TGx-DDI Biomarker Data for EMGS Bioinformatics Challenge

Li, HH. *et al*. (2015). **Development of a Toxicogenomics Signature for Genotoxicity Using a Dose-Optimization and Informatics Strategy in Human Cells.** *Environmental and Molecular Mutagenesis* 56: 505-519.

Study Compounds:

Compound	Genotoxic or Non-Genotoxic (DDI or non-DDI)	Concentration Selected for Gene Expression Analysis
Antimycin A	non-genotoxic	100 µM
Apicidin	non-genotoxic	1 µg/ml
Cytosine arabinoside (AraC)	genotoxic	50 µM
Bleomycin	genotoxic	10 µg/ml
Cadmium chloride	non-genotoxic	50 µM
Camptothecin	genotoxic	125 nM
Cisplatin	genotoxic	80 µM
Colchicine	non-genotoxic	250 ng/ml
2-Deoxy-D-glucose (2-DG)	non-genotoxic	20 µM
Docetaxel	non-genotoxic	50 nM
Ethanol	non-genotoxic	2%, 4%
Etoposide	genotoxic	200 nM
5-Fluorouracil (5-FU)	genotoxic	25 µg/ml
Gamma irradiation (γ ray)	genotoxic	4 Gy
HC Toxin	non-genotoxic	20 ng/ml
Heat shock	non-genotoxic	47°C for 20 min
Hydrogen peroxide (H_2O_2)	genotoxic	80 µM
Hydroxyurea	genotoxic	0.5 mM
Methotrexate	genotoxic	100 µM
Methyl methanesulphonate	genotoxic	100 µg/ml
Oxamflatin	non-genotoxic	1 µM
Paclitaxel	non-genotoxic	50 nM
Potassium chromate (VI)	genotoxic	100 µM
Sodium Arsenite	genotoxic	30 µM
Thapsigargin	non-genotoxic	250 nM
Trichostatin A (TSA)	non-genotoxic	20 ng/ml
Tunicamycin	non-genotoxic	2.5 µg/ml
Vinblastine	non-genotoxic	200 ng/ml

Time Point: 4 hr (no S9) for gene expression

GEO Accession Number: GSE58431

GEO Link: https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE58431

Link to Publication: https://www.ncbi.nlm.nih.gov/pubmed/25733355

Buick, J.K., *et al*. (2015). **Integration of Metabolic Activation With a Predictive Toxicogenomics Signature to Classify Genotoxic Versus Nongenotoxic Chemicals in Human TK6 Cells.** *Environmental and Molecular Mutagenesis* 56: 520-534.

Study Compounds:

Aflatoxin B1 – 0, 0.025, 0.075, 0.1 µM

Benzo[a]pyrene – 0, 0.45, 1.4, 10 µg/mL

Cisplatin – 0, 24 µg/mL

Dexamethasone – 0, 0.63, 1, 7.5 mM

Phenobarbital – 0, 1, 3.2, 10 mM

Time Points:

4 hr, 8 hr, 24 hr (with S9)

GEO Accession Number: GSE51175

GEO Link: https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE51175

Link to Publication: https://www.ncbi.nlm.nih.gov/pubmed/25733247

Yauk, C.L. *et al*. (2016). **Application of the TGx-28.65 Transcriptomic Biomarker to Classify Genotoxic and Non-Genotoxic Chemicals in Human TK6 Cells in the Presence of Rat Liver S9.** *Environmental and Molecular Mutagenesis* 57: 243-260.

Study Compounds:

Acetaminophen – 0, 1, 3.2, 10 mM

2-Aminoanthracene – 0, 0.75, 1.5, 2 µg/mL

Cyclophosphamide – 0, 1, 5, 20 µM

Dibenz[a,h]anthracene – 0, 1, 20, 280 µg/mL

Dimethylnitrosamine – 0, 1, 5, 10 mM

Furan – 0, 2, 3, 5 mM

2-Nitrofluorene – 0, 10 , 50, 300 µM

Phenanthrene – 0, 8, 40, 100 µg/mL

Sucrose – 0, 1, 3.2, 10 mM

Time Points:

7-8 hr (with S9) for gene expression

GEO Accession Number: GSE74216

GEO Link: https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE74216

Link to Publication: https://www.ncbi.nlm.nih.gov/pubmed/26946220

Buick, J.K. *et al*. (2017**). Integration of the TGx-28.65 genomic biomarker with the flow cytometry micronucleus test to assess the genotoxicity of disperse orange and 1,2,4-benzenetriol in human TK6 cells.** *Mutat Res Fund Mol Mech Mutagen* 806: 51–62.

Study Compounds:

Disperse orange azo dye – 0, 50, 500, 750 µg/ml (0, 130, 1297, 1946 µM)

1,2,4-Benzenetriol – 0, 15, 20, 30 µg/ml (0, 119, 159, 238 µM)

Benzo[a]pyrene - 10 µg/ml

Time Points:

7 hr (with S9) for gene expression

GEO Accession Number: GSE95192 for DO and BT and GSE51175 (SubSeries: GSE51173 for BaP)

GEO Link: https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE95192;

https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE51173

Link to Publication: https://www.ncbi.nlm.nih.gov/pubmed/29017062

Li, HH. et al (2017). **Development and validation of a high-throughput transcriptomic biomarker to address 21st century genetic toxicology needs.** *Proc Natl Acad Sci USA.* 114(51): E10881-E10889.

Study Compounds:

Class 1 (DDI agents that interact directly with DNA)
N-ethyl-N-nitrosourea (ENU) - 500 µM

Mitomycin (MMC) - 10 µM
Ethyl methanesulfonate (EMS) - 2 mM
Bleomycin - 20 µM
Nitrogen mustard - 200 nM
Chlorambucil - 4 µM
Busulfan - 10 µM
Hydroquinone - 20 µM
Class 2 (DDI agents that interact indirectly with DNA)
Class 2 Topoisomerase inhibitors
Doxorubicin - 1.2 µM
Genistein - 20 µM
Topotecan - 400 nM
Norfloxacin - 1 mM
Ciprofloxacin - 100 µM
Class 2 Antimetabolites
5-Fluorouracil (5-FU) - 400 µM
Thioguanine (6-TG) - 4 µM
Thiopurine (6-MP) - 1 mM
Azidothymidine (AZT) - 1 mM
5-Azacytidine (5-AzaC) - 10 µM
Class 3 (agents that interact indirectly with DNA via effects on the cell cycle, regulation of apoptosis, and interaction with the mitotic apparatus)
Class 3 Antimitotic agents
Diethylstilbestrol - 40 µM
Nocodazole - 30 µM
Benomyl - 1 mM
Class 3 Kinase inhibitors
Dasatinib - 20 µM
Imatinib mesylate - 400 µM
Sorafenib - 20 µM
Class 4 (non-DDI compounds with a clean genotoxicity profile, including negativity in vitro CD assays)
Class 4 Kinase inhibitors
Sunitinib maleate - 20 µM
Gefinitib - 100 µM
Class 4 Nongenotoxic carcinogens
Progesterone - 1 mM
Diethanolamine - 1 mM
Melamine - 1 mM
Class 4 Antibiotics
Ampicillin - 1 mM
Erythromycin stearate - 500 µM
Class 4 Other
D-Mannitol - 1 mM
n-Butyl chloride - 1 mM
Methyl carbamate - 1 mM
Class 5 (compounds known to have irrelevant positive results in in vitro genotoxicity assays)
Phenobarbital - 1 mM
Esomeprazole - 200 µM
Donepezil - 1 mM
Cyclohexamide - 10 µM
2,4-Dinitrophenol (2,4-DNP) - 1 mM

Olmesartan - 0.16 µM
Exemastan - 100 µM
Rabeprazole-NA - 0.8 µM
Rotigotin - 100 µM
Dexamethasone - 1 mM
Staurosporine - 30 nM

Time Points:

4 hr (no S9) for gene expression analysis

GEO Accession Number: GSE107162

GEO Link: https://www.ncbi.nlm.nih.gov/geo/query/acc.cgi?acc=GSE107162

Link to Publication: https://www.ncbi.nlm.nih.gov/pubmed/29203651