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| **Table S2 Preclinical models with a cause-effect relationship between commensals and anticancer effects.**  |
| **Cancer models** | **ATB/FMT** | **Drugs** | **Commensals** | **Commensal Regimen** | **Effect** | **Mode of action** | **Reference** |
| **NATURAL IMMUNOSURVEILLANCE** |
| Pre-leukaemic myeloproliferation (PMP)in *Tet2*-/-mice | ATB and GF and IL-6R wt versus KO bone marrow | None | Differences assigned to *Lactobacilli reuteri, L. johnsonii, L. intestinalis* | None | Accelerated and increased incidence of PMP development, Tet2 deficiency-induced gut permeability and translocation of Lactobacilli in secondary lymphoid organs | TLR2L and IL-6- induced myeloproliferation, expansion of IL-6Ra expressing GMP  | (Meisel et al. 2018) |
| Ovarian and breast tumors in *Tlr5-/-*mice | Tlr5 wt versus Tlr5 KO miceTlr5−/− γδ-deficient miceCo-housing experiments | None | Differences assigned to genera of Allobaculum, Bacteroides, and Lactobacillus | None | Deleterious role of flagellin-harboring gut commensals on (IL-6 or IL-17 driven) peripheral inflammation | Crosstalk between MDSC and γδ-T cells related to gut commensals. Role of IL-6 and IL-17 in tumor-induced inflammation and propagation. | (Rutkowski et al. 2015) |
| KP autochthonous lung cancer model | SPF | None | *Veillonella parvula*Increased total bacterial burden and reduced diversity *(*enrichment with *Herbaspirillum* and *Sphingomonadaceae,* and reduced *Aggregatibacter* and *Lactobacillus)* | Interalveolar spreading in lower airway tract | Enhancing tumor engraftment and local dissemination | Induction of PD-L1 on tumor cells and IL-17 local inflammation and turning on the MAPK/mTOR pathway. γ6δ1 T cells producing IL-17 triggered by neutrophils | (Tsay et al. 2020)(Jin et al. 2019) |
| \*BRPKp110 HR+ mouse mammary cancer\*PyMT mammary tumors\*LKRasG12Dp53flx/flxL-Stop-L-Myristoylated p110a\_GFP. mice | ATB (bacitracin, neomycin)and FMT | Dysbiosis prior to tumor inoculation | ATB-induced drop in bacterial richness | Oral administration of dysbiotic caecal content | Increased fibrosis and collagen deposition in mammary gland and TME | Dysbiosis+tumor inoculation increased Cxcl2 and CCL2 and Cxcl10 in the mammary gland and IL-23, Arg1, IL-6 producing myeloid MDSC recruitment in tumor beds leading to increased stromal inflammation | (Buchta Rosean et al. 2019) |
| \*CT26 and MC38 colon cancers\*4T1 mammary cancer | SPF mice | None (eubiosis) | Nanoparticles from Gram negative bacteria and E. coli ΔmsbB OMV | Intravenous injection of outer membrane vesicles from E. coli (OMV) every 3 days for 20 days | Cxcl10 and IFNγ systemic secretionT and NK cell stimulation | T and NK cell dependent tumor growth retardation with OMV | (Kim et al. 2017) |
| **IMMUNOTHERAPY** |
| ***Immune Checkpoint inhibitors (ICI) +/- chemotherapy*** |
| \*Melanoma B16.SIY \*Bladder cancer MB49  | SPF Taconic (TAC) vs Jackson (JAK) labno ATB | anti-PD-1 mAbs  | *Bifidobacterium* spp cocktail (*B. breve, B. longum*) | Oral gavage with anti-PD1 mAbs  | Restoring efficacy of ICIin mice coming TAC vendor | Enhanced DC functions and CD8+ T cell priming and CTL recruitment in the TME | (Sivan et al. 2015) |
| \*MCA-205 sarcoma\*RET melanoma\*MC38 colon carcinoma | GF or ATB and FMT from melanoma patients  | anti-CTLA-4 mAbs | Bacteroidales or Burkholderialesorder(*B. fragilis, B.thetaiotaiomicron) B. cepacia)* | Oral gavage with anti-CTLA-4 mAbs  | Restoring therapeutic response to anti-CTLA-4 mAb in FMT- or ATB treated mice | Maturation of tumor DC and induction of IL-12-dependent systemic TH1-immune responses  | (Vétizou et al. 2015) |
| \*MCA-205 sarcoma\*MC38 MSI colon carcinoma \*CT26 MSS colon cancer  | GF recipient or ATBSPF or FMT from colon cancer patients | Sequential oxaliplatin chemotherapy and anti-PD-1 mAbs | ErysipelatotrichaceaeBacteroidaceae FusobacteriaceaePrevotellaceaefamily members. (*B. fragilis, E.ramosum,**P. clara, F. nucleatum*) | Combinations of ileal commensals+oxaliplatinum-anti-PD1 mAbs in MSS colon cancers | Synergistic effects of OXA+anti-PD1 in the presence of immunogenic ileal commensals  | Ileal apoptosis+ ileal immunogenic bacteria induce IL-1β and IL-12 DC release and elicitation of B cells, IgG2b serum levels and TFH immunity associated with tumor regression. | (Roberti et al. 2020; Picard et al. 2020)  |
| \*BP melanoma | FMT from R and NR melanoma patients | anti-PD1 mAbs | Oral gavages of hosts with FMT from melanoma patients |  *None*  |  Increased responsiveness to anti-PD1 mAbs  | Immune changes in gut, spleen and TME: increased of TH1 and decrease of TH17 TILs in TME, ascribed to enrichment in *Faecalibacterium* spp. | (Gopalakrishnan et al. 2018; Rutkowski et al. 2015)  |
| \*MCA-205 sarcoma\*RET melanoma \*Orthotopic LLC lung carcinoma  | GF or ATB in SPF or prior to FMT from NSCLC NR patients  | anti-PD-1 mAbs+/- anti-CTLA4 Abs | *Akkermansia muciniphila (Akk)* (+/-*Enterococcus hirae*)  | FMT from NR-NSCLC patients in avatar micesupplemented with oral gavages of Akk during anti- PD-1 mAb+/- anti CTLA4 Ab-based therapy | Compensation of dysbiosis and restoration of response to anti-PD-1 mAbs | \*Recruitment of CCR9+CXCR3+CD4+ T cells in the TME via IL-12\*Increased CD4/Foxp3 ratio in TILs | (Routy et al. 2018) |
| \*Orthotopic RENCA kidney carcinoma  | ATB or FMT from R vs NR RCC cancer patients | antiPD-1 mAbs + antiCTLA 4 mAbs | *Akkermansia muciniphila* or *B. salyersae* | FMT from NR-RCC patients in avatar micesupplemented with oral gavages of Akk during anti- PD-1 mAb+/- anti CTLA4 mAbs | Restoring responses to combination of ICI  | Not done | (Derosa et al. 2020) |
| \*MC38 colon carcinoma\*Braf V600E Pten-/- melanoma  | GF or SPF conditions without antibiotics | anti-PD-1 oranti-CTLA 4 mAbs | Mixture of a 11 bacteria consortium | Repetitive oral supplementation early after tumor inoculation  | Enhancing the efficacy of ICI | Induction of colonic and intratumor IFN𝛄 producing CD8+ T lymphocytes, activation of systemic DCMetabolomic changes with the bacteria consortium | (Tanoue et al. 2019) |
| \* CT26 and MC38 colon cancer\**Msh2LoxP/LoxPVillin-Cre autochthonous colon cancer* model | ATB  | anti-CTLA4, CpG and chemotherapy | *Bifidobacterium pseudo longum and Akkermansia* (gut or possibly intratumoral bacteria) | Oral *B. pseudolongum, L. johnsonii, Olsenella spp.+ICI* |  DC exposed to *B. pseudolongum* or A.muc produce IL-12 which, through IL-12Rβ cosignaling with A2AR on T cells induce TH1 differentiation | Anticancer metabolite inosine translocates from gut to tumor beds.Inosine (ip, iv or per os) synergized with anti-CTLA4 mAbs in an IL-12 and A2AR-dependent manner | (Mager et al. 2020) |
| \*MC38 colon cancer | ATBGFTac versus Jax mice and Ifnarf/fCd11cCre mice | anti-CD47 mAbs | Oral inoculation of *Bifidobacteria* | Oral administration of Bifidobacterium and i.t. injection of anti-CD47 mAbs | Stimulation of the STING signaling pathway | Induction of IFNβ in tumor DC. Intratumoral (i.t) elimination of Bifidobacterium by an antibiotic cocktail reduced the cross-priming ability of tumor DCs | (Y. Shi et al. 2020) |
| \* Preinvasive and invasive pancreatic ductal adenocarcinoma (PDA)\*orthotopic KPC | ATB | anti-PD1 mAbs | TRAF6 inhibitors decreased while TLR2 and TLR5 ligandsincreased PDA aggressiveness | Oral administration of protumorigenic *B. pseudolongum* | MDSC and TLR signaling.*Proteobacteria and B. pseudolongum* more abundant in gut and tumor and accelerated oncogenesis in a TLR-dependent manner | Reprogramming of M2 into M1, and TH1+ cytotoxic CTL in PDA. Combination of ATB and PD-1 blockade reduce PDA growth | (Pushalkar et al. 2018) |
| \*RET melanoma\*TC1 iv metastases\*RENCA kidney cancer\* Humans in carb free diet interventions | Ketogenic diet (KD)or 3OH butyrate (3HB) in SPF mice | anti-PD1 mAbs+/-anti-CTLA-4 mAbs | Nutritional interventions (Ketogenic dietor 3OH butyrate (3HB° ip, iv, or per os) | Diet-induced changes of microbiota composition (richness in *Eisenberghiella massiliensis*) |  3HB-induced TH1 differentiationwithout upregulation of PDL-1 on tumor cells nor CD86 on spleen macrophages | Increased efficacy of ICI by prophylactic diet interventionsT cell dependent activity of KD or 3HB | (Ferrere et al. 2021) |
| ***Adoptive Cellular Therapy (ACT)*** |
| \*Large B16F10 melanoma | ATB or polymyxin or TLR4 or CD14 wt versus TLR4 or CD14 KO miceRag2–/–γc–/– mice | 5 Gy TBI and ACT (p-mel-1 specific CTL) | Ultrapure LPS | Effects of host conditioning with TBI prior to ACT | Enhanced efficacy of ACT in the setting of TBIdue to translocation of Enterobacter cloacae, E. coli, Lactobacillus, and Bifidobacterium bacteria into mLN after TBI | Bacterial and LPS dependent increase of host spleen CD11c+CD86high DCs and serum levels of IL-12 | (Paulos et al. 2007) |
| \*MPKAS tumors | Tlr5 wt versus Tlr5 KO miceTlr5−/− γδ-deficient miceCo-housing experiments | Spontaneous tumor growth | Differences assigned to genera of Allobaculum, Bacteroides, and Lactobacillus | Extra-intestinal tumor growth kinetics between TLR5 wt and gene deficient littermates | Deleterious role of flagellin-harboring gut commensals on (IL-6 or IL-17 driven) peripheral inflammation | Cross-talk between MDSC and γδ-T cells related to gut commensals. Role of IL-6 and IL-17 in tumor-induced inflammation and propagation. | (Rutkowski et al. 2015) |
| \*sc B16.SIY melanoma | SPF C57BL/6  | SVY (*B. breve* epitope)-expanded T cells targeting the SIY -expressing tumor cells  | *Bifidobacterium breve* | ACT injection at day 8 post tumor inoculation, followed by 2 injections of IL-2 | Delay tumor growth | TILs stimulation via cross-reactivity between SVY commensal epitope and SIY melanoma neoantigen  | (Bessell et al. s. d.) |
| \*sc TC1 cells, HPV E6/E7 gene transduced cervix /lung cancer cells  | ATB regimen(vancomycine, versus neomycine,versus metronidazole) | HPV-E6/E7-specific ACT  | Vancomycine (killing unknown specific Gram+bacteria from the Bacteroides genus) | Oral vancomycine (but not metronidazole or neomycine) for 10 days before ACT  | Vancomycin increased the efficacy of ACT | Increased systemic CD8 ⍺ DC numbers resulting in enhanced efficacy of ACT in an IL-12 dependent manner | (Uribe-Herranz et al. 2018, 12) |
| ***Cytokine or TLR agonists*** |
| \*sc MC38 colon carcinoma, \*B16.F10 melanoma  | ATB pre-exposed mice | CpG-ODN combined to anti-IL10R | *Alistipes shahii and Ruminococcus genus* were pro-inflammatorywhileL. murinum, L. intestinalis, and L. fermentumwere anti-inflammatory mediators*.* | Oral administration of 5 or 8 doses, after one week of antibiotic cessation | TNFα-induced tumor necrosisfollowing CpG+anti-IL-10R mAbs | Increased TNF production by tumor associated myeloid cells in response to anti-IL10R/CpG-ODN | (Iida et al. 2013) |
| \*B16F10 melanoma\*CT26 sc colon cancer\*Human colon cancer tissues | SPF mice on ex vivo organotypic cultures |  rIL-2  | *A. muciniphila (Akk)* or TLR2 *Akk* agonist | Oral gavages with *Akk* every three days for 20-25 days with ip administration of rIL-2 | *Akk* induced tumor cell apoptosis, increased CD8/Treg ratio, activation of intratumor DCs | Increased Tc1 CTLs in tumor bedsReduction of TregIncreased ratios between TNFα/TGFβ in tumor beds | (L. Shi et al. 2020) |
| **CHEMOTHERAPY or TARGETED THERAPIES** |
| \*sc EL4 thymoma |  ATB or GFand TLR4 wt versus KO mice | Oxaliplatinum (OXA) | Not done | Oxaliplatinum in GF or ATB treated mice | Deficient production of reactive oxygen species and cytotoxicity after chemotherapy in ATB or TLR4 KO mice | ABX attenuated induction of Nox1 and Cybb encoding ROS-generating NADPH oxidase 2 (NOX2) and of the ROS-responsive Nos2, Sod1, and Sod2 after OXA | (Iida et al. 2013) |
| \*MCA-205 sarcoma \*B16.F10 melanoma  | C57BL/6J miceGerm free or ATB treated mice in SPF conditions | Cyclophosphamide (CTX) | *Enterococcus hirae* and *Lactobacillus johnsonii* | Oral gavages the day after CTX administration  | Elicitation of pTH17 cells compensating the loss of CTX activity in ATB-treated mice. | CTX-induced Gram-positive translocation from gut to splenocytes and subsequent systemic priming of pTH17 and memory TH 1 immune correlating with therapeutic efficacy of CTX. | (Viaud et al. 2013) |
| \*MCA-205 sarcoma \*MC38 colon cancer\*HPV16 TC1 lung cancer  | ATB or SPF | CTX | *Enterococcus hirae* or *Barnesiella intestinihominis*  | Oral gavage the day after CTX administration or vaccination  | *B. intestinihominis* restores efficacy of a cancer vaccine*E. hirae* restores efficacy of CTX in ATB treated mice  | *\*E. hirae* increased intratumoral CD8/Treg ratio. \*B. intestinihominis stimulated IFN**𝛄** producing 𝛄𝝳 Tcells in the TME. \*Both commensals mounted effector and memory CD4+TH1, CD8+ Tc1 lymphocytes | (Daillère et al. 2016) |
| \*MCA205 sarcoma\*TC1 lung cancer | ATB | CTX or anti-PD-1 Abs | Various strains of *E. hirae* containing or not a Siphoviridae phage sequence |  *E. hirae* spp. harboring various genetic sequences and CTX or anti-PD-1 mAbs |  H-2Kb-restricted CTL responses in spleen and tumor beds | Molecular mimicry between *E. hirae* TMP1 antigen and PSMB4 oncogenic driver | (Fluckiger et al. 2020) |
| \*YUMM1.5 melanoma\*NRASQ61Kmouse melanoma cells | Prebiotics in SPF mice | Mucine or Inulin | None | Oral gavage of prebiotics in conjunction with MEK or BRAF inhibitors(mucin (3% in drinking water) or inulin (15% w/w in chow) starting 2 weeks before sc inoculation of melanoma tumor cells  | Changes of the microbiota composition with prebiotics (mucin and Akk, inulin and Biifidobacteria) | Systemic Il-1a and Cxcl13 with mucin. TH1 cells and DC maturation with both prebiotics.Inulin attenuated resistance of melanoma to MEK inhibitors | (Li et al. 2020) |
| **RADIATION THERAPY**  |
| \*B16-OVA melanoma, \*TC1 cervix/lung carcinoma  | SPF and vancomycine treated mice | External beam radiotherapy (RT) on tumor beds | Gram positive bacteriaand SCFA | Oral vancomycine before tumor inoculation | Enhanced local and abscopal anti -tumor effects of RT | Increases local cross- presentation of tumor antigen-specific T cellsInhibitory effects of distinct Gram+ bacteria and butyrate | (Uribe-Herranz et al. 2020) |
| \*Elite mice subjected to sublethal irradiation\*B16F10\*EL4\*21 leukaemia patients at strat of TBI for pre-HSCT | FMT and dirty cage sharing | Partial or total body irradiation | Lachnospiraceae and Enterococcaceae | Oral gavages with Lachnospiraceae family members  | Gut metabolic changes such as increased Propionate and H-Indole 3- carboxaldehyde Kynurenic acid that protect mice against DNA damage and ROS release | Increased hematopoiesis and intestinal barrier recovery post-sublethal irradiation | (Gao et al. 2018) |
| **STEM CELL TRANSPLANT (SCT)** |
| Major-histocompatibility-complex (MHC)-matched minor-antigen-mismatched allo-HCT model (C57BL/6→129S1/Sv)  | Broad spectrum ATBcompared with T cell repleted grafts | Allogeneic bone marrow transplantation (BMT) | *Enterococcus faecalis* | Dietary lactose depletion or elimination of Enterococci growth post-all BMT | Graft-versus-host disease (GVHD) modulated with enterococci relative overgrowth in colon LP | Disaccharide lactose-induced Enterococci overgrowth, creating elevated IFN**𝛄** serum levels, TH17 colonic accumulation and recirculation of CD4+ T cells  | (Stein-Thoeringer et al. 2019; Iida et al. 2013) |
| Mice irradiated (TBI) and transplanted with B10.BR BM and T cells 7 days ampicillin, before BMT | C57BL/6J mice | Allogeneic bone marrow transplantation (BMT) | *Lactobacillus johnsonii* | Oral reintroduction every other day for 14 days before BMT | Protection against Graft-versus-host disease (GVHD)  | Unknown | (Jenq et al. 2012) |
| Mice irradiated (TBI) and transplanted with BM 7 days ampicillin, before BMT | C57BL/6J mice | Allogeneic bone marrow transplantation (BMT) | *Lactobacillus rhamnosus GG* | Oral administration 7 days prior to BMT or in post transplantation period proceeded by 7 days of ciprofloxacin | Reduced mortality post BMT and protect against GVHD | Unknown | (Gerbitz et al. 2004) |