595 Stratum corneum lipid biomarkers at two months of age predict future onset of atopic dermatitis

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RATIONALE: It has been hypothesized that skin barrier function in early human life determines the onset of atopic dermatitis (AD) and atopic march. Finding early signs of skin abnormalities in newborns before the onset of AD may identify infants at risk to develop AD who can benefit from skin barrier enhancing therapies.

METHODS: Newborns (n=119) with and without family history of atopic diseases (risk group, n=79, control group, n=40) were enrolled in Seoul, Republic of Korea. Skin tape strips (STS) were collected from the volar area of the forearm at the age of two months before any signs of clinical AD, and children were clinically monitored until their age of two years. STS were subjected to lipidomic and proteomic analyses by the LC/MS/MS.

RESULTS: Overall, 21/79 (26.6%) and 5/40 (12.5%) infants developed AD in the high-risk group and the control group, respectively (P=0.079). Univariable Cox regression analysis did not reveal significant predictive clinical factors for the development of AD. Lipidomics identified a decrease in the content of total protein-bound ceramides (median values 5360 vs 3864 pmol/mg protein, p=0.0001, healthy versus future AD subjects, respectively) as one of the strongest parameters associated with higher risk of AD development. Increased content of unsaturated sphingomyelin species and short-chain NS-and AS-ceramides were also associated with higher risk of AD development. Proteomics revealed a decreased expression of ALOX12B, ALOXE3, and SDR9C7 enzymes needed to form protein-bound ceramides in future AD subjects.

CONCLUSIONS: Early life STS lipidomic analyses can identify infants at risk of future development of AD.

596 Association of Atopic Dermatitis with Proximity to Major Roads

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RATIONALE: The clinical association between traffic-related air pollution (TRAP) and atopic dermatitis (AD) was recently described in urban cohorts in Asia. The goal of our study was to determine if a similar effect is observed in a large clinical population in Colorado, USA, including both urban and rural residents.

METHODS: A 13-year retrospective chart review was completed of patients aged 0-18 years presenting to a pediatric department in Denver, Colorado. Patients were identified with AD using a search of diagnostic codes and compared to an age and sex matched control group of children without AD. Patient residential addresses were geocoded to coordinates and distance from a major road with an average annual daily traffic of over 10,000 vehicles was calculated using The R Project for Statistical Computing (R). Traffic data was obtained from the Colorado Department of Transportation (CDOT). Linear regression was completed with distance from a major road as a predictor of AD.

RESULTS: Residential distances to major roads were calculated for 7384 AD patients and 7241 controls. An 18.8% decrease in odds of AD for each factor 10 increase in distance from a road (p=0.000015) was noted. Children living greater than or equal to 1000 m from the nearest major road had a 26.1% (95% CI: 13.4, 36.9; p=0.0002) lower odds of AD than patients living within 500 m from the nearest major road.

CONCLUSIONS: Increasing distance from a major road is associated with decreasing risk of AD. Future studies are needed to determine the pathophysiological mechanisms of this clinical association.

597 Dupilumab Reduces Exacerbations And Improves Lung Function Regardless Of Prior Asthma Exacerbation Status: LIBERTY ASTHMA TRAVERSE Open-Label Extension Study

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RATIONALE: Prior asthma exacerbations have been associated with lung function decline and increased risk of future exacerbations. Dupilumab, a human monoclonal antibody, blocks IL-4/IL-13, key central drivers of type 2 inflammation. We investigated the relationship between prior exacerbations and lung function in patients with moderate-to-severe type 2 asthma (blood eosinophils ≥150cells/μL or FeNO ≥25ppb at parent study baseline [PSBL]) from QUEST (NCT02414854) who enrolled in TRAVERSE (NCT02134028).

METHODS: Patients on dupilumab in QUEST continued in TRAVERSE up to 96 weeks (dupilumab 300mg q2w; dupilumab/dupilumab arm); patients on placebo in QUEST initiated dupilumab on entering TRAVERSE (placebo/dupilumab arm). Endpoints were: annualized severe exacerbation rates (AER) and change from PSBL in pre-bronchodilator percent-predicted (pp) FEV_1 in non-exacerbators (0 exacerbations) and exacerbators (≥1 exacerbations) during QUEST.

RESULTS: In QUEST, dupilumab significantly reduced AER and improved lung function. During TRAVERSE, dupilumab further reduced AER in the exacerbator group (0.78 and 0.56 in dupilumab/dupilumab and placebo/dupilumab arms, respectively), and maintained low AER (0.11 and 0.17, respectively) in the non-exacerbator group. Dupilumab sustained lung function improvements during TRAVERSE. Mean (SD) $ppFEV_1$ at TRAVERSE Week 0 was 65.0 (17.3) and 73.3 (15.8) in dupilumab/dupilumab arm, and 60.4 (16.0) and 68.0 (16.0) in placebo/dupilumab arm in exacerbator and non-exacerbator groups. By Week 96, dupilumab improved $ppFEV_1$ to 67.2 (17.1) and 72.8 (16.2) in the dupilumab/dupilumab arm, and 70.8 (15.2) and 71.4 (17.3) in the placebo/dupilumab arm, respectively.

CONCLUSIONS: Dupilumab significantly reduced AER, improved lung function in the placebo/dupilumab arm, and showed sustained improvement in the dupilumab/dupilumab arm regardless of prior exacerbation status.

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