

Supplementary Table 1. Therapeutic Agents Targeting NETs in Cancer

Target molecules	Agents	Mechanism/Results	Cancers	References
PAD4 inhibitors				
PAD4	Chloroquine	Reduce NET formation through inhibiting TLR9 and PAD4 inhibitory.	Pancreatic cancer	1
PAD4	ZD-E-1	Inhibited tumor growth and metastasis by reduce PAD4 activity and NETs formation.	Lung cancer, Breast cancer	2
PAD4	BB-Cl-amidine	Decreased NF-κB activation and tumor metastasis.	Breast cancer	3
PAD4	GSK484	As immunotherapeutic synergy to inhibit NET-mediated barrier protection.	Breast cancer	4
PAD4	GSK484	Inhibit tumor metastasis by deplete NETs.	Hepatocellular carcinoma	5
DNA inhibitors				
DNA	DNase1	Inhibit NET formation and decrease tumor growth.	Nonalcoholic steatohepatitis to hepatocellular carcinoma	6
DNA	DNase 1	Disrupt NET-driven tumor cell capture and metastasis.	Colorectal cancer	7
DNA	DNase + PD-1	Reversal of anti-PD-1 blockade resistance through	Colorectal cancer	8

			increasing cytotoxicity.		
DNA	AAV-DNase I		Inhibite neutrophil infiltration and NET formation	Colorectal cancer	9
DNA	DNase I		Reduce lung metastases.	Breast cancer	10
DNA	DNase I		Improve overall radiation response via inhibiting NETs formation.	Bladder cancer	11
Chemokines					
IL-8、CXCL2	IL-8 antibody、CXCR2 antibody		Promote Diffuse Large B-cell Lymphoma Progression via blocking IL8-CXCR2 axis.	Diffuse large B-cell lymphoma	12
IL-8	IL-8 antibody		Regulate the HMGB1/RAGE/IL-8 axis via neutralizing IL-8.	Glioma	13
CXCR1/2	Reparixin		As CXCR1/2 inhibitor to inhibite NET-mediated barrier protection.	Breast cancer	4
IL-17	IL17/IL17R antibodies		Increase immune checkpoint blockade sensitivity via IL17/IL17R neutralization.	Pancreatic cancer	14
TCM					
ROS	Danshen(Sal B and DHT I)		Inhibite NETs formation via blocking the activity of MPO and NADPH.	Gastric cancer	15
Related to the deactivation of PAD4	Huang Decoction	Qin	Inhibits the initiation of colitis associated carcinogenesis by	Colorectal cancer	16

		decreasing NETs formation.		
NADPH/ROS-NETs signalling	Kaempferol	Decreased NET formation and tumour metastasis via suppressing ROS production.	Breast Cancer	17
Nanodrugs				
DNA	mP-NPs-DNase/P TX	Degrade NETS structure.	Non-small cell lung cancer and breast cancer	18
DNA	GODM-gel	Buffer tumor acidity and degrade NETs to enhance NK cell cytotoxic function.	Hepatocellular carcinoma	19
DNA	PLGA-PD-DNase 1	Inhibit tumor metastasis by degrading NETs structure.	Lung metastasis of breast cancer	10
DNA	PR@DNase I-PLGA@Gel	Wreck NETs and inhibit lung metastasis	Lung cancer	20
DNA	PAAP/DNase 1	Induce tumor-cell apoptosis and decompose NETS-DNA to prevent NETs-induced tumor metastasis to the liver.	Liver metastasis in CT26 colon cancer and 4TI breast cancer	21
DNA	DNase 1+AuPB/mPDA shell	Degrade NETs to expose tumors to immune cells and prevent circulating tumor cells capture.	Colorectal cancer	7

NETosis	ZD-E-I	Reduce the growth and metastasis of tumors by Inhibiting histone-3 citrullination and NETs.	Solid tumorst	2
NETosis	LA/DOX NPS	Inhibit NETs generation by blocking the NF-kB signaling pathway and P-SEL.	Breast cancer	22

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