

WG1-WG2-WG3-WG4-WG5-WG6-WG7

Ege University Translational Pulmonology Group's Ongoing Projects and Future Expectations

Ozlem Goksel¹, Levent Pelit², Fusun Pelit², F. Nil Ertas², Burak Ordin³, Arif Gursoy³, Sinan Akgol⁴, Emir Caliskan⁴, Ulku Yavasogullari⁵, Cumhur Gunduz⁶, Emin Karaca⁷, Asude Durmaz⁷, Ayca Aykut⁷, Ali Veral⁸, Deniz Nart⁸, Yasemin Baskin⁹, Gizem Calibasi⁹, Canan Demir¹⁰, NeJdiye Mazican¹⁰, Nur Toreyin¹⁰, Meral Turk¹⁰, Tuncay Goksel¹

¹Ege University, Faculty of Medicine, Department of Pulmonary Medicine, Division of Immunology and Allergy ⁶Ege University, Faculty of Medicine, Department of Medical Biology
²Ege University, Faculty of Science, Department of Chemistry ⁷Ege University, Faculty of Medicine, Department of Genetics
³Ege University, Faculty of Science, Department of Mathematics ⁸Ege University, Faculty of Medicine, Department of Pathology
⁴Ege University, Faculty of Science, Department of Biochemistry ⁹Dokuz Eylul University, Oncology Institute, Division of Immuno-Oncology
⁵Ege University, Faculty of Science, Department of Biology ¹⁰Ege University Faculty of Medicine, Department of Public Health and Occupational Health&Diseases

Spin-off projects of CA 15129

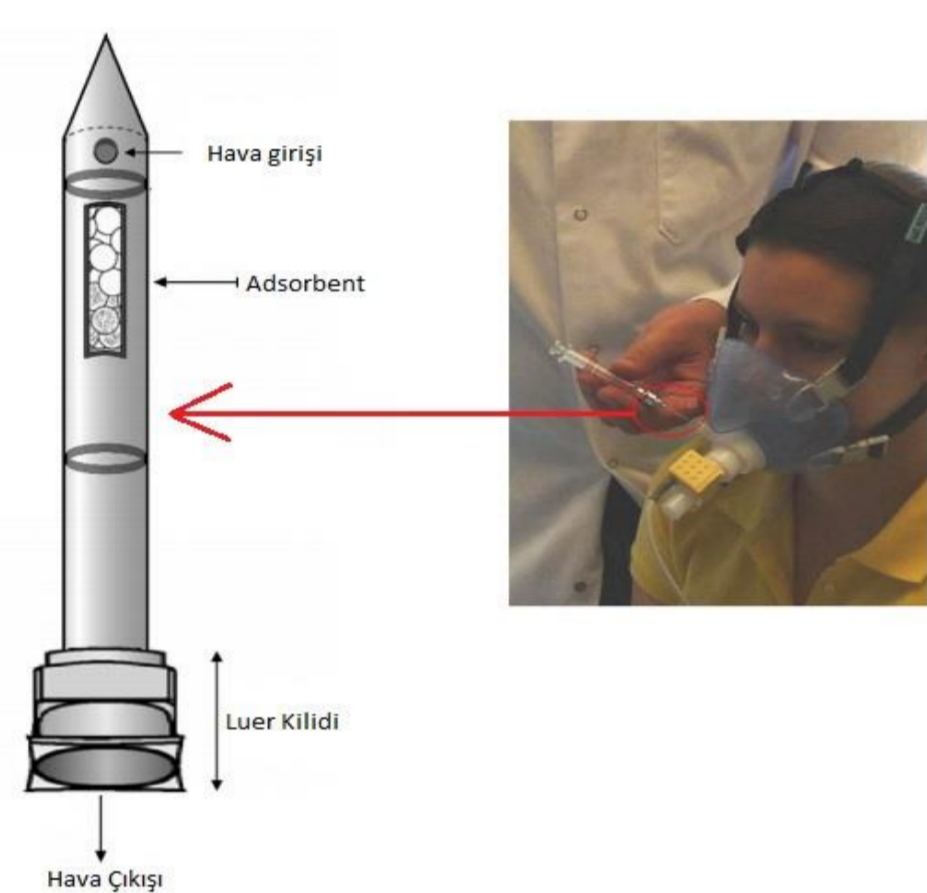
Candidates

DETERMINATION OF MOLECULAR ASTHMA ENDOTYPES BY EXHALED VOLATILE ORGANIC COMPOUNDS AND PERIPHERAL BLOOD MICRORNA BIOMARKERS (VOC/micRNA-Endotype)

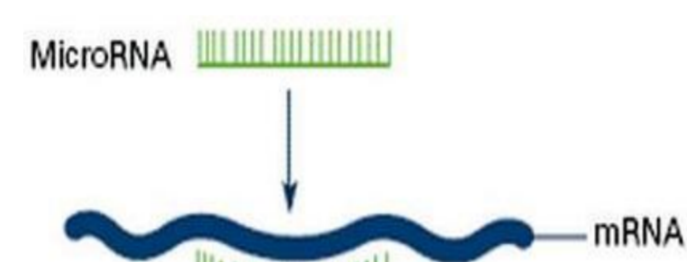
TUBITAK (Scientific and Technological Research Council of Turkey)-COST 2515 Connection Project

Aim: Molecular endotyping and biomonitoring of asthmatic patients via molecular biomarkers; exhaled VOCs and peripheral blood miRNAs were targeted for this research.

Method: After entering detailed data regarding demographical features of patients and clinical presentations of asthma, Exhaled Breath Nitrous Oxide (FeNO) levels, induced sputum inflammatory cell amounts, VOC analyses by GC-MS matched needle trapped selective adsorbent systems (NTD) and peripheral blood microRNAs are going to be assessed in both asthma patients (250 patients) and healthy controls (100 Controls).



VOC	Tipi
1,1,1,1-Tetra(cyclopentane)	Sikloalkan
1,2-dimethylsiloxane	Aromatik hidrokarbon
2,2-dimethyl heptane	Alkan
2,4-dimethylpentane	Alkan
2,6,10-trimethyl dodecane	Alkan
2,6,11-trimethyl dodecane	Alkan
2-methylpentane	Alkan
2-methylpentane	Alkan
2-undecenal	Aldehit
3,7-dimethyl undecane	Alkan
4-methyl-2-pentanol	Aldehit
4-methylöctane	Alkan
acetic acid	Karboksilik asit
allyl methyl sulfoxide	Miscellaneous
benzyl alcohol	Aromatic alkol
ethylacetone	Aromatic alkol
isoprene	Ketma
limonene	Aromatik hidrokarbon
naphthalene	Aromatik hidrokarbon
propylalcol	Alkol
n-pentane	Alkan
Octane	Alkan
terpeneol	Ketma
tridecane	Alkan



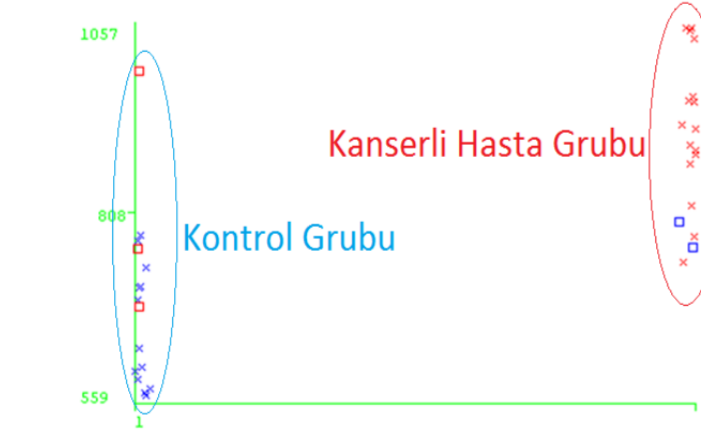
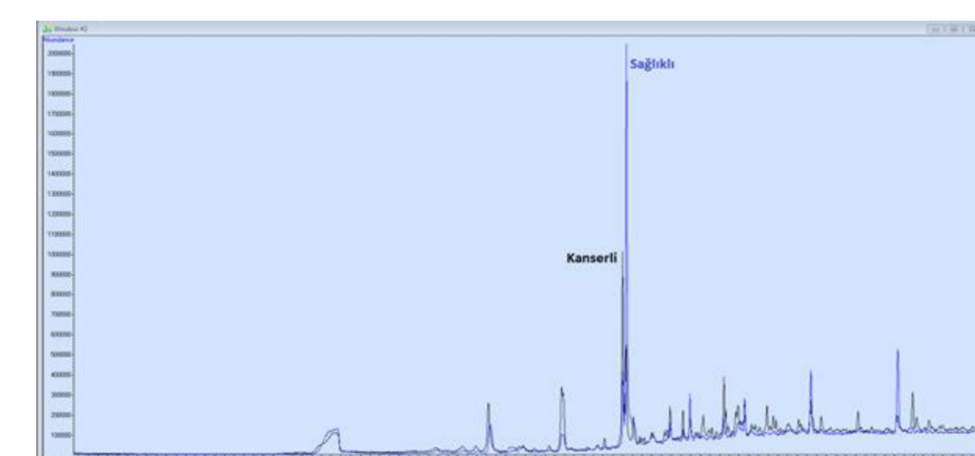
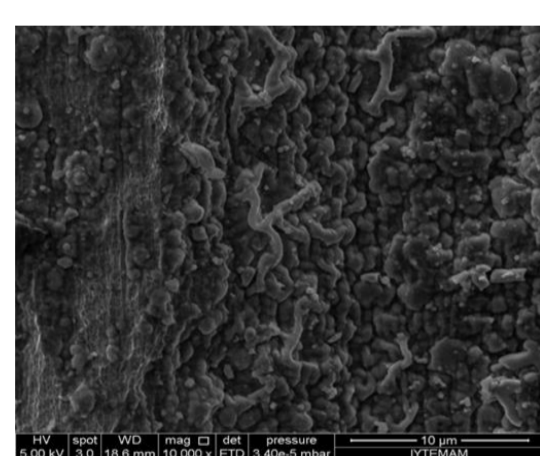
Let-7, miRNA-126, miRNA-10a, miRNA-708, miRNA-133a, miRNA-17, miRNA-19a, miRNA-21, miRNA-106a, miRNA-145a, miRNA-155, miRNA-221 are miRNAs going to be studied (miRNAs that are shown as linked with asthma in the literature)

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Grant: 130.000 Euro
Duration: 3 years
Ethical approval: Ege University Ethical Committee (February 2016)

DEVELOPMENT OF A NONINVASIVE METHOD FOR BIOMARKER DETERMINATION IN HUMAN BREATH FOR EARLY DIAGNOSIS OF LUNG CANCER (VOC-Lung Cancer)

Aim: Lung cancer is the major cause of cancer death in the World. Low dose CT screening for early diagnosis has still had some problems due to high rate of false-positive results. There is urgently need to new, in particular non-invasive biomarkers in the early diagnosis of lung cancer. The main objective of this study is to detect role of volatile organic compounds (VOCs) as potential biomarkers in early diagnosis of lung cancer.

Method: The thin film of polymers were coated electrochemically on a stainless steel wire by using cyclic voltammetry (CV) and following the surface characterization by using several techniques, the fibers were placed in breath masks to enrich the analytes in human breath. Newly diagnosed lung cancer patients and healthy and asthmatic controls included into this prospective-case control study. Breath samples were collected via lab-made sample collector where the VOC content was enriched on a lab-made polythiophene solid phase microextraction (SPME) fibers. Then, the VOC content was analyzed by inserting into injection port of a gas chromatography coupled with mass detector (GC-MS) allowing



Funded by: TUBITAK
Grant: 130.000 Euro
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VOC-Severe Asthma (ERS 2016)

Defining severe allergic asthma by molecular fingerprints may help developing proper protective measurements and individualized treatments. Volatile Organic Compounds (VOCs) are the most studied biomarkers in exhaled breath samples today and they seem promising for molecular endotyping of asthma. Objective of this study is defining molecular endotypes of severe allergic asthma patients via VOCs fingerprint in exhaled air. Severe allergic asthma patients according to the GINA2015 were included in this prospective case-control study, along with healthy controls. Atopic status was determined by skin-prick testing/specific IgE measurements in patients' blood. Breath samples were collected via lab-made sample collector where the VOC content was enriched on a polythiophene solid phase microextraction (SPME) fibers. Then, the VOC profile was analyzed by inserting into injection port of a gas chromatography coupled with mass detector (GC-MS) allowing thermal desorption. Commercial Carboxen/Polydimethylsiloxane SPME fiber was also utilized. A total of 27 severe allergic asthma patients along with 42 healthy controls' breath samples were collected and analyzed. The results were interpreted with chemometric approach by using Neural Network classification algorithm in WEKA. According to the first preliminary results of the study; this technique is able to significantly discriminate between patients with asthma and controls with greater accuracy. There was significantly different signal level of VOCs mixture in NN classification algorithm. The using algorithm in WEKA gave a sensitivity of 95.6%, a specificity of 95.8% with a success rate of 88.6% in the training set.

USAGE OF LIQUID AND VOLATILE BIOPSY IN PERSONALIZED MOLECULAR DIAGNOSIS AND BIOMONITORING OF LUNG CANCER PATIENTS (Lung Cancer/Liquid and Volatile Biopsies)

Under leadership of EGE Translational Pulmonology Research Group (EGE TPRG), we are preparing a new multi-institutional collaborative project proposal to present the Scientific and Technological Research Council of Turkey (TUBITAK). This multi-institutional collaborative group will include 4 universities, 13 departments and 30 investigators (pulmonologists, medical and basic oncologists, geneticists, molecular biologists, pathologists, chemists (30 investigators). If the project will be found as successful in initial evaluation by the TUBITAK, the detailed negotiations will start for final evaluation.

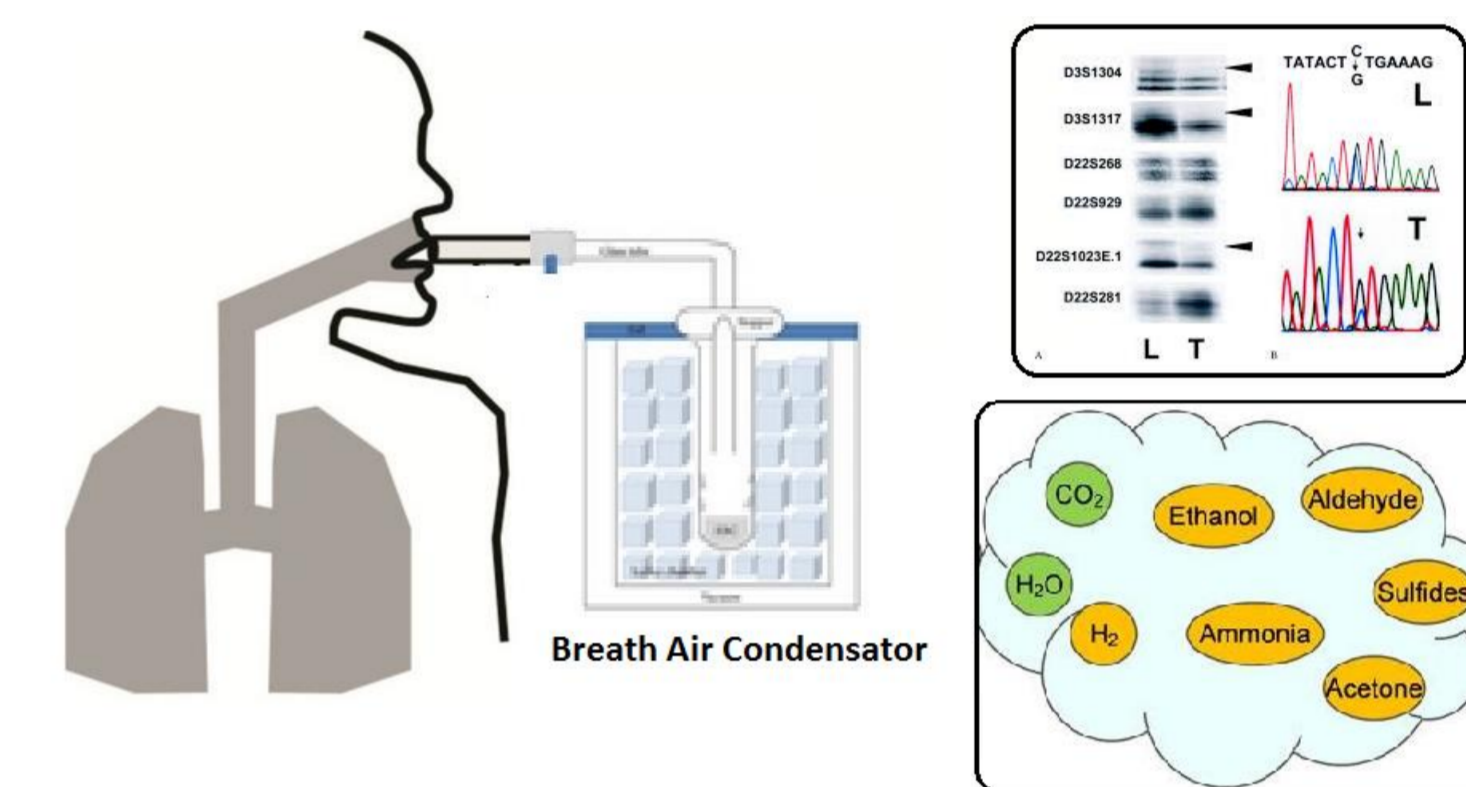
Aim: The main objective of this project; to develop a new non-invasive methodology using exhaled breath and bloods for early molecular diagnosis and biomonitoring of lung cancer.

Method: In this project, driver mutations will be investigated in cfDNA obtained blood (liquid biopsy) and exhaled breath condensate (volatile biopsy)

Demand budget: 300.000 Euro

Duration: 36 months

Ethical approval: Ege University Ethical Committee (02/06/2016; NO: E.90181)



EXPOSURE TO INDOOR AIR POLLUTANTS AND THEIR EFFECTS ON CHRONIC RESPIRATORY DISEASES (Indoor pollutants and chronic airway diseases)

Aim: We aim to investigate the possible causality reasons between exposure to indoor particulate matters and emerging chronic airway diseases from randomly selected homes near 50 m border of one of big-highways of Izmir City (Indoor environment monitoring). We also aim to observe possible reflections of these exposures on the patients breath VOCs analyses who will be determined as having asthma/COPD (Monitoring) during the study.

Method: Step 1. Observational cross sectional part. Number 220, 221, 223 and 263 have been selected as statistically by public health specialist to represent the area. All off these streets are located 50 m. next to the highway and consisted of 58 buildings and 398 apartments with 1271 habitants (Population Directorate of Izmir Municipality, 2016). At least 318 sampling has been targeted with minimum 143 sampling size. To spend at least 8 hours in a day in the same house and being resident in this house for at least 1 year are the inclusion criterias including subjects into the study.

Indoor environment monitoring for PM2.5, PM4.0, PM10.0 particulate matters, toxic gases, CO2 and selected some common VOCs such as ethan, penthane, benzene, methylene chloride, styrene, tetrachloroethylene, toluene, m-p-xylene, o-xylene etc. from bedrooms of homes for at least 4 hours per one day and will be repeated at every 6 months during 3 years.

Step 2. Nested case control part. European Respiratory Health Survey will perform to study population. Demographic variable, comorbidities, indoor environment variables will be recorded. Among subjects a further spirometric analyses are planned to whom having positive questionnaire results suggest chronic airway diseases asthma/COPD. Remain willing ones, with normal survey results, considering age and gender will generate a well-matched Control Group. Both Study and Control Groups will evaluate with exhaled breath analysis. The specific methodology previously described by our chemistry group valid also for this study.



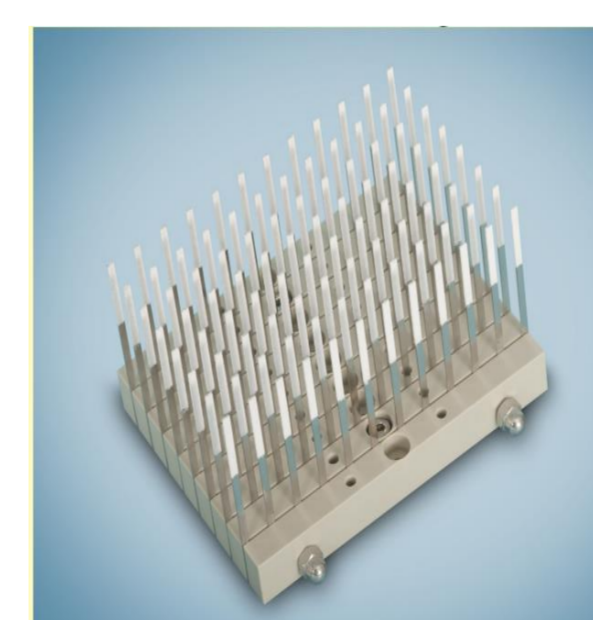
The 3M EVM-7 environmental monitor simultaneously measures particulates, volatile organic compounds (VOCs) with PID, toxic gas, carbon dioxide, relative humidity, temperature, and air velocity. EVM-7 is for worksite monitoring, industrial hygiene surveys, air quality assessment, VOC screening and monitoring.

Granted by: Ege University Scientific Research Commission
Budget: 1500 Euro
Duration: 36 months
Ethical approval: Ege University Ethical Committee (January 2016)

DEVELOPMENT OF 96 WELL PLATE THIN FILM EXTRACTION RODS FOR THE DETERMINATION OF SPECIFIC BIOMARKERS PROFILE OF LUNG CANCER PATIENTS (Biomarkers and lung cancer)

Aim: To develop non-invasive, inexpensive, rapid and highly sensitive thin-film micro extraction (IFME) strips for easy screening of different metabolite groups in lung cancer patients.

Method: a total of 96 IFME strips will made a plate system which is able to measure several types of metabolites from patients urine and saliva samples at the same time. The most specific metabolites in patient's urine and saliva samples for lung cancer have been chosen from the literature. Adsorbed metabolites to plate system will be analyzed with LC-GC/QTOF and LC-MS systems after desorbed in a suitable solvent within small volumes.



2-methoxy benzoic acid, 3-methoxy benzoic acid, α-N-phenylacetyl-L-glutamine, betaine, bilirubin, citric acid, creatine, D-proline, glycine, glycolic acid, hippuric acid, Hipoksant'sant's, indoxyl, L-Alanine, L-Carnitine, Levoglukos which, L-proline, N6, N6, N6-trimethyl-L-lysine, N-Asetilglutamine, nicotinamide, pipercolic acid, succinic acid, Taurine, Trigonella of L-Phenylalanine and VOCs such as alcohols, aldehydes, ketones and hydrocarbons were frequently considered as metabolites.

Funded by: TUBITAK and Ege University Scientific Research Commission
Grant: 160.000 Euro
Duration: 2 years
Ethical approval: Ege University Ethical Committee (October 2015)

