor growth in Ang-2 inhibitor monotherapy and combination therapy with Ang-1 inhibitor | (Falcon et al., 2009) |
| Lewis lung carcinoma, MT-ret melanoma, and B16F10 melanoma in Ang-2 knockout mice | N/A | Ang-2 knockout | Smaller microvessels, higher PC coverage and more mature PCs | Decreased tumor growth rate in all types of tumors in Ang-2 knockout mice | (Nasarre et al., 2009) |
| Breast cancer in orthotropic mouse model | Murinized anti-ANG2 neutralizing antibody; imatinib | Ang-2; PDGFR | Anti-ANG2 antibody restores the integrity of PC-depleted leaky BV | Anti-ANG2 therapy significantly reduces the frequency of lung metastasis; combination of anti-ANG2 and imatinib treatment shows synergic effect on inhibiting primary tumor growth and lung metastasis as compared to imatinib monotherapy | (Keskin et al., 2015) |
| Melanoma lung metastatic experimental mice | TH10-DTX-NPg | NG2-positive PC | Reduced PC density and microvessel density in the lung metastases | Extended tumor bearing mouse survival with no obvious toxicity and enhanced antitumor effect | (Guan et al., 2014) |
| Human NSCLC xenograft model | tTF-TAAh | NG2-positive PC | Activated coagulation within the microvasculature | Suppressed tumor growth | (Brand et al., 2016) |
| Human breast cancer xenograft model | Z-GP-DAVLBHi | FAPα-positive PC | Disrupted blood vessels in tumor core and periphery | Inhibited tumor growth or induced tumor regression | (Chen et al., 2017) |
| CRC in subcutaneous mouse model | Z-hTRAILj | PDGFRβ-positive PC | N/A | Increased tumor uptake and enhanced antitumor effect of hTRAIL contribute to tumor regression | (Tao et al., 2017) |
| BV: blood vessel; RENCA: murine renal carcinoma; CRC: colorectal cancer; CTX: cyclophosphamide; DLK: dual leucine zipper kinase; IH: infantile hemangioma; LLC, Lewis lung carcinoma; NSCLC: non-small-cell lung cancer; PDGF: platelet-derived growth factor; PDGFR: platelet-derived growth factor receptor; RCC: renal cell carcinoma; SCC: squamous cell carcinoma; VEGFR: vascular endothelial growth factor receptor |

1. A fully human neutralizing antibody that directs against PDGFRβ;
2. Transgenic mice that express viral thymidine kinase under the PDGFRβ promoter as an alternative model for PC depletion;
3. An anti-human CD248 antibody Fb5;
4. A specific anti-VEGF-A antibody that neutralizes both murine and human VEGF-A;
5. A novel DNA oligonucleotide aptamer highly selective PDGF-B;
6. A human anti-angiopoietin 2 monoclonal antibody;
7. TH10 peptide conjugated nanoparticles loading docetaxel (TH10-DTX-NP) target the NG2 proteoglycan to facilitate nanoparticle internalization in PCs resulting in DTX-induced PC apoptosis;
8. tTF-TAA consisting of the extracellular domain of tissue factor (TF) and the peptides which represent ligands of NG2 target to PC leading to tumor vessel infarction;
9. Z-GP-DAVLBH hydrolyzed by FAPα to release vascular disrupting agent DAVLBH in order to disrupt the cytoskeleton of PC to overcome VDA treatment resistance;
10. Fused ZPDGFR affibody mediates PC-targeted delivery of hTRAIL.

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