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MIR-26A DESENSITIZES NON-SMALL CELL LUNG CANCER CELLS TO TYROSINE KINASE INHIBITORS BY TARGETING PTPN13

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Background and Aims: Epidermal growth factor receptor (EGFR)-targeted tyrosine kinase inhibitors (TKIs) have emerged as first-line drugs for non-small cell lung cancers (NSCLCs). However; the resistance to TKIs represents the key limitation for their therapeutic efficacy. This paper is going to study the molecular mechanism and the effect of miR-26a on the development of EGFR-TKI resistance in NSCLCs.
Methods: Cell culture; bioinformatic analysis; molecular biological technologies and xenograft modoels were employed in this study to elucidate the regulatory function of miR-26a to PTPN13 expression and its role in the acquirement of EGFR-TKI resistance.
Results: We found that miR-26a was upregulated in gefitinib-refractory NSCLCs; miR-26a is downstream of EGFR signaling and directly targets and silences protein tyrosine phosphatase non-receptor type 13 (PTPN13) to maintain the activation of Src; a dephosphorylation substrate of PTPN13; thus reinforcing EGFR pathway in a regulatory circuit. miR-26a inhibition significantly improved NSCLC responses to gefitinib.
Conclusions: This study unraveled the regulatory roles of miRNA(s) in EGFR-TKI responsiveness of NSCLCs; and thus hold out great promise for miR-26a as a potential target for treatment of EGFR-TKI resistant NSCLCs.

ORAL PRESENTATION 12 - CLINICAL RESPIRATORY MEDICINE + PULMONARY CIRCULATION + RESPIRATORY STRUCTURE AND FUNCTION: ADVANCED IN PULMONARY LABORATORY

APSR6-0157

REFERENCE VALUES OF IMPULSE OSCILLOMETRY IN HEALTHY PRESCHOOL CHILDREN FROM SOUTHEAST CHINA

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Background and Aims: The impulse oscillometry system (IOS) is a simple and noninvasive technique for measuring lung function during tidal breathing. However, the reference values available in Chinese preschool children are limited. The purpose of our study was to present the reference equations of IOS parameters in healthy preschool children in Southeast China.
Methods: IOS was performed in healthy Chinese children aged 3-6 years to measure respiratory resistance (Rrs) and respiratory reactance (Xrs) at various frequencies, respiratory impedance (Zrs), and resonance frequency (RF). The relationships between IOS value and demographic data (age, height, and weight) were analyzed by regression analyses.
Results: IOS was performed in 537 (287 boys,250 girls) healthy Chinese children The IOS measurements were presented as means and standard deviations. Linear regression identified height as the best predictor of Rrs and Xrs. Using multiple regressions based on age, height, and weight, we determined regression equations and coefficients of determination (R^2) for boys ($Rrs_5 = 3.451 - 0.024 \times Height + 0.015 \times Weight - 0.003 \times Age$, $R^2 = 0.510$) and for girls ($Rrs_5 = 3.380 - 0.025 \times Height + 0.017 \times Weight$, $R^2 = 0.482$).
Conclusions: This study provided reference values for IOS measurements of healthy preschool children from Southeast China. These data provide references for diagnosing and monitoring respiratory diseases in preschool children.

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REFERENCE DATA FOR BABYBODY PLETHYSMOGRAPHIC MEASUREMENTS IN CHINESE CHILDREN UNDER 2 YEARS OLD

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Background and Aims: Population-specific pulmonary function reference data are essential to identify the nature and severity of respiratory disease. However, there is a lack of reference data for Chinese neonates and infants.To develop reference data for tidal breathing and plethysmographic measurements for Chinese infants during the first 2 years of life.
Methods: Data of tidal breathing and plethysmography from healthy Chinese neonates and infants using the Jaeger MasterScreen BabyBody were collated. Data were excluded if gestational age was <37 weeks or birth weight was <2.5 kg or a positive history of neonatal respiratory distress or prior respiratory tract infection. Multiple linear analyses were performed to determine various parameters of the pulmonary function measurements. Reference equations for outcomes were constructed via multilevel-multivariable analysis. The LMS (lambda-mu-sigma) method was used for calculating smoothed reference percentiles.
Results: Four hundred and ten healthy children were tested; acceptable and repeatable measurements of tidal breathing analysis and plethysmography outcomes respectively were 396(96.6%) and 370(90.4%). Normal reference data, reference percentiles and equations for main parameters of tidal breathing and plethysmography were derived from test occasions of 211 neonates and 185 infants beyond the neonatal period. Bodyweight, crown–heel length and age were significantly associated with infant lung function, of which length was the strongest predictor. The first 12 months after birth were the peak time of lung development, especially during the first 6 months, during which values of FRC_P and VT had the most marked rise. Reference equations were developed as follows: $FRC_P = 3.87\ L + 2.37A - 142.4$, $Reff = 9.61 - 0.093\ L$, $VT = 0.81\ L + 3.12\ W + 0.58A - 25.6$ and $TEF_{25} = 1.2\ L - 26.9$.
Conclusions: This study provides reference standards for BabyBody -plethysmographic measurements in healthy Chinese children in the first 2 years of life, highlighting the importance of using population-specific data.

APSR6-0402

SPIROMETRY REFERENCE NORMS FOR 13-14 YEAR OLD SRI LANKAN CHILDREN

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Background and Aims: Spirometry reference norms have only been reported for Peak Expiratory Flow Rate (PEFR) in Sri Lankan children. The aim of this study was to construct prediction equations for spirometry in Sri Lankan children aged 13-14 years.
Methods: Spirometry was performed in 2078 healthy 13-14 year old Sri Lankan children (1023 boys (49.2%) and 1055 (50.8%) girls) according to American Thoracic Society guidelines. Forced Vital Capacity (FVC), Forced Expiratory Volume in the first second (FEV_1), PEFR and Forced Mid-Expiratory Flow Rates (FEF25-75%) were measured. Correlation coefficients were established between each parameter and standing height, weight, and age. The functions were regressed over all possible combinations of variables separately for boys and girls.
Results: There were significant correlations between spirometry parameters and height and weight in both genders. There were significant correlations between age and PEFR, FEF25 and FEF50 in males and age and FEV_1, PEF and FEF25-75% in females. The prediction equations in males for FVC: 0.047height + 0.0007age– 4.66; for FEV_1: 0.041height + 0.016age – 4.22; for PEFR: 0.074height + 0.123age – 7.59 and FEF25-75%: 0.042height + 0.066 age – 4.36.
The equations in females for FVC: 0.028height + 0.031age – 2.36; for FEV_1: 0.027height + 0.047age – 2.57; for PEFR: 0.038height + 0.159age – 2.93 and FEF25-75%: 0.02height + 0.136age – 3.18.
Conclusions: Height and age influence ventilatory parameters and could be used to assess lung functions in Sri Lankan children.