

Table S1: List of Perfluoroalkyl and Polyfluoroalkyl Substances (PFAS) as stressors

<b>Stressors</b>
Perfluoro-n-butanoic acid
Perfluoropentanoic acid
Perfluorohexanoic acid
Perfluoroheptanoic acid
perfluoro-heptanesulfonate
Perfluoropentanesulfonic acid
Perfluorooctanoic acid
Perfluorononanoic acid
Perfluoro-n-decanoic acid
Perfluorononanesulfonic acid
Perfluoro-n-undecanoic acid
Perfluorododecanoic acid
Perfluoro-1-butanesulfonate
perfluoro-1-decanesulfonate
Perfluoro-1-hexanesulfonate
Perfluorooctane sulfonic acid
perfluorooctane sulfonate
2-(N-Methyl-perfluorooctane sulfanamido) acetic acid
2-(N-ethyl-perfluorooctane sulfanamido) acetic acid
Perfluoro(2-ethoxy-2-fluoroethoxy)acetic acid ammonium salt
Perfluorotetradecanoic acid
perfluoro-n-tridecanoic acid
perfluoro-n-tetradecanoic acid
Krytox-H
Perfluorooctanesulfonamide
2-(Perfluorohexyl)ethyl acrylate
Polyfluoroalkyl phosphate mono-esters
Polyfluoroalkyl phosphate di-esters
Polyfluoroalkyl phosphate tri-esters
2-(Perfluoro-n-octyl)ethanol
2-(Perfluorodecyl)ethanol
2-(Perfluorooctyl)ethane-1-sulfonic acid
h,1h,2h,2h-Perfluorooctanesulfonic acid
Perfluoro-3,5,7,9-tetraoxadecanoic acid
Perfluoro-3,5,7,9,11-pentaoxadodecanoic acid
Ammonium 4,8-dioxa-3H-perfluorononanoate
Nafion Byproduct 2
6:2 chlorinated polyfluorinated ether sulfonic acid
Ammonium perfluoro-2-methyl-3-oxahexanoate
8:2 chlorinated polyfluorinated ether sulfonic acid
Trifluoroacetate
TFAA
C4-C4-PFPiA
Bis(nonafluorobutyl)phosphinic acid

C6-C8-PFPiA  
Bis(perfluorohexyloctyl)phosphinic acid  
C8-C8 PFPiA  
Bis(perfluorooctyl)phosphinic acid  
4-2 fluorotelomer sulfonic acid  
3,3,4,4,5,5,6,6,6-Nonafluoro-1-hexanesulfonic acid  
4-2 FTSA  
Hexafluoropropylene Oxide Trimer Acid  
HFPO-TA  
Perfluorooctylphosphonic acid  
2-(Perfluorohexyl)ethyl phosphonic acid  
PFOPA  
FL16.119  
N-(2-methylcyclohexyl)-2,3,4,5,6-pentafluorobenzamide  
PFECA  
Perfluoro-1,2-propylene glycol and perfluoro-1,1-ethylene glycol, terminated with chlorohexafluoropropoxy groups; Perfluoro(2-ethoxy-ethoxy)acetic acid, ammonium salt  
Perfluoro-2-methyl-3-oxahexanoic acid  
PMOH  
GenX  
3H-perfluoro-3-(3-methoxypropoxy) propanoic acid  
PMPP  
ADONA  
OBS  
p-perfluorous nonenoxybenzenesulfonate  
1-Octanol, 3,3,4,4,5,5,6,6,7,7,8,8,8-tridecafluoro-  
6-2 FTOH  
Perfluorotributylamine  
FC43  
Perfluoro-3,5,7-trioxaoctanoic acid  
PFO3OA  
1,1,2,2-tetrafluoro-2-(1,2,2,2-tetrafluoroethoxy)ethanesulfonic acid  
NVHOS  
4-defluoro-3-oxa-PFPeS  
Hydro-EVE  
polyfluoroalkyl ether carboxylic acid  
2,2,3,3-tetrafluoro-3-((1,1,1,2,3,3-hexafluoro-3-(1,2,2,2-tetrafluoroethoxy)propan-2-yl)oxy)propanoic acid  
Potassium 9-chlorohexadecafluoro-3-oxanonane-1-sulfonate  
6-2 Cl-PFESA  
Potassium 11-chloroeicosafluoro-3-oxaundecane-1-sulfonate  
8:2 Cl-PFESA  
Pentafluoropropionic acid  
N-methylperfluoro-1 octanesulphonamide 1,1,2,2,3,3,4,4,5,5,6,6,7,7,8,8,8-  
Heptafluoro-N-methyl-1-octanesulfonamide (IUPAC)  
n-MeFOSA  
N-EtFOSA,  
SULFLURAMID

N-EtFOSE  
 N-MeFOSE  
 PFODA  
 PfHxDA

Table S2: List of biological events

List of AOP-wiki events	List of HBM4EU events
stabilization PPAR alpha co-repressor PPAR-gamma activation Increased Reactive oxygen species Increase FA Influx Activation FAS Activation Glucocorticoid Receptor Up Regulation SREBF2 Up Regulation Unsaturated fatty acid Down Regulation GSS gene Down Regulation GST gene Glutathione synthesis Activation 3-hydroxy-3-methylglutaryl-CoA reductase gene Perturbation of cholesterol Glutathione homeostasis Hepatotoxicity Increase cytosolic fatty acid Inhibit serotonin transporter activity Decreased serotonin transporter activity Decreased extracellular sodium Decreased extracellular Na <sup>+</sup> Decreased extracellular chloride Decreased extracellular Cl <sup>-</sup> Increased extracellular serotonin Increased intracellular sodium Increased intracellular Na <sup>+</sup> Increased intracellular chloride Increased intracellular Cl <sup>-</sup> Decreased intracellular serotonin Decreased packaged serotonin Decreased synaptic release Increased 5-HT <sub>3</sub> Increased 5-hydroxytryptamine Inactivated 5-HTR (serotonin receptors) Reduce expression BDNF Reduce expression Brain-derived neurotrophic factor Decreased neuroplasticity	Insulin Resistance Syndrome Syndrome X Dysmetabolic Syndrome X Metabolic Cardiovascular Syndrome Type 2 Diabetes Mellitus Insulin Sensitivity Glucose Intolerances Hyperglycemia Insulin Resistance Metabolic syndrome Dyslipidemias Dyslipoproteinemias Hyperlipidemias High Blood Pressure Hypertension Abdominal Obesity Central Obesity Liver Diseases Thyroid Diseases

Increase cortisone  
Reduced BDNF  
Reduced Brain-derived neurotrophic factor  
Activation 5-HT2A (Serotonin 2A)  
Activate PLC  
Activate Phospholipase C  
Increase inositol triphosphate  
Increase intracellular calcium  
Activate calmodulin  
Increase myosin light chain phosphorylation  
Increase vascular smooth muscle contraction  
Increase hypertension  
Decreased extracellular serotonin  
NFE2/Nrf2 repression  
Increased steatosis  
Reduced FXR activity  
Reduced SHP activity  
Activated LXR  
Reduced PPARalpha  
Reduced HSD17B4 activity  
Reduced fatty acid beta oxidation  
obesity  
activation of CCAAT/enhancer-binding protein alpha  
increased adipogenesis  
decreased dopamine  
decreased reward  
decreased DNA methylation of tyrosine hydroxylase  
decreased methylation of dopamine transporter promoter  
chronic high fat diet  
Steatohepatitis  
Inhibition Fatty Acid Beta Oxidation  
Increased Oncotic Necrosis  
Tissue resident cell activation  
Increased Pro-inflammatory mediators  
Leukocyte recruitment  
Leukocyte activation  
Fatty Acid Beta Oxidation Decreased  
Endocytotic lysosomal uptake  
Activation LXR  
Damaging Mitochondria  
Mitochondrial dysfunction 1  
Decreased Mitochondrial fatty acid beta-oxidation  
Activation AhR

Peptide Oxidation  
Decreased PCK1 expression  
Activation PPAR $\alpha$   
peroxisome proliferator activated receptor  
promoter demethylation  
Alkylation Protein  
Activation PXR/SXR  
Activation SCD-1  
Activation SREBP-1c  
Activation Stellate cells  
Accumulation Triglyceride  
Accumulation Fatty acid  
Liver fibrosis  
Liver Steatosis  
Suppression VLDL secretion  
Inhibition Mitochondrial fatty acid beta-oxidation  
Increased Triglyceride formation  
Accumulation Liver lipid  
Suppression NR1H3  
Activation SREBF1  
Increased De Novo FA synthesis  
Increased Liver Steatosis  
Increased Liver Steatosis  
Suppression HNF4alpha  
Up Regulation SCD-1  
Up Regulation FAS  
Increased FA Influx  
Up Regulation LDLR  
Up Regulation low density lipoprotein receptor  
Increased LDL uptake  
Inhibition PPAR alpha  
Up Regulation Acetyl-CoA carboxylase-1  
Up Regulation ACC-1  
Inhibition FoxA2  
Down Regulation CPT1A  
Down Regulation HMGCS2  
Decreased Ketogenesis  
Activation NRF2  
Activation NR1H4  
Activation SHP  
Decreased DHB4/HSD17B4  
Activation LXR alpha  
Up Regulation CD36  
Cell injury  
Cell death  
Decreased Cholesterol  
Decreased De Novo Biosynthesis of

<p>Cholesterol Decreased Uptake of Lipoproteins Decreased Transport of Cholesterol to the Inner Mitochondrial Membrane Decreased Testosterone Production by Adult Leydig Cells Decreased sperm quantity and/or quality in the adult testis Activation ChREBP Accumulation Collagen Up Regulation CYP1A1 Decreased PPARalpha transactivation of gene expression Decreased Ketogenesis Decreased production of ketone bodies Not Increased Circulating Ketone Bodies Increased Catabolism of Muscle Protein Decreased Body Weight Inhibition SREBP1c Activation MTTP Increased ApoB100 Increased Triglyceride Disruption Lysosome Synthesis De Novo FA S-Glutathionylation eNOS Uncoupling eNOS Depletion Nitric Oxide Decrease Tetrahydrobiopterin Decrease GTPCH-1 Impaired Vasodilation Increase Vascular Resistance Hypertension Decrease AKT/eNOS activity Binding of antagonist PPAR alpha</p>	
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