

Supplement Table S1. List of anticancer foods with the bioactive molecules, mechanism of action and function endpoints.

Food	Functional Molecules	Targets and Mechanism of Action	Level of Evidence	Functional Endpoints	References
Edible Mushroom	B-glucans	TLRs0Myd88-NFκB-TNFα/IL6/IL12	Clinical, <i>in vitro</i> , and <i>in vivo</i> studies	Prime innate & adaptive immune cells	[S1 – S5, S57]
		Dectin-Syk-NLRP3-IL1β*to	Clinical, <i>in vitro</i> , and <i>in vivo</i> studies	Reduce immunosuppressive cells	[S6]
		MDSCs, M2 Macrophage*to			
	Conjugated Linoleic acid	Inhibitor aromatase, 5α-reductase and androgen receptor*‡	<i>In vitro</i> and <i>in vivo</i> studies	Inhibit E2/DHT formation Inhibit AR/PSA production	[S4, S5]
	Phytosterols (Tocopherols)	Inhibit tyrosinase*	<i>In vitro</i> studies	Suppress cell growth	[S4, S5]
	Ergosterol	Signaling molecules from Fox03: ± Fas, FasL, BimL & SimS*	<i>In vitro</i> studies	Inhibit cell growth	[S2, S4, S7]
	Flavonoids (myricetin, catechin)	Potent immune stimulants Protect against free radical damage*	<i>In vitro</i> studies	Promote immune response, disrupt redox homeostasis	[S2, S4, S56]
Broccoli	Food Extract	Suppress prostaglandin E2, Ki67, DNA topoisomerase 2α*‡	<i>In vitro</i> and <i>in vivo</i> studies	Inhibit cell growth	[S8, S9]
		± Nfr2 transcriptional pathway*	<i>In vitro</i> studies	Eliminate redox reaction	[S29, S30]
	Flavonoid (Kaempferol)	Inhibit NF-κB pathway*	<i>In vitro</i> studies	Decrease inflammation and redox activities	[S29, S30]
		Activates mitogen-activated protein kinase (MAPK) signaling pathway*	<i>In vitro</i> studies	Inhibit cell growth	[S29, S30]
		↓ VEGF expression/ ∓HIF-1α* G2/M phase cell cycle arrest* ∓ epithelial-mesenchymal transition (EMT)-related markers* ∓ PI3K/protein kinase B signaling pathways* ∓ ER signaling pathway*	<i>In vitro</i> studies	Obstruct redox activities	[S29, S30]
		AITC-SiQDs, nanoscale system, disrupt ROS homeostasis*	<i>In vitro</i> studies	Obstruct redox activities	[S29, S30]
	Allyl isothiocyanate	Activate Nrf2 to	Clinical trial and <i>in vivo</i> studies	Eliminate redox reaction	[S31]
	Sulforaphane	Target DNA methyltransferases (DNMTs), histone deacetyltransferases (HDACs) & noncoding RNAs*	<i>In vitro</i> studies	Epigenetics, cell cycle arrest	[S32]
	Glutathione	± antioxidant genes, such as Gclc, Gclm, heme oxygenase-1 (Hmox1), and NADPH quinone oxidoreductase-1 (Nqo1)*	<i>In vitro</i> studies	Disrupt redox homeostasis resulting in higher immune activities	[S33, S34]
	Allyl isothiocyanate nanoparticles	Inhibit TNF-α, IL-6, NO & iNOS production*	<i>In vitro</i> studies	cell growth inhibition, anti-inflammation, and redox activity suppression	[S35]
Garlic	Amino acids (Alliin, Allicin)	G2/M arrest* ± Bax & FasL expressions ‡ ± caspase-3, -8, & -9*	<i>In vivo</i> and <i>in vitro</i> studies	Inhibit cell growth	[S25, S26]
	Diallyl trisulfide (DATS)	↓ G1, M, & S phases *‡ ↑ Caspase-3 activity *‡ Sustain cyclin B1 expression *‡ Inhibit spindle formation *‡	<i>In vivo</i> and <i>in vitro</i> studies	Inhibit cell growth	[S27]
	Saponins	Inhibit intracellular ROS* ↓ γH2AX, prevent H2O2-induced DNA damage* ↑ antioxidant enzyme heme oxygenase-1 (HO-1)* Activate Nrf2/HO-1 pathway*	<i>In vitro</i> studies	Eliminate redox activities	[S28]
	Flavonoid (Kaempferol)	± Nfr2 transcriptional pathway*	<i>In vitro</i> studies	Eliminate redox reaction	[S29, S30]
		Inhibit NF-κB pathway*	<i>In vitro</i> studies	Decrease inflammation and redox activities	[S29, S30]
		Activates mitogen-activated protein kinase (MAPK) signaling pathway* ↓ VEGF expression/ ∓HIF-1α*	<i>In vitro</i> studies	Inhibit cell growth	[S29, S30]

		G2/M phase cell cycle arrest* ⇐ epithelial-mesenchymal transition (EMT)-related markers* ⇐ PI3K/protein kinase B signaling pathways*			
Berries	Quercetin	⇐ cyclin B1 & CDK1* Inhibit topo II activity ‡ DNA damage via ROS generation*	<i>In vivo and in vitro studies</i>	Inhibit cell growth	[S49]
			<i>In vitro studies</i>	Low amounts inhibit cell cycle progression but not induce cell death	[S49]
	Anthocyanin	Activate caspase 3-pathways* ↓ cell proliferation* ↓ PI3K/AKT & NFκB activation & phosphorylation *‡ ↓ Ki-67 expression, ↑ caspase-3 expression/apoptosis ‡ ↓ AKT & p65 NF-κB signaling proteins ‡ ↑ anti-inflammatory cytokines in serum (MIG, IP-10, IL-12, IL-2, TNF-α)*	<i>In vivo and in vitro studies</i>	Inhibit cell growth	[S50 – S53]
	Food extract (Jamun, blueberry)	Inhibit cell growth/proliferation, ↑ apoptosis *‡	<i>In vivo and in vitro studies</i>	Inhibit cell growth	[S53, S55]
Pomegranate	Anthocyanidins (Delphinidin, Cyanidin, Pelargonidin)	DNA damage in cancer cells via ROS generation* ↓ VEGF*	<i>In vitro studies</i>	Oxidative stress and inflammation	[S10]
			<i>In vitro studies</i>	Inhibit cell growth	[S11]
	Polyphenol (Ellagitannin, Ellagic Acid)	↓ specificity protein (Sp) transcription factors & Sp-related genes *‡ ↓ miR-27a*‡, ⇐ miRNA0155*	<i>In vivo and in vitro studies</i>	Inhibit cell growth	[S12]
			<i>In vivo and in vitro studies</i>	Regulate gene expression	[S12]
		⇐ cyclin A, B1, ⊥ cyclin E*	<i>In vitro studies</i>	Inhibit cell cycle	[S11]
		Inhibit AKT activity, NF-κB activation, and COX-2 expression*	<i>In vitro studies</i>	Oxidative stress and inflammation	[S13]
	Metabolite (Urolithin A & B)	Reduces IL-6, IL-1β, NOS2*	<i>In vitro studies</i>	Disrupt redox homeostasis	[S11, S14, S15]
		Inhibit aromatase activity*	<i>In vitro studies</i>	Inhibit E2 formation	[S11, S14, S15]
Tomato	Flavonoid (kaempferol, quercetin, naringenin)	Induce autophagy*	<i>In vitro studies</i>	Inhibit cell growth	[S17, S36]
	Carotenoid (Lycopene, Phytoene, Phytofluene, α- and β-carotene, βcryptoxanthin, Lutein, Zeaxanthin)	Activate antioxidant enzymes (glutathione, glutathione peroxidase, & glutathione-S-transferase) ‡ (Epre/ARE) activation* Inhibit ERK phosphorylation* Androgen receptor inhibition*	<i>In vivo and in vitro studies</i>	Disrupt redox homeostasis	[S36 – S39]
			<i>In vitro studies</i>	Inhibit cell growth	[S36 – S39]
			<i>In vitro studies</i>	Inhibit AR activity	[S36 – S39]
Walnut	Polyphenol (Ellagitannin)	↓ cyclin B1 protein*	<i>In vitro studies</i>	Inhibit cell growth	[S40]
	Vitamins (Tocopherol, Niacin)	⊥ PPAR activity*	<i>In vitro studies</i>	Inhibit cell growth	[S41]
	Flavonoid (quercetin, catechin)	Induce autophagy*	<i>In vitro studies</i>	Inhibit cell growth	[S17]
	Phytosterol (stigmasterol, campsterol, sitosterol)	Activate ER-mitochondrial axis to induce cell death* ⇐ TNF-α & VEGFR-2*	<i>In vitro studies</i>	Inhibit cell growth	[S42, S43]
	Juglone	Enhance the level of Fox03a & Fox01 in cells* Induce G2/M phase cell cycle arrest* Activate JNK pathway & ROS-mediated p38 to initiate autophagy*	<i>In vitro studies</i>	Disrupt the DNA replication and cell cycle division	[S44]
			<i>In vitro studies</i>	Inhibit cell growth	[S44]
	Metabolites (Urolithins-A, -C, & IsoUro-A)	⇐ mRNA & protein level in PSA & AR*	<i>In vitro studies</i>	Reduce PSA & AR activities	[S45]

		↓ Bcl-2 protein levels*	<i>In vitro</i> studies	Inhibit cell growth, induce apoptosis	[S45]
Ginger	Paradol	↓ EGFR protein expression* Inactivate PI3K/AKT signaling*	<i>In vitro</i> studies	Inhibit cell growth	[S46, S47]
	Zingiberene	Damage microtubules*	<i>In vitro</i> studies	Inhibit cell growth	[S46]
	1-monolinolein	⊣ NF-κB activation* ↑ caspase-3/7 activation for apoptosis*	<i>In vitro</i> studies	Inhibit cell growth	[S45, S48]

Note: ‡ in animal model; * in cell line; o clinical trial; ↑ increase; ↓ decrease; ⊣ down-regulate; ⊕ up-regulate.

Comment: The biological activities being studied are mainly from *in vitro* models and that no references to animal models have shown to reduce the growth of xenografted tumors or PDX grafts, but the targets and mechanism of action are sometimes both observed and corresponded to each other in both *in vitro* and *in vivo* studies. Although clinical trials do not specify that the botanical foods are proven to have anti-cancer activities, some trials have shown that patients receiving botanical foods and/or botanical food agents along with chemotherapy have prolonged the cancer patient's survival (e.g., references S1 & S57). Many clinical trials could not conclude that botanical foods do reduce tumor growth, as they claim a larger sample size is needed for a higher level of evidence.

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