timely treatment, thereby escalating deterioration and worsens outcome. Hence, therapeutic hypothermia has been explored in this study as a potentially simple and effective method to preserve liver functions. Hitherto the concept of hypothermia for toxicity management has been contentious and we aim to debunk the conflict with a systematic investigation of hypothermic effects in an acetaminophen (APAP)-induced liver injury model.

Methods: Cytotoxic levels of APAP (1–10 mM) was used to induce liver injury of different severities in TAMH. The temporal relationship between moderate hypothermia, 32 °C for 24 h, and onset of hepatotoxicity was explored for any protective (i.e. hypothermia induced before toxicity), preservative (i.e. hypothermia induced during toxicity) or recovery (i.e. hypothermia induced after removal of toxicants) effects. The extent of hypothermic effects was also investigated by rewarming cells back to 37 °C for 24 h. Both the extent of cell viability and cell death was examined and we attempted to elucidate its protective mechanism with gene and protein expression of cold shock proteins (CSPs), caspase 3 activity, microarray and cell-cycle analysis.

Results: Moderate hypothermia could promote liver preservation, with most prominent effect seen in 5 mM APAP-induced liver injury. The increased cell viability and reduced cell death continued for 24 h after rewarming. These cytoprotective effects could stem from different mechanisms as seen with differential gene expressions and distinct contrast in caspase 3 activity following temperature transition – with a predominant CSPs-induced translational regulation and mRNA stabilization during hypothermia and a complex interplay with transcriptional regulation upon rewarming, involving Tsc22 leucine zipper domains, independent of heat shock.

Conclusion: Moderate hypothermia may effectively alleviate liver injury in an unconventional way and allow lasting protection beyond treatment duration. This study thus unveils a prelude for an efficient drug-free approach to attenuate injury.

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P23-06
Toxicity of synthetic cathinones in human kidney (HK-2) cells

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Synthetic cathinones, also known as bath salts, emerged in the recreational drug market in the mid-2000s as alternatives to illicit drugs such as amphetamines and cocaine and represent nowadays a large class of new popular drugs of abuse. The use of synthetic cathinones is associated with adverse health effects, including renal injury, although the underlying mechanisms are not yet understood. The aim of this study was to evaluate the potential nephrotoxic effects of five commonly used cathinone synthetic derivatives, namely 3,4-methylenedioxypyrovalerone (MDPV), methylone, pentedrone, 3,4-dimethylmethcatinone (3,4-DMMC) and 4-methylethcatinone (4-MEC), using the human kidney (HK-2) cell line as an *in vitro* model. The HK-2 cells were exposed to a wide range of concentrations, specifically 0.01–3 mM for 3,4-DMMC and 0.1–10 mM for all the others synthetic cathinones, for 24 and 48 h. Cytotoxicity was evaluated by measuring by measuring mitochondrial reduction of 3-(4,5-dimethythiazol-2yl)-2,5-diphenyl tetrazolium bromide (MTT) and by assessing lysosomal uptake of neutral red (NR). It was observed that all tested compounds induced cell death in a concentration- and time-dependent manner. 3,4-DMMC was found to be the cathinone derivative that exhibited the highest toxicity for HK-2 cells, followed by MDPV, pentedrone, methylone, and 4-MEC. To the best of our knowledge, this is the first study to demonstrate the *in vitro* nephrotoxic potential of synthetic cathinones.

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P23-07
Protective effects of SIRT1 antagonist on diabetic-induced renal fibrosis

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Chronic kidney disease (CKD) is a leading cause of mortality in patients with diabetes mellitus (DM). Recent studies have shown that SIRT1 is closely related to the occurrence and development of diabetic nephrotoxicity. Silent information regulator 2 (Sir2) is a nicotinamide adenine dinucleotide- (NAD^+-) dependent deacetylase. The homology of SIRT1 and Sir2 has been extensively studied. SIRT1 deacetylates target proteins using the coenzyme NAD^+ and is therefore linked to cellular energy metabolism and the redox state through multiple signaling and survival pathways. In the kidneys, SIRT1 may inhibit renal cell apoptosis, inflammation, and fibrosis. Therefore its activation may also become a new therapeutic target in the patients with CKD including diabetic nephropathy. Here, we evaluated the roles of SIRT1 on the kidney fibrosis in diabetic animal model. We found that acetylation of p65 and STAT3 was increased in the kidney of high fat diet-induced ZDF rats. The expression of a-SMA, collagen I, and fibronectin levels were markedly increased in diabetic-induced ZDF rats. Furthermore, SIRT1 inhibitor attenuated the diabetic-induced kidney fibrosis. Our findings strongly support that SIRT1 inhibitor may use as a protective agent for renal fibrosis in chronic hyperglycemia condition.

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P23-08
Effects on cigarette smoke extract on cell proliferation and apoptosis in mouse embryonic stem cells via reactive oxygen species-induced endoplasmic reticulum stress signaling pathways

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Cigarette smoke contains thousands of chemicals, and many components have reproductive and developmental toxicity that is harmful to humans and animals. Previous studies have reported that cigarette smoke or cigarette smoke extract (CSE) have negative effects on embryo development through *in vivo* and *in vitro* studies. However, there is no mechanism study on how CSE affects the cellular signaling pathway for apoptosis and oxidative stress in embryonic cells, or how the two pathways cross-link. Therefore, we investigated the effects of CSE on apoptosis and oxidative stress