ABSTRACT WITHDRAWN

TRPV4 AND FGF2 MAY BE IMPLICATED IN BRONCHIAL WALL REMODELLING UNDER MECHANICAL STRESS IN THE AIRWAYS OF ASTHMA AND COPD PATIENTS

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Background and Aims: Mechanical compression of the bronchial walls occurring during bronchoconstriction in asthma and COPD and often referred as mechanical stress may cause airway remodelling with progressive loss of lung function over time. The aim of the present study was to explore the molecular aspects of airway remodelling under mechanical stress in vivo in patients with asthma and COPD.

Methods: The study enrolled 60 patients including 28 with asthma, 22 with COPD and 10 with chronic bronchitis (CB). Mechanical stress was simulated by 5-min isocapnic (5% CO2) inspiratory resistive breathing with load at 45% of maximum inspiratory pressure. Concentrations of TGFβ1 and FGF2 were measured in exhaled breath condensate by ELISA before and after the challenge. Airway remodelling was assessed directly by CT (WA%) and indirectly by reversibility test with salbutamol. Expression of TRP channels was quantified in nasal epithelium by qRT-PCR.

Results: In response to the challenge TGFβ1 increased by ≥20% in 41% of CB, 23% of asthma and 26% of COPD patients. Corresponding increase of FGF2 was observed in 30% of CB, 21% of asthma and 50% of COPD cases. In general, TGFβ1 and FGF2 responses were interrelated (r=0.26, P=0.04). Relative change in FGF2 concentration (∆FGF2) was inversely correlated with the response to bronchodilator (ΔFEV1 r=−0.3, P=0.02), especially in the patients with baseline FEV1<−80% (ΔFEV1 r=−0.46, P=0.006). Furthermore, ∆FGF2 was significantly correlated with bronchial wall area (WA10b r=0.44, P=0.002). At the same time, the response of FGF2 was related to the expression of TRPV4 (r=0.6, P=0.002) and TRPV2 (r=0.4, P=0.03).

Conclusions: Airway remodelling developing under mechanical stress in asthma and COPD may be mediated by excessive production of FGF2 which in turn may arise from upregulation of TRPV4 or TRPV2 mechanosensitive channels in the airway epithelium. The study was supported by RSF (project 18-75-10028).

ABSTRACT WITHDRAWN

ALPHA-MANGOSTIN INHIBITS CD4+ T CELL AND MAST CELL ACTIVATION VIA THE CA2+ RELEASE ACTIVATED CA2+ CHANNEL

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Background and Aim: Intracellular calcium signalling cascades are crucial for early and late allergic responses involving mast cell degranulation and type 2 helper T cell activation, respectively. Both responses are accompanied by calcium movement through the calcium release activated calcium (CRAC) channel, encoded by the ORAI1 gene. Moreover, patients with genetic defects affecting ORAI1 exhibit severe combined immune deficiency syndrome and deficits in CRAC channel function. Therefore, inhibitors of the ORAI1 channel represent an attractive therapeutic target for the alleviation of inflammatory diseases.

Xanthones are natural organic compounds isolated from the pericarp of mangosteen (Garcinia mangostana L.). Among the xanthones, α-mangostin exhibits anti-inflammatory and anti-allergic effects; however, its effects on calcium signalling have not been reported. This study investigated whether α-mangostin reduces CRAC currents (ICRAC), and thus, inhibits mast cell degranulation and T cell activation.

Methods: Human STIM1 and ORAI1 co-expressing HEK293T cells were treated with α-mangostin for an electrophysiological study. Modulation of ICRAC activity was examined using a conventional whole-cell patch-clamp technique. Jurkat T cells (human immortalized T lymphocyte cell line) and RBL-2H3 cells (rat basophilic leukemia cell lines) were treated with α-mangostin for proliferation assay and β-hexosaminidase assay.

Results: We found that α-mangostin significantly inhibited ICRAC activity in STIM1 and ORAI1 co-expressing HEK293T cells and T lymphocytes (Jurkat T lymphocytes, IC50: 1.29 ± 0.06 μM). In addition, we showed that the elevation of intracellular free Ca2+ concentration in anti-CD3/CD28 co-stimulated T lymphocytes was significantly inhibited by α-mangostin (10 μM). T cell proliferation induced by co-stimulation with anti-CD3/CD28 and RBL-2H3 mast cell degranulation by stimulation of high affinity IgE receptor were both inhibited after treatment with 10 μM α-mangostin (89.4 ± 1.93% inhibition).

Conclusions: Our findings suggest that α-mangostin is a promising therapeutic agent for the prevention and treatment of allergic diseases.

GHRELIN ATTENUATES LIPOPOLYSACCHARIDE-INDUCED ACUTE LUNG INJURY INDEPENDENTLY OF VAGUS NERVE CIRCUIT

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Background and Aims: Ghrelin, an endogenous ligand for the growth hormone secretagogue receptor (GHSR), is produced in the stomach, stimulates food intake by neural activity via vagus nerve. We previously reported ghrelin suppresses lung inflammation in mice with bleomycin induced lung injury (Eur J Pharmacol. 2011; 672: 153-8). In this study, we investigated whether ghrelin attenuates acute lung injury through vagus nerve activity by using mice with lipopolysaccharide (LPS) induced lung injury.

Methods: We administered ghrelin (10 nmol/mouse, twice a day) or PBS intraperitoneally to the 10-weeks-old C57BL6 mice with or without bilateral cervical vagotomy. Mice were intratracheally administered 5 mg/kg of LPS or PBS. At 24 hours after administration of LPS or PBS, mice were anesthetized by intraperitoneal injection of medetomidine, midazolam and butorphanol and sacrificed. Measurements of ghrelin levels were analyzed by two-site immunoenzymometric assay. The expression levels of pro-inflammatory cytokines in lungs were examined by quantitative real-time PCR. The concentration of pro-inflammatory cytokines in BALF was measured by ELISA.

Results and Conclusions: The plasma ghrelin levels in the LPS injected mice and ARDS patients were significantly lower than those in PBS injected mice and healthy volunteers, respectively. In LPS injected group, ghrelin-treated mice without vagotomy had smaller reductions in food intake and body weight than PBS-treated mice. The effects of ghrelin on food intake and body weight reduction were diminished in vagotomized...
mice. On the other hand, ghrelin treatment decreased the expression levels of IL-1β, IL-6, TNF-α, and CXCL2 mRNA in lungs and concentration of IL-6, TNF-α and CXCL2 in BALF in LPS injected mice with or without vagotomy. Our data indicated that the anti-inflammatory effect of ghrelin is independent of vagus nerve circuit and to restore ghrelin level may be an attractive therapeutic target in the patients with ARDS.

AP1652

EGFR MUTATIONS IN TISSUE SAMPLES AND RELATED FACTORS IN VIETNAMESE NON-SMALL CELL LUNG CANCER PATIENTS OVER 60 YEARS OLD
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Backgrounds and Aims: Non-small cell lung cancer (NSCLC) is one of the most common cancers and high mortality rates. The majority of patients is the elderly, diagnosed at advanced stages because initial symptoms are common poor and vague, the elderly tending to be less tolerated with chemotherapy. Targeted therapy is a effective new treat-ment for NSCLC patients with EGFR mutations. This study aims to describe EGFR mutation status detected in tissue samples and analyse some related factors in Vietnamese NSCLC patients over 60 years old.

Methods: A total 351 tissue samples collected from 351 NSCLC patients over 60 years old diagnosed at The Nuclear Medicine and Oncology Center, Bach Mai Hospital during 2017 – 2018. Detect EGFR mutations by combining PCR with Hybrid Molecular Probe method, use EGFR XL StripAssay Kit for testing tissue samples.

Results and Conclusions: EGFR mutations were discovered in 38.2% (134/351) NSCLC patients. The EGFR mutation were exon 19 deletion mutations (48.6%), exon 21-point mutations (41.6%), exon 18 point mutations (4.9%), resistant mutation T790M on exon 20 (4.9%). The mutant rate in females was higher than in males (66.7% versus 27.5%); and higher rate in non-smokers compared to smokers (53.3% versus 30.3%). In conclusion, the EGFR mutation ratio in NSCLC patients over 60 years was relatively high, the frequent mutant sites were exon 19 and 21. Mutations are more common in women and non-smokers.

AP1655

CHARACTERISTICS OF EGFR MUTATIONS IN PLASMA SAMPLES FROM VIETNAMESE NON-SMALL CELL LUNG CANCER PATIENTS
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Backgrounds and Aims: Detection for EGFR mutation in plasma samples on non-small cell lung cancer (NSCLC) patients have recently been widely used to assess the suitability of targeted therapy by tyrosine kinase inhibitors (TKIs) and follow-up treatment response. The research aims to describe EGFR mutation status detected in plasma samples and analyse some related factors in Vietnamese NSCLC patients.

Methods: A total 136 plasma samples were collected from 136 NSCLC patients diagnosed at Bach Mai Hospital during 2017-2018. Detecting EGFR mutations by Real-time PCR technique, using cobas® EGFR mutation Test v2 kit for plasma samples.

Results and Conclusions: EGFR mutations were detected in 56/136 (41.2%) plasma samples. T790M mutation accounted for 24% of 75 mutations detected. The rate of EGFR mutations in females was higher than in males (50.8% versus 33.8%); and show higher rate in non-smokers compared to smokers (49.4% versus 30.5%); the T790M mutation rate in treated patients with TKIs was more common than in non-treated patients (20.5% versus 0.0%). In conclusion, the rate of EGFR mutations in plasma samples was relatively high. The distribution of mutations shows mainly exon 19 frame deletion, L858R on exon 20, T790M mutations were common in treated patients with TKIs.

Clinical Allergy and Immunology

AP1027

AIRWAY MUCIN MUC5AC PRODUCTION IS INCREASED IN PATIENTS WITH CHRONIC EOSINOPHILIC PNEUMONIA
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Background: Eosinophilic pneumonia (EP) is characterized by massive infiltration of eosinophils into the lungs. Although eosinophils have been linked to mucus plug formation, the production of airway mucins in eosinophilic pneumonia is unknown.

Aims: To examine whether concentration of airway secreted mucin MUC5AC is elevated in the bronchoalveolar lavage fluid (BALF) of patients with EP.

Methods: Diagnostic bronchoalveolar lavage (BAL) was performed via fibreoptic bronchoscopy in according to established guidelines. After the BAL, patients who met criteria for EP (elevated BAL eosinophil count greater than 25%) and patients who showed no apparent lung disease (control, n=8) were enrolled to this study. The absolute concentration of MUC5AC in BAL fluids was measured by ELISA.

Results: EP patients were clinically diagnosed with chronic eosinophilic pneumonia (CEP, n=5), drug-induced pneumonia (n=2), acute eosinophilic pneumonia (AEP, n=1). All CEP patients were diagnosed with asthma. The mean percentage of eosinophils in BAL fluids in EP was 60±24%, the data that were not signifi-cantly different among the diseases. The MUC5AC levels were significantly higher in patients with CEP

Figure 10271

Respirology (2019) 24 (Suppl. 2), 98–261