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International Agency for Research on Cancer

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Table S4.21 Alterations in cell proliferation, cell death, or nutrient supply in human immortalized cells exposed to cobalt

End-point	Tissue, cell line	Results[a]	Concentration (LEC or HIC)	Comments	Reference
Angiogenesis					
VEGF levels	Choroidal vascular endothelial cell line RF/6A	+	200 µM for 24 h		Balaiya et al. (2013)
VEGF levels, through its promoter activation	Human microvascular endothelial cell line HMEC-1	+	250 µM for 24 h		Loboda et al. (2005)
VEGF levels	Human Müller cell line MIO-M1	+	100 µM for 48 h	Statistical analysis was not performed.	Sears & Hoppe (2005)
VEGF expression	Osteoblast-like cell line Saos-2	+	75 µM for 4 h	Statistical analysis was not performed.	Kim et al. (2002)
VEGF expression	Human retinal pigment epithelial cell line ARPE-19	+	200 µM for 6–24 h		Oh et al. (2013)
VEGF expression	Human retinal pigment epithelial cell line ARPE-19	+	300 µM for 24 h	Non-cytotoxic concentration.	Zheng et al. (2016)
VEGF expression	Human retinal pigment epithelial cell line ARPE-19	+	200 µM for 24 h	Non-cytotoxic concentration.	Park et al. (2015)
VEGF expression	Human retinal pigment epithelial cell line ARPE-19	+	100 µM for 12 h	Non-cytotoxic concentration.	Alzhrani et al. (2017)
VEGF expression	Human retinal pigment epithelial cell line ARPE-19	(+)	150 µM	Results presented in equivocal way in figure. Increase in VEGF expression could be due to co-exposure to low glucose. Absence of $CoCl_2$-only treated cells.	Chen et al. (2017b)
VEGF expression	Human retinal pigment epithelial cell line ARPE-19	+	200 µM for 6–18 h	Non-cytotoxic concentration.	Wang et al. (2016b)
VEGFC and VEGFR-3 expression	Human retinal pigment epithelial cell line CRL-2302	+	200 µM for 48 h		Zhao et al. (2015b)
Induces nuclear HMGB1, decreases SIRT1 expression HMGB1 nucleocytoplasmic relocation and extracellular release	Human retinal pigment epithelial cell line ARPE-19	+ +	100 µM for 6 h	HMGB1 is pro-angiogenic factor.	Chang et al. (2017)
VEGF expression and tube formation	Human retinal vascular endothelial cells (HRVECs)	+	150 µM for 24 h		Li et al. (2022)
VEGF expression	Human cervical cancer-derived cell line ME-180	+	100 µM for 20 h	$CoSO_4·7H_2O$; Sigma, USA; 99% purity) was also tested.	Xia et al. (2009)

Table S4.21 (continued)

End-point	Tissue, cell line	Results[a]	Concentration (LEC or HIC)	Comments	Reference
VEGF expression	Human endometrial cancer cell line ECC-1	+	100 µM for 2 h		Molitoris et al. (2009)
VEGF expression	Human cervical cancer cell line HeLa	+	100 µM	Statistical analysis was not performed.	Wang et al. (2013a)
VEGF expression	Human cervical cancer cell line HeLa	+	200 µM for 4 h	$CoCl_2$ increased translation of VEGFA mRNA dependent on HuR (mass spectrometry).	Osera et al. (2015)
VEGF expression	Human colon adenocarcinoma cell line HCT 116	+	100 µM for 24 h		Law et al. (2012)
VEGF expression	Human mesothelioma cell line H2452	+	50 and 75 µM for 24 h	Non-toxic concentration. Effects of $CoCl_2$ on HIF-2α/VEGF pathway is dependent on activation of Yes, a member of the Src family of kinases.	Sato et al. (2014)
VEGF expression	Pancreatic cancer cell line PANC-1, lung cancer cell line A549, and cervical cancer cell line HeLa	+	100 µM for 8 h	Statistical analysis was not performed.	Dai et al. (2008)
VEGF expression	Pancreatic cancer cell line PANC-1	+	100 µM for 24 h	Non-cytotoxic concentration.	Wen et al. (2016)
VEGF expression	Pancreatic cancer cell line PANC-1 and prostate carcinoma cell line PC-3	+	100 µM	Effect dependent on p-STAT activation, that binds VEGF promoter.	Gray et al. (2005)
VEGF expression	Prostate carcinoma cell line DU145	+	100 µM for 12 h	Effect dependent on AMPK.	Lee et al. (2006)
VEGF expression	Neuroblastoma cell lines BE(2)-C and SK-N-AS	+	100 µM		Rellinger et al. (2015)
VEGF expression	Melanoma cells, hepatic carcinoma cell line Hep-G2, and cervical cancer cell line HeLa	+	100 µM for 18 h	Statistical analysis was not performed.	Minchenko et al. (1994b)
VEGF expression	Human hepatoma cell lines SMMC 7721 and MHCC 97H	+	200 µM for 48 h	Non-cytotoxic concentration.	Xu et al. (2014)
VEGF expression through VEGF promoter activation	Human oral squamous cell carcinoma cell line SCC-9	+	100 µM for 24 h		Slomiany et al. (2006)
VEGF expression Decreased collagen XVIII and CBP2/Hsp47	Human oral squamous cell carcinoma cell line SCC-9	+ +	100 µM for 24 h	Effect dependent on PI3K signalling pathway. Statistical analysis was not performed.	Stewart et al. (2003)
Secretion of endocan (endothelial cell-specific molecule-1), a proangiogenic factor	Human glioblastoma cell line U-118 MG	+	100–200 µM for 24 h	Statistical analysis was not performed.	Maurage et al. (2009)

Table S4.21 (continued)

End-point	Tissue, cell line	Results[a]	Concentration (LEC or HIC)	Comments	Reference
Glycolysis					
GLUT1 and hexokinase II expression	Human cervical cancer cell lines HeLa and SiHa	+	150 μM		Cheng et al. (2013)
GLUT1 expression	Breast cancer cell lines derived from primary (HCC1395 and HCC1937) and metastatic sites (MCF7 and MDA-MB-231)	+	150 μM for 24 h		Chen et al. (2010a)
GLUT-1 and BCRP/ABCG2 expression	Human renal proximal tubular cell line HK-2	+	300 μM for 48 h		Nishihashi et al. (2017)
Cell proliferation					
Cell number	Human retinal endothelial cells HRECs	+	150 μM for 48 h		Wang et al. (2014)
Cell viability	Human retinal vascular endothelial cells HRVECs	(+)	150 μM for 24 h	Cell viability as an indirect measure of cell proliferation.	Li et al. (2022)
Cell viability	Human retinal pigment epithelial cell line ARPE-19	+	50–200 μM for 6–24 h	Cell viability as an indirect measure of cell proliferation.	Wang et al. (2016b)
Cell number	Pulmonary artery smooth muscle cells PASMCs	+	25–100 μM for 18–30h	Effect dependent on PGI2 downregulation and H_2S levels.	Li et al. (2014)
Cell number Increased ERK-MAPK signalling transduction pathway	Human gastric adenocarcinoma cell line (SGC-7901)	+	100 μM for 24 h		Bi et al. (2010)
Cell viability	Human gastric cell line (BGC-823)	(+)	100 μM for 24 h	Statistical analysis was not available for $CoCl_2$ effects on increased cell viability, as the focus was on diosgenin and/or HIF-1α statistically significant decreases in $CoCl_2$-induced cell viability. Cell viability as an indirect measure of cell proliferation.	Mao et al. (2012)
SP cells in cancer cells but not in normal cells	Cancer stem cells from papillary thyroid cancer-derived cell line BCPAP and anaplastic thyroid cancer-derived cell line SW1736 as SP cells (a putative stem cell population	(+)	100 μM for 48 h	$CoCl_2 \cdot 6H_20$. Although there was a 400% increase for BCPAP and of 120% for SW1736 SP cells, these changes were not significant using a two-sided *t*-test.	Mahkamova et al. (2018)
Cell viability and colony formation	Human cervical cancer cell lines HeLa and SiHa	+	150 μM for 24–72 h	Statistical analysis was not performed.	Cheng et al. (2013)

Table S4.21 (continued)

End-point	Tissue, cell line	Results[a]	Concentration (LEC or HIC)	Comments	Reference
Cell number	Human pancreatic cancer cells MIA PaCa-2	+	40–80 µM for 24 h		Chen et al. (2018a)
Cell number in 786-O cells, but not in A498 cells	Renal cell carcinoma cell lines A498 and 786-O	+	50–200 µM	Concentration higher than 250 µM decreased cell viability in both cell lines.	Zhang et al. (2017)
Decreased p53 expression mediated by its promoter repression, possibly through HIF-1α	Human cervical cancer cell line HeLa	+	1–100 µM for 16 h	Statistical analysis was not performed	Lee et al. (2001)
Decreased cell viability	Human colorectal cancer cell line LOVO	(–)	100–250 µM for 7 d	Cell viability as an indirect measure of cell proliferation.	Yang et al. (2016)
Decreased cell viability	MCF10A cells used as a normal non-malignant breast cell line pII (ER–), EII (ER+), and YS1.2 (ER+) derived from MCF7 (ER+) human breast cancer cell line	(–)	100 µM for 24 h	Cell viability as an indirect measure of cell proliferation.	Barrak et al. (2020)
Decreased cell viability	Human fetal mesencephalic neural progenitor cells	No changes	10 µM	Cell viability as an indirect measure of cell proliferation.	Milosevic et al. (2009)
Decreased cell number	Hodgkin lymphoma cell line (L-428)	No changes	200 µM for 48 h	Statistical analysis was not performed.	Kewitz et al. (2016)
Cell number	Ovarian serous carcinoma OVCAR3 and clear cell carcinoma ES2 cell lines	No changes	100 µM for 48 h	Statistical analysis was not performed.	Nunes et al. (2018)
Cell death					
Apoptosis	Human hepatoma SMMC 7721 and MHCC 97H cell lines	No changes	200 µM	Statistical analysis was not performed.	Xu et al. (2014)
Increased apoptosis	Human cervical cancer cell lines Hela and SiHa		150 µM	Statistical analysis was not performed.	Cheng et al. (2013)

ABCG2, ATP-binding cassette subfamily G member 2; AMPK, 5′AMP-activated protein kinase; BRCP, breast cancer resistance protein; CBP2, cytochrome B pre-mRNA-processing protein 2; ER, estrogen receptor; ERK, extracellular signal-regulated kinase 1/2; GLUT1, glucose transporter 1; HIF-1/2α, hypoxia-inducible factor-1/2 alpha; HMGB1, nuclear high mobility group box 1; H_2S, hydrogen sulfide; Hsp47, heat shock protein 47; HuR, human antigen R; MAPK, mitogen-activated protein kinase; mRNA, messenger RNA; PGI2, prostaglandin I2; PI3K, phosphoinositide 3-kinase; p-STAT, phosphorylated signal transducer and activator of transcription; SIRT1, sirtuin 1; SP, side population; VEGF, vascular endothelial growth factor; VEGFA, vascular endothelial growth factor A; VEGFR-3, vascular endothelial growth factor receptor-3.

[a] +, positive; –, negative; (+) or (–), positive or negative in a study of limited quality.

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