gentamicin treatment a subset of rats were sacrificed and their kidneys used for histology. With the purpose of identifying biomarker of predisposition, proteomic studies were performed before gentamicin administration at week 21. Chronic administration of UN in drinking water during 21 weeks did not modify renal function or renal tissue integrity. However, when rats exposed to UN during 21 weeks where challenged with low doses of gentamicin, they developed an overt renal failure as shown by an increase in creatinine, urea and by histological alterations. These alterations were not observed in the control group. Using a proteomic analysis, hemopexin was detected which was validated by Western blot. Urinary excretion of hemopexin was statically higher in the exposed group than in the control group. Our results suggest that chronic exposure to UN, at doses that apparently does not produce damage, predisposes to AKI when animals were subjected to a second insult at subtoxic doses. Hemopexin protein might be potentially used as marker of chronic predisposition to ARF. This new diagnostic tool might help to reduce AKI incidence and severity, and also the associated sanitary and socioeconomic costs.

http://dx.doi.org/10.1016/j.nhtm.2014.11.047

Listening to shiny body: In vivo photoacoustic tomography

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Abstract

High-resolution volumetric optical imaging modalities, such as confocal microscopy, two-photon microscopy, and optical coherence tomography, have become increasing important in biomedical imaging fields. However, due to strong light scattering, the penetration depths of these imaging modalities are limited to the optical transport mean free path (~1 mm) in biological tissues. Photoacoustic imaging, an emerging hybrid modality that can provide strong endogenous and exogenous optical absorption contrasts with high ultrasonic spatial resolution, has overcome the fundamental depth limitation while keeping the spatial resolution. The image resolution, as well as the maximum imaging depth, is scalable with ultrasonic frequency within the reach of diffuse photons. In biological tissues the imaging depth can be up to a few centimeters deep. In this presentation, the following topics of photoacoustic imaging will be discussed: (1) multi-scale photoacoustic imaging systems, (2) morphological, functional, and molecular photoacoustic imaging, (3) potential clinical applications, and (4) contrast agents for photoacoustic imaging.

http://dx.doi.org/10.1016/j.nhtm.2014.11.048

Melanoxoin reduces tumor growth in xenograft animial model and inhibits cell migration in human lung cancer cell lines.

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Abstract

Natural products remain the best sources of drugs and drug leads. Various anticancer drugs are derived from the natural products. In our previous studies, we found that methanol extract of Pterocarpus santalinus exhibited potent cytotoxicity and anti-inflammatory activities. Among the series of compounds isolated from Pterocarpus santalinus, melanoxoin demonstrated the highest cytotoxic effects with a IC50 of 1.98 Î¼g/ml in human non-small cell lung cancer H1299 cells. The results showed that melanoxoin regulated the transcription of several cell cycle regulators in H1299 cells. Melanoxoin induced tubulin depolymerization, suggesting that melanoxoin causes G2/M arrest thus increasing apoptosis in tumor cell. The results of neutral comet assay showed that treatment with melanoxoin induced significant DNA damage in H1299 cells, while the in vivo efficacy of melanoxoin was revealed by the mice xenograft models. Clinical data showed that an increase (61%) of MET expression was observed in non-small cell lung cancer samples compared with adjacent normal tissues. HGF/c-Met signaling is involved in the cancer progression, metastasis and gefitnib resistance. In particular, we also found that melanoxoin can inhibit HGF-induced cell migration using the wound healing and transwell migration assay. Altogether, our results indicated that melanoxoin displays an outstanding inhibitory activity toward tumor growth and metastasis. Thus, it exerted great potential to be developed into novel anti-cancer agent.

http://dx.doi.org/10.1016/j.nhtm.2014.11.049

Regulation of renal fibrosis by the transforming growth factor beta-1 receptor Alk1

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Abstract

Tubulointerstitial fibrosis –a common end-stage feature of chronic kidney disease- is characterized by the presence of renal myofibroblasts and excessive accumulation of extracellular matrix proteins (ECM) in the renal tubular interstitium. The cytokine transforming growth factor beta 1 (TGF-β1) promotes myofibroblast activation and ECM proteins expression through intracellular Smads activation, having an important role in renal fibrosis. We have recently reported that the heterozygous disruption of the TGF-β1 receptor activin receptor-like kinase 1 (ALK1) leads to an increase in TGF-β induced renal fibrosis after ureteral obstruction. Thus, we analyzed the effect of ALK1 heterozygosity in TGF-β1 induced signaling and its consequent fibrotic response in mouse embryonic fibroblasts (MEFs). We have analyzed Smad signaling pathaways in ALK1 heterozygous MEFs (ALK1+/-) and their respective controls (ALK1+/+) in basal conditions and after TGF-β1 treatment by Western blot and immunofluorescence. Moreover, we have analyzed collagen I, fibronectin and connective tissue growth factor (CTGF) expression in basal conditions, after TGF-β1 stimulation and after ALK5 inhibition –with SB431542- and Smad3 inhibition –with SIS3-. TGF-β1 stimulation induced Smad2 and Smad3 phosphorylation and Smad2/3 translocation into the nucleus in ALK1+/+ and ALK1+/- MEFs, being this increase higher in ALK1+/- MEFs. Basal Smad2 and Smad3 phosphorylation was higher in ALK1 heterozygous fibroblasts. TGF-β1 stimulation did not induce Smad1 phosphorylation in ALK1+/- MEFs and a very small Smad1 phosphorylation in ALK1+/- MEFs. ALK1 heterozygous MEFs expressed more collagen I, fibronectin and CTGF than their respective controls in basal conditions. Stimulation with TGF-β1 lead to an increase in collagen I, fibronectin and CTGF, being the increase in fibronectin and CTGF higher in ALK1+/- MEFs. Inhibition of ALK5 and Smad3 reversed the ALK1+/- phenotype. Summarizing, ALK1 heterozygous disruption leads to an impairment of TGF-β1 signaling and increased TGF-β1-induced fibrotic response in mouse embryonic fibroblasts.

http://dx.doi.org/10.1016/j.nhtm.2014.11.050