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J Clin Toxicol 2017, 7:3(Suppl)
DOI: 10.4172/2161-0495-C1-025

9th Euro-Global Summit on

Toxicology and Applied Pharmacology

June 22-24, 2017 Paris, France

Interest of cytometry in toxicology testing

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What is the best way to analyze toxicity in human? Human cells provide closest tools to analyze toxicity in human at low cost, low ethical issue and cytometry is the ideal tool for this. What is cytometry? Cytometry includes several techniques that measure quantitatively cells, individually and on multiple parameters simultaneously. Image cytometry gives precise location of cellular targets. Flow-cytometry (FCM) is the most useful, high content, high performance, high speed technique giving direct information on cell status and at relatively low cost for clinical or preclinical screening applications. High throughput analysis is possible for large scale screening. Recent disrupting innovation has combined FCM with image (Imagestream™) or mass spectrometry that is a bit less sensitive but gives the possibility to analyses much more parameters simultaneously. FCM is particularly adapted for blood samples and any biological fluids (broncho-alveolar lavage, bone marrow, stem cells) but can also be used in dissociated tissues or their representative cell lines. Other types of cells can also be analyzed from animals, vegetal, algaes and even bacteria. Applications in toxicology: FCM is routinely used for precise counting and eventually measuring maturation break or lineage specific damages of immune and hematopoietic cells in drug development and clinical research such as biotherapy. Cell damages and eventual repair cell death, apoptosis, necrosis, autophagy can be identified under experimental or accidental exposure. But FCM can also help identifying the mechanism involved in toxic effect by analyzing the some basic cell functions such as mitochondrial respiratory chain, production of oxygen or nitrogen free radicals, lysosome activity, fatty acid metabolism and peroxysome, signaling, caspases, calcium influx, or cytokine profiles. Typical examples are shown. Quality assurance procedures have been developed. In conclusion, flow cytometry is a precious technique that can help in toxicology addressing specific or global cell effects in high scientific/economic efficiency.

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Activation of FGF2-FGFR1 axis by visceral fat is responsible for malignant transformation of epithelial cells in mice kept on high fat diet

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Increased adiposity plays a crucial role in the pathogenesis and prognosis of different types of cancers, especially in obese individuals. Epidemiological evidence suggests visceral adipose tissue (VAT) and high-fat diets (HFD) are associated with increased cancer risk however, the mechanism is not well understood. The aim of this study was to explore the factors in VAT that stimulate malignant transformation. We modeled visceral adiposity-stimulated malignant transformation using our novel ex vivo system of VAT-condition medium stimulated epithelial cell transformation (measured by growth in 3D cell culture model of soft agar) and our *in vivo* murine lipectomy model of ultraviolet light B (UVB)-induced, VAT promoted skin tumor formation. We found that VAT from mice and obese human donors stimulated malignant transformation of non-tumorigenic epithelial cells. Moreover, the VAT of obese mice fed a HFD [not VAT from low-fat diet (LFD) fed mice] stimulated malignant transformation. Furthermore, human VAT stimulated both skin and mammary epithelial cell transformation. The differences in VAT activity between LFD and HFD fed mice and human donors were associated with the levels of FGF2. Circulating levels of FGF2 were associated with non-melanoma tumor formation *in vitro*. Human and mouse VAT failed to stimulate transformation in FgfR1(-/-) cells and do not form tumors when injected in Nude mice *in vivo*. Collectively, our data show FGF2 released from VAT and its interaction with FGFR1 is a novel and potential direct path of VAT-enhanced tumorigenesis. Blocking the FGF2-FGFR1 axis in VAT of abdominally obese individuals may be an important cancer prevention strategy as well as an adjuvant therapy for improving outcomes following cancer diagnosis.

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