Supplementary file 1

Revolutionizing cancer therapy: Monoclonal antibodies in radiosensitization

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Table. S1. Summary of Studies on Antibody-Mediated Radiosensitization in Cancer Therapy

Radiation Characteristics	Mechanism of Action	In Vivo/In Vitro	Cells and tumor models	Cancer type	Composition Details	Accompanying Agents	Molecular Target	Role of antibody	Antibody	Year [Ref]
8 Gy × 3	↑immune response by inducing local inflammation, ↓hypoxia, activating ADCC, and triggering innate and adaptive immunity	In Vivo	4T1, CT26/ BALB/C mice	Breast, colon	-	Bifidobacterium infantis	*Bifidobacterium infantis*	targeting B. infantis, PD-1	Specific monoclonal antibody for B. infantis, αPD-1	2024 [75]
4 Gy	↑DNA damage and suppresses TME; G2/M arrest reversal via CDK1 inhibition; TME modulation by PD-1 blockade	In Vivo/In Vitro	HepG2, Hepa1-6, and H22/ Balb/c mice,	**Hepatoma**	AZD1775: Wee1 inhibitor	AZD1775	PD-1	Targeting PD-1	Anti-PD-1	2024 [76]
2.5 to 10 Gy	↑H3K9ac and α-tubulin acetylation; inhibiting migration/metastasis pathways	In Vivo/In Vitro	T24, UMUC-3, BFTC909/ C57BL/6 mice	MIBC	Tubacin: HDAC6 Inhibitor, Panobinostat: Pan-HDAC Inhibitor	Tubacin, Panobinostat	CXCL1	Targeting CXCL1	Anti-CXCL1	2023 [77]

X-ray energy: 6 MV, 18 MV; doses: 2, 4, 8 Gy	↑cytotoxicity	In Vitro	SKBr-3	Breast	Diameter: 41.5 nm, PEGylation; OPSS-PEG-SVA for conjugation	Fe3O4@Au core-shell NPs	HER-2	targeting HER-2 and NPs delivery	Trastuzumab	2023 [78]
6 MV X-ray, (10 Gy in 5 days; 2 Gy/day)	eradicated tumor cells, ↓ vascularization, proliferation, and repair	In Vivo/In Vitro	U87, Athymic nude mice	GBM	GNPs coated with insulin to cross BBB	TMZ, GNPs	EGFR	blocking EGFR	Cetuximab	2022 [79]
200 keV to 1 MeV, 3 and 5 Gy	produce CD8 T cell and immunologic memory, ↓ DNA repair	In Vivo/In Vitro	LL/2, MOC1 ، MOC2, B16/ C57BL/6	Oral, melanoma	linked to CDX3379 via MC-VC-PABC and tracked using Cy5 labeling	MMAE	HER3	targeting of HER3	CDX3379	2022 [80]
Energy: 220 kV, Dose: 0-15 Gy	↑ROS and impairing DNA repair, blocking the PD-L1/PD-1 immune checkpoint, reversing the immunosuppressive effects caused by TAMs	In Vivo/In Vitro	B16F10	melanoma	MRI imaging, radiosensitization, drug delivery, PD-L1 targeting, and immune modulation	antiPD-L1-SPIOs@PLGA@Au	PD-L1	Targeting and blocking the PD-L1/PD-1 signaling pathway	Anti-PD-L1	2022 [81]

Energy: 6 MV, Dose: 0-8 Gy	↑ROS	In Vitro	LNCaP	prostate	-	PEGylated AuNPs	PSMA	Targeting PSMA and delivery NPs	PSMA	2022 [82]
200-kVp, 2-6 Gy	↓ tyrosine and serine/threonine kinase activity	In Vitro	MiaPaCa-2	PDAC	-	Only antibody	β1 integrin	Targeting β1 integrin	AIIB2, mAb13	2022 [83]
0.0682 Gy/s (in vitro), 0.0167 Gy/s (in vivo)	leading to cell cycle arrest and cytotoxicity	In Vivo/In Vitro	A549, H1299/ Athymic nude mice	Lung	cytotoxic drug, DAR = 4.25	MMAE	TIP1	Targeting TIP1 for binding, endocytosis	7H5	2021 [73]
10 Gy	↓tumor hypoxia and ↑ DNA damage	In Vivo	LLC/ C57BL/6 mice	lung	Bacteria accumulate in hypoxic regions, antibody binds, radiation destroys	Bifidobacterium infantis	*Bifidobacterium infantis*	targeting B. infantis	Specific monoclonal antibody for B. infantis	2021 [84]
γ-rays: 0-10 Gy	↓hypoxia	In Vivo/In Vitro	HeLa, DU145, U2OS, HEK293TN/ BALB/c nu/nu	Cervical adenocarcinoma, Prostate adenocarcinoma, Osteosarcoma	-	Only antibody	SPINK1	neutralizing SPINK1	Anti-SPINK1	2021 [68]

0-6 Gy	Cell cycle arrest in G2/M phase	In Vitro	HCC1954, ZR-75-1, MDA-MB-453, BT474, SKBr3, MDA-MB-231	Breast	T-DM1 (trastuzumab conjugated with DM1	T-DM1	HER2	targeting HER-2 and drug delivery	Trastuzumab	2021 [85]
0-12 Gy	GSH depletion; Fenton reaction; ROS generation (hydroxyl radicals)	In vitro/ in vivo	HeLa P3 cells	Cervical cancer	catalytic property	$Fe_4Se_2W_{18}$ NCs	PD-L1	Targeting PD-L1	Anti-PD-L1	2021 [86]
2-2.5 Gy	blocking cells in G2–M phase	In Vivo/In Vitro	HCT116 NCI-N87 OE19/ athymic nu/nu mice	Esophageal, Colorectal and Gastric cancer	conjugated to anti-HER2 antibodies via cleavable linker	MMAF/MMAE	HER2	targeting HER2 and delivering MMAF or MMAE	Trastuzumab, Pertuzumab	2020 [87]
Energy: 6 MV, Dose: 0-8 Gy	inhibiting the **MAPK** and **AKT** signaling pathways**, ↑DNA damage** and **ICD**	In Vivo/In Vitro	**A431, CaSki**	cervical epi dermoid carcinoma	-	**Cisplatin**	**EGFR** and **HER3**	dual-targeting **EGFR** and **HER3**	MEHD7945A	2020 [88]
0-4 Gy	inhibition of DNA damage response	In Vivo/In Vitro	CAL27, A549, PANC1, HCT116, LN229/ athymic nu/nu mice	HNSCC, lung, pancreatic, colorectal, glioma	a **DNA damage checkpoint kinase inhibitor**	AZD7762	EGFR	targeting EGFR and delivering drugs	Cetuximab	2020 [89]

Proton irradiation**: 1.3 MeV,** 2 Gy/min	↑accumulation and cell killing	In Vitro	A431, MDA-MB-453	Carcinoma, breast	Diameter: 4-5 n.m	GNPs	EGFR	targeting of EGFR and delivery GNPs	cetuximab	2019 [90]
3 Gy (in vitro), 5 Gy (in vivo)	↑cytotoxicity through ROS generation	In Vivo/In Vitro	SK-OV3/nude mice	ovarian cancer	Diameter: 15 n.m	AuNP-PEG-HER2ab	HER2	targeting HER2; facilitates endocytosis	Anti-HER2	2019 [91]
Total 25 Gy	Ab wasn't effective	In Vivo	p53FRT/FRT mice	**STS**	-	Only Ab	PDGFRα	Targeting PDGFRα	1E10Fc	2019 [92]
0-6 Gy	mTOR and KEAP1 inhibition	In Vitro	UTSCC14, UTSCC15, UTSCC45 and SAS	HNSCC	-	mTOR Inhibitors, KEAP1 Inhibitors	EGFR, β1 Integrin	Targeting EGFR, β1 Integrin	Cetuximab, AIIB2	2018 [93]
High RT doses (12 Gy, 5×3 Gy, 20 Gy) and low RT doses (6 Gy, 5×2 Gy)	PD-L1 blockade enhances T-cell activation and reduces myeloid cell infiltration	In Vivo	KPC, Pan02/ C57BL/6 mice	PDAC	A chemotherapeutic agent	gemcitabine	PD-L1	↑T-cell activation and reducing myeloid cells	Anti-PD-L1	2017 [94]

0-3 Gy (10 Gy total)	Suppression of PI3K/Akt/mTOR signaling; ↑apoptosis	In Vivo/In Vitro	D54, U251, A549, H460/ Athymic nude mice	NSCLC, GBM	-	Only Ab	GRP78	Targets and Inhibits GRP78 activity	anti-GRP78	2017 [95]
Energy: 200-kV, Dose: 1.3 Gy/min	↑DSBs via NHEJ pathway	In Vivo/In Vitro	UTSCC15 and Cal33/ (nu/nu) mice	HNSCC	PARP inhibitor	Olaparib	β1 integrin	blocking β1 integrin	AIIB2	2016 [96]
Gy6-0	↑G2/M arrest and DNA double-strand breaks	In Vivo/In Vitro	CAL-27, SCC-25, SCC-35, SCC-61, SQ-9G, A549, CALU3, HCT-116, NCI N87, LN229, BT474, and OE19/ athymic nude mice	Human HNC, NSCLC, Colorectal, Gastric, Glioma, Breast, Esophageal Cancer	Anti-tubulin drugs (auristatins, maytansinoids)	T-DM1	ErbB receptors (specifically HER2)	target tumor cells expressing ErbB receptors, directing the radiosensitizer	anti-ErbB	2016 [97]
200 kV X-Ray unit at 100 cGy/minute	ADAM17 shedding of survival factors; ErbB pathway activation	In Vivo/In Vitro	A549, NCI-H125, H460, Calu-3, Calu-6, A431/ athymic nude mice	NSCLC, epidermoid carcinoma	Radiation causes activation of ADAM17 via furin-mediated cleavage	Only antibody	ADAM17; ErbB signaling	targeting EGFR	Cetuximab	2016 [98]
Total dose 30 Gy	Activation of T cells by checkpoint inhibition	In Vivo	Oral cavity squamous cell carcinoma/	oral	-	Only Ab	PD-1	Facilitates immune checkpoint blockade	Pembrolizumab	2016 [71]

			human case study							
Energy: 6 MV, dose: 1.4 Gy per minute	**↑apoptosis, angiogenesis inhibition,** and **↓DNA repair**	In Vivo	A431/ nude mice	HNSCC	Diameter: 30 n.m	GNPs	EGFR	targeting EGFR and delivering NPs	Cetuximab	2016 [99]
Energy:12 5 kV, Dose: 0-8 Gy	inducing apoptosis and blocking pro-survival signaling	In Vivo/In Vitro	FaDu, CAL27, RPMI2650, SCC4, SCC15, SQ20B/ Foxn1nu mice	HNSCC	a SMAC-mimetic drug	Debio 1143	TNF-a	Blocking TNF-a for finding the role of Debio 1143	TNF-a-blocking antibody	2015 [100]
Energy: 200 kV, Dose: 1.2 Gy/min	G1 arrest	In Vivo/In Vitro	A549, H460, H1299, H3122/ nude mice	NSCLC	EGFR blocking: Erlotinib**,** BIBX1382BS/ siRNA: knockdown p21	Erlotinib**,** BIBX1382 BS, siRNA	EGFR	Targeting EGFR	Cetuximab	2015 [101]
10 Gy	↑DSBs and ROS	In Vivo/In Vitro	U87MGEGFRvIII/ nude mice	GBM	Simultaneously detection by MRI and targeted therapy	IONPs	EGFRvIII	targeted and therapeutic delivery	Cetuximab	2015 [102]
0-6 Gy	↑Cytotoxicity, blocking the survival signals	In Vivo/In Vitro	UTSCC45, UTSCC15, UTSCC14, UTSCC8,	HNSCC	-	Only antibody	β1 integrin and EGFR	Targeting β1 integrin and EGFR	AIIB2 and cetuximab	2015 [69]

	mediated by FAK and Erk1		UTSCC5, SAS, Cal33, FaDu, HSC4, XF354/ nu/nu mice							
6 MV, 45 Gy in 25 fractions	EGFR inhibition and plasma ligand modulation (e.g., TGF-α, EGF)	In Vivo (clinical trial)	KRAS wild-type	LARC	-	Only Ab	EGFR	Blocks EGFR signaling	Panitumumab	2015 [70]
6 Gy	inhibiting the c-MET-PI3K-AKT pathway and ↑ apoptosis		A973	lung	Inhibition of c-MET-PI3K-AKT pathway	erlotinib	c-MET-PI3K-AKT pathway	Blockade of c-MET activity	anti-c-MET	2014 [103]
200 kV X-rays, 1.2 Gy/min	Cetuximab had no effect; Olaparib alone and combined enhanced radiosensitivity via ↓ DNA repair	In Vitro	93-VU-147T, UM-SCC-47, UTSCC-45, UD-SCC-2, and UPCI-SCC-154, F180 & F184	HPV-positive HNSCC	Olaparib (PARP inhibitor) PF-00477736 (Chk1 inhibitor)	Compare Ab with: Olaparib + PF-00477736	EGFR	Targeting EGFR	cetuximab	2014 [104]

Ab: Antibody, **DAR:** Drug-to-Antibody Ratio, **TMZ**: temozolomide, **GNPs:** gold nanoparticles, **BBB**: Blood–Brain Barrier, **GBM:** glioblastoma, **DSBs**: DNA double-strand breaks, **ROS:** reactive oxygen species, **IONPs:** iron oxide nanoparticles, **MRI:** magnetic resonance imaging, **SPINK1**: Serine Protease Inhibitor Kazal type I, **MMAE:** monomethyl auristatin E, **HER3**: Human Epidermal Growth Factor Receptor 3, **MMAF**: monomethyl auristatin F, **NSCLC**: Non–small cell lung cancer, **ADAM17:** A Disintegrin and Metalloprotease 17, **HNSCC:** head and neck squamous cell carcinomas, **PDAC:** Pancreatic ductal adenocarcinoma, **MIBC:** muscle-invasive bladder cancer, **LARC**: Locally Advanced Rectal Cancer, **PDAC**: Pancreatic Ductal

Adenocarcinoma, **GRP78:** glucose regulated protein 78, **SPIOs**: Superparamagnetic iron oxide nanoparticles, **TAMs:** tumor-associated macrophages, **PSMA:** Prostate-Specific Membrane Antigen, **ICD: immunogenic cell death, TME:** tumor microenvironment**, NCs:** nanoclusters, **STS:** Soft Tissue Sarcoma**, NHEJ:** Non-Homologous End Joining**.**