

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

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