

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

Stressors
<p> 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-butanefulfonate  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 </p>

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-perfluorooxanonenoxybenzenesulfonate  
 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
<p>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</p>	<p>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</p>

<p>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</p>	
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<p> Peptide Oxidation  Decreased PCK1 expression  Activation PPAR<math>\alpha</math>  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 HNF4<math>\alpha</math>  Up Regulation SCD-1  Up Regulation FAS  Increased FA Influx  Up Regulation LDLR  Up Regulation low density lipoprotein receptor  Increased LDL uptake  Inhibition PPAR <math>\alpha</math>  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 <math>\alpha</math>  Up Regulation CD36  Cell injury  Cell death  Decreased Cholesterol  Decreased De Novo Biosynthesis of </p>	
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<p>Choleseterol</p> <p>Decreased Uptake of Lipoproteins</p> <p>Decreased Transport of Cholesterol to the Inner Mitochondrial Membrane</p> <p>Decreased Testosterone Production by Adult Leydig Cells</p> <p>Decreased sperm quantity and/or quality in the adult testis</p> <p>Activation ChREBP</p> <p>Accumulation Collagen</p> <p>Up Regulation CYP1A1</p> <p>Decreased PPARalpha transactivation of gene expression</p> <p>Decreased Ketogenesis</p> <p>Decreased production of ketone bodies</p> <p>Not Increased Circulating Ketone Bodies</p> <p>Increased Catabolism of Muscle Protein</p> <p>Decreased Body Weight</p> <p>Inhibition SREBP1c</p> <p>Activation MTTP</p> <p>Increased ApoB100</p> <p>Increased Triglyceride</p> <p>Disruption Lysosome</p> <p>Synthesis De Novo FA</p> <p>S-Glutathionylation eNOS</p> <p>Uncoupling eNOS</p> <p>Depletion Nitric Oxide</p> <p>Decrease Tetrahydrobiopterin</p> <p>Decrease GTPCH-1</p> <p>Impaired Vasodilation</p> <p>Increase Vascular Resistance</p> <p>Hypertension</p> <p>Decrease AKT/eNOS activity</p> <p>Binding of antagonist PPAR alpha</p>	
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