CHEMICAL CARCINOGENESIS - REACTIVE OXYGEN SPECIES

Metals (Lead: IARC Group 2B) (Lead compounds, inorganic: IARC Group 2A) (Lead compounds, organic: IARC Group 3)

Halogen compounds (IARC Group 2A) p,p'-DDT

(Iron and steel founding: IARC Group 1) Fe(III)

(Nickel compounds: IARC Group 1) Ni(III)

Metals (IARC Group 1) As(V) — GSH, GSSG, AS3MT, GSTO1, MMA(III), MMA(V), SAM, SAH, DMA(V), DMA(III), (Fenton-type reaction)

(IARC Group 1) Cd

(IARC Group 2B) Co(I) — Co(I), Co(II), Co(III), (Fenton-type reaction)

(IARC Group 1) Cr(VI) — SLC26A2, GSH, GS•, Cr(VI), Cr(V), Cr(IV), Cr(III), (Fenton-type reaction)

Mitochondria: Mitochondrial dysfunction, Oxidative Phosphorylation, Cx I, Cx II, Cx III, Cx IV, Cx V, MnSOD, MPTP

Antioxidant defense system: SOD1, GPX1, GST

Reactive oxygen species (ROS) — Damage to bio-macromolecules, Gene mutations, Altered gene expression, Activation of oncogenic pathways

Non-small cell lung cancer; Small cell lung cancer; Prostate cancer; Renal cell carcinoma; Hepatocellular carcinoma

Aromatic amines/amides: (IARC Group 1) 4-Aminobiphenyl — CYP1A2 — N-Hydroxy-4-aminobiphenyl — Hydronitroxide radical — 4-nitrosobiphenyl — Bladder cancer

Aromatic hydrocarbons: (IARC Group 1) Pentachlorophenol — CYP1A2 — Tetrachlorohydroquinone — Tetrachloro-1,4-semiquinone — Tetrachloro-1,4-benzoquinone — Non-Hodgkin lymphoma, Multiple myeloma, Soft tissue sarcoma

(IARC Group 1) Benzene — CYP2E1, CYP2F1 — Benzene oxide — Phenol — CYP2E1 — Hydroquinone — Benzosemiquinone — Benzoquinone — Acute myeloid leukemia; 1,2,4-Benzenetriol

Metabolism of xenobiotics by cytochrome P450

(IARC Group 1) Benzo[a]pyrene — CYP1A1, CYP1B1 — B[a]P-7,8-oxide — EH — B[a]P-7,8-diol — AKR — B[a]P-7,8-catechol — Semiquinone — Redox-cycling — B[a]P-7,8-dione — Skin cancer, Lung cancer, Gastric cancer

AhR; Chemical carcinogenesis - receptor activation

Dioxins: (IARC Group 1) TCDD — AhR

Estrogen analogues: (Estrogen therapy, postmenopausal: IARC Group 1) 17β-estradiol (E2) — CYP1B1, CYP1A1 — 2-OHE2, 4-OHE2 — LPO — E2-2,3-semiquinone, E2-3,4-semiquinone — E2-2,3-quinone, E2-3,4-quinone — Breast cancer

Alcohols: (IARC Group 1) Ethanol — CYP2E1 — Acetaldehyde — Hepatocellular carcinoma

Flame retardants: PBDE-47

NADPH oxidase (Nox4-based): Nox4, p22phox

(Nox1-based): Nox1, p47phox, p22phox, NOXO1, p67phox

NBP: (IARC Group 1) NNK, B[a]P; (IARC Group 2B) PhIP — Breast cancer

EGF, HGF, EGFR, MET, Grb2, Sos, Ras, Raf, MEK, ERK, MAPK signaling pathway, AP-1, DNA

PI3K, PIP3, PDK1, PTEN, PKB/AKT, PDK1, PI3K-Akt signaling pathway, FOXO, Bad, Cell survival

Rac1, Ask-1, MKK4/7, JNK, p38, NF-κ B signaling pathway, IKK, IκBα, NFκB, Inflammatory response, Cancer proliferation, angiogenesis and metastasis

PKCδ, PTP, Src, Abl, PKD, FAK, PLD, NIK, HIF-1α, HIF-1 signaling pathway, HIF-1β, VEGF signaling pathway, VEGF, Angiogenesis, Cancer cell adhesion and migration

KEAP1, Nrf2, NQO1, AKR, HO-1 (Phase II detoxing enzymes & antioxidants)

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