20th World Congress on

Toxicology and Pharmacology

May 06-07, 2019 Tokyo, Japan

Poster

I-Chen Kung et al., Toxicol Open Access 2019, Volume 5
DOI: 10.4172/2476-2067-C1-009

A novel synthetic LSD1 inhibitor with anticancer activity in prostate cancer cells

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In United States during 2018 an estimated 164,690 new cases and 29,430 deaths of prostate cancer. Prostate cancer ranks as the first of new cases and the second of deaths from cancer in the US during 2018. The lysine-specific demethylase 1A (LSD1/KDM1A) is the first histone demethylase discovered and it can remove mono or di-methyl groups from lysine K4 or K9 on histone H3. LSD1 expression is increased in malignant prostate cancer. Overexpression of LSD1 enhances cell growth and cancer metastasis. Therefore, we want to treat prostate cancer by inhibiting cell growth or inducing cell death or suppressing cell migration and Epithelial–Mesenchymal Transition (EMT) through the inhibition of LSD1. We synthesized a new compound (Compound X) for LSD1 inhibition, and we compared with a well-known LSD1 inhibitor, SP2509. SP2509 can inhibit cell growth in prostate cancer cell PC3 and DU145 with micromolar GI50 value (1.34 and 2.12 μM), and Compound X can inhibit cell growth in PC3 and DU145 with submicromolar GI50 value (0.34 and 0.89 μM) by SRB assay. Our results showed that Compound X induces sub G1 phase of cell cycle arrest in a time-dependent manner and induces caspase-dependent apoptosis and inhibits migration and EMT more than SP2509 in PC3 and DU145 cells. Knockdown of LSD1 enhances Compound X-induced cell apoptosis and suppression of migration in PC3 and DU145 cells. It has been reported that N-Myc Downstream-Regulated Gene 1 (NDRG1) is a potent metastatic suppressor in prostate and colon cancer cells. Our data showed that Compound X increase NDRG1 expression, therefore we will also investigate if NDRG1 plays an important role in the inhibition of migration and EMT by treated with Compound X. These data show that our new Compound X is more potent than well-known LSD1 inhibitor, SP2509.

Biography

I-Chen Kung has completed her graduation from the Department of Medical Laboratory Science and Biotechnology, Taipei Medical University. She is a Medical Technologist in Taiwan. She is currently pursuing her Masters in the Institute of Pharmacy, Taipei Medical University and also is a Member in the Clinical Drug Discovery Lab.

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Accepted Abstracts

Toxicol Open Access 2019, Volume 5
DOI: 10.4172/2476-2067-C1-009

Production of avant-garde sensors for the identification and termination of toxic gases

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This study explains a process which significantly explores the application of mass spectroscopy, Fabry-Perot interferometer and the Atume's configuration of gases in the production of sophisticated sensors that analyzes toxic gases. Basically, the molar masses of gases in an environment is predicted by means of an embedded and portable mass spectrometer, that is linked to a sensor which utilizes its transmission spectrum as a function of wavelength, exhibiting peaks of large transmission, corresponding to resonance of the Fabry-Perot assembly and a scanning along with advanced spectral processing. A programming is carried out such that corresponding wave lengths and molar masses are compared to the Atume's configuration of gases which involves all possible molecular quantization for each gas. This process is based on the principle that, no two gases can have all the same number of quantum parameters. The avant-garde sensor periodically sends results of every analysis to cell phones, suggesting ways of terminating the toxic gases that were identified and in very serious cases, an alarm will sound.

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Toxicol Open Access 2019, Volume 5
DOI: 10.4172/2476-2067-C1-009

Investigating brain tissue damage following respiratory contact with carbon nanotubes in rat using isolated lung mitochondria

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Objective: The main aim of this study is to investigate the lung toxicity following the respiratory contact with Multi-Wall Carbon Nanotubes (MWCNTs) in male Wistar rats.

Method: Rats were exposed to 5 mg/m3 MWCNT aerosol in different size and purity for 5 hours/day, 5 days/week for 2 weeks in a whole-body exposure chamber. After two weeks exposure, the rats of all groups was necropsied the animals lungs were removed. Then we separated the left and right lungs and mitochondria of them were isolated and parameters of mitochondrial toxicity including mitochondrial succinate dehydrogenase (complex II) activity, generation of Reactive Oxygen Species (ROS), Mitochondrial Membrane Potential (MMP) collapse, mitochondrial swelling and cytochrome c release were evaluated.

Result: Our results demonstrated that MWCNTs with different characteristics, in size and purity, significantly ($P<0.05$) decreased mitochondrial succinate dehydrogenase activity and mitochondrial ROS production. Induced mitochondrial swelling, MMP collapse and cytochrome c release mitochondria and right lung had seen more damage.

Conclusion: We concluded that MWCNTs with different characteristics, in size and purity because damage in varying degrees on the mitochondrial respiratory chain and induce ROS mediated cytotoxicity by directly targeting mitochondria lung tissue. It seems that the right lung has been more damaged due to the larger size of the left lung.

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Toxicol Open Access 2019, Volume 5
DOI: 10.4172/2476-2067-C1-009

Blood lymphocytes cytotoxicity monitoring of hospital nurses occupationally exposed to anti-neoplastic drugs

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Anti-neoplastic agents are extremely active biological compounds and their action is non-selective. Oncology nurses are exposed at the workplace to a wide spectrum of these agents in sub therapeutic concentrations might face unknown biological consequences which are always a serious health problem. The purpose of this study is to assess biological and cellular alteration in blood lymphocytes of nurses who work in chemotherapy wards and compare the obtained data to those of nurses who work in other wards. All nurses who work in chemotherapy wards were selected with enter and exit criteria clarified by medical and para medical tests. Demographic data such as age, sex, time of exposure, smoking status and alcohol drinking were collected and blood samples were taken. Control nurses who work in other wards of hospitals were chosen by the same criteria imposed for oncology nurses. All cytotoxicity parameters (cell viability, ROS formation, MMP collapse, lysosomal membrane damage, lipid peroxidation, caspase 3 activity and apoptosis phenotype) in exposed oncology nurses were significantly ($p<0.001$) higher than those of unexposed control nurses. Our results indicate that the lymphocytes of oncology nurses exposed to anti-neoplastic drugs are more susceptible to oxidative stress than controls group. Hence, we should prevent hospital oncology nurse from contacting with possible risks such as inhalation of aerosols, particles and droplets via. direct skin or eyes contact by spraying, swallowing of chemotherapeutic agents due to poor health conditions or dispersal of anti-cancer drug, or injection as a result of scarring by the sharp tools.

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Toxicol Open Access 2019, Volume 5
DOI: 10.4172/2476-2067-C1-009

Arsenic trioxide induces structural perturbation of hen egg white lysozyme towards oligomers formation

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Arsenic trioxide is one of the most common metallic pollutants entering the food chain both by human activities and nature. Its introduction to living organism and accumulation is known to manifest several metabolic and hormonal disorders; however its role in protein misfolding and aggregation followed by neurodegenerative disorders is not fully elucidated. In the present study by employing several biophysical techniques, we reveal the aggregation mechanism of Hen Egg White Lysozyme (HEWL) in presence of Arsenic Trioxide (As_2O_3) at physiological condition and characterized the aggregates. Our ThT fluorescence and scattering data shows that As_2O_3 promote the *in vitro* aggregation of HEWL in concentration dependent manner. Early phase of aggregation was observed to be induced by exposure of hydrophobic surfaces which later reorganized to promote further self-association leading to β sheet structure which was evident by CD spectroscopy. Presence of lower ordered oligomers after two days and higher ordered oligomers along with amorphous aggregates, as evident by AFM after week long incubation, indicate that As_2O_3 drives the self-assembly of lysozyme towards oligomers form. It is now been believed that not the mature fibrils but the transiently formed oligomers are the real culprit of several neurodegenerative disorders. Though we did not observed any mature fibrils in present study, presence of oligomers of Rh ~62 nm and ~222 nm indicate that heavy metal promotes small and medium sized oligomers which could be potential toxic species of arsenic mediated toxicity. With the fact that several environmental pollutants including heavy metals are continually entering the living organism resulting into various chronic disorders, present study provides a new insight about arsenic driven protein aggregation and toxicity associated with that.

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Toxicol Open Access 2019, Volume 5
DOI: 10.4172/2476-2067-C1-009

Therapeutics effect of Idebenone in murine colitis

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Idebenone short chain quinone has been described as a potent antioxidant and mitochondrial electron donor. Its therapeutical potential has been described extensively in numerous pathological conditions ranging from neurodegenerative, neuromuscular to diverse metabolic conditions. There is also some emerging evidence that Idebenone has some anti-inflammatory activity. Oxidative stress is one of the key players of the inflammatory cascade responsible for the initiation of Ulcerative Colitis (UC). Therefore, we investigated the anti-oxidative and anti-inflammatory properties of Idebenone in Dextran Sodium Sulfate (DSS) induced mouse model of acute colitis. Acute colitis was introduced in female C57BL/6J mice by administering 2.5% of DSS in autoclaved water continuously for seven days. Changes in body weight, Disease Activity Index (DAI), colon length and histopathological parameters were evaluated and scored. Colonic contents of Malondialdehyde (MDA), a marker of lipid peroxidation were also examined as a parameter of disease-associated redox state. Protein expression of the oxidative stress induced redox factor NAD(P)H dehydrogenase Quinone-1 (NQO-1) was determined by western blot, while the levels of various pro-inflammatory cytokines were quantified using Bio-Plex assay. On Oral administration of Idebenone at a dose of 200 mg/kg body weight significantly against body weight loss and improved DAI, colon length and histopathology. Idebenone also significantly reduced MDA content as well as pro-inflammatory cytokine levels such as IL-1α, TNF-α, G-CSF, GM-CSF, MIP-1α, MIP-1β, RANTES and EOTAXIN and furthermore, Idebenone upregulated NQO1 protein levels. These results suggest that Idebenone could represent a promising therapeutic strategy to interfere with disease pathology in UC by inducing anti-oxidative and anti-inflammatory pathways.

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