

Potential impact of diet, nutrition, physical activity and height in increasing susceptibility to cancer

Exposure	Systemic impact	Cell function	Hallmarks possibly affected
Greater body fatness	Hyperinsulinemia	mTOR/PI3K/AKT, MAPK	Reduced apoptosis; increased proliferation; genome instability
	Increased oestradiol	MAPK/ERK/PI3K	Increased proliferation in ER-positive tissues; genome instability
	Inflammation	STAT3/NF-κB	Reduced apoptosis; increased cell division; altered macrophage function; genome instability
		WNT, P53	Cellular energetics
Greater height	Higher IGF-I	mTOR/PI3K/AKT, MAPK	Reduced apoptosis; increased proliferation
Greater physical activity	Reduction in insulin	mTOR/PI3K/AKT, MAPK	Increased apoptosis; reduced proliferation; less genome instability
	Reduction in oestradiol and testosterone	MAPK/ERK/PI3K	Reduced proliferation in ER-positive tissues; reduced genome instability
	Reduced inflammation (long term); improved immune function	STAT3/NF-κB	Increased apoptosis; increased cell division; altered macrophage function; reduced genome instability
		WNT, P53	Cellular energetics
Greater intake of red and processed meat	Elevated exposure to nitrites; endogenous N-nitroso compound formation	DNA adduct formation -> mutations in p53, KRAS	Reduced apoptosis; increased proliferation; genomic instability
		Oxidative stress, inflammation	Increased inflammation; genomic instability
Greater intake of dairy foods	Higher IGF-I	mTOR/PI3K/AKT, MAPK	Reduced apoptosis; increased proliferation
Lower vegetables and fruit intake	Folate deficiency	DNA uracil misincorporation	Genome instability
	Low dietary fibre intake	Low butyrate	Reduced apoptosis; increased proliferation
	Low levels of carotenoids, vitamins A, C, E	Oxidative stress, inflammation	Increased inflammation; genomic instability; reduced apoptosis; increased proliferation
Greater alcohol intake	Elevated acetaldehyde	Oxidative stress, lipid peroxidation	Increased inflammation; genomic instability
	Increased oestradiol	MAPK/ERK/PI3K	Increased proliferation in ER-positive tissues
	Inflammation	STAT3/NF-κB	Reduced apoptosis; increased cell division; altered macrophage function
	Folate deficiency; interference with 1-carbon metabolism	DNA uracil misincorporation	Genome instability

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Abbreviations: AKT, also known as protein kinase B; DNA, deoxyribonucleic acid; ER+, oestrogen receptor positive; ERK, extracellular signal-regulated kinases; IGF-I, insulin-like growth factor 1; KRAS, please see glossary; MAPK, mitogen-activated protein kinase; mTOR, mechanistic/mammalian target of rapamycin; NF-κB, nuclear factor kappa-light-chain-enhancer of activated B cells; P53, tumour protein p53; PI3K, phosphoinositide 3-kinase; STAT3, signal transducer and activator of transcription 3; WNT, Wingless-related integration site.