ТРАКИЙСКИ УНИВЕРСИТЕТ

Научен Семинар „Европа в моя регион“
05.07.2017 год. , Стара Загора

COST Акция BM1201 Developmental origins of chronic lung disease (CLD) – възможности за споделяне и обмяна на знания и умения и за съвместни научни изследвания.

Проф. Татяна Влайкова

Относно COST

- COST е междудържавна рамкова програма за Европейска координация в областта на науката и технологиите.
- Позволява координиране на Европейско ниво на национално финансираните научни изследвания в определени области.
- Допринася за ограничаване на фрагментирането на Европейските средства за научни изследвания и създава възможности за кооперирание на Европейските учени.

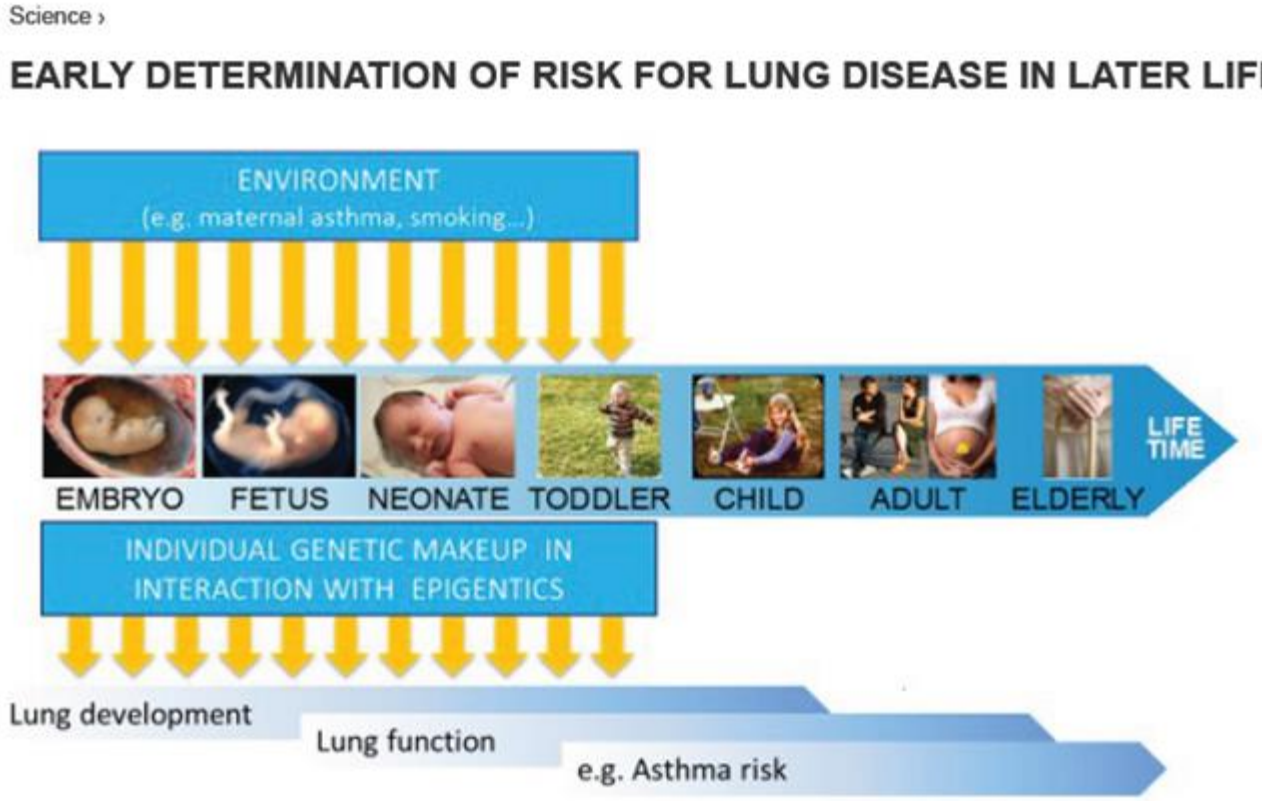
English

DEVELOPMENTAL ORIGINS OF CHRONIC LUNG DISEASE
COST ACTION BM1201

PUBLIC SCIENCE

- COST Акция BM1201 “Developmental origins of chronic lung disease (CLD)” е COST акция в областта на Биомедицината и Молекулярно-биологичната наука (Biomedicine and Molecular Biosciences)

- COST Акция BM1201 имаше за цел обединяване и координиране на Европейски учени от 28 страни проучващи молекулните механизми водещи до повишаване на риска за развитие на хроничните белодробни болести при пре- и ранната постнатална експозиция на организма на увреждащи фактори.



BMBS COST Action BM1201

Parties

Action details

MoU	4116/12
CSO Approval date	07/06/2012
Start of Action	12/12/2012
End of Action	11/12/2016

Biomedicine and Molecular Biosciences COST Action BM1201

Description
Parties
Management Committee

Parties

Country	Date	Country	Date	Country	Date	Country	Date
Austria	05/11/2012	Belgium	03/10/2012	Bosnia and Herzegovina	27/03/2013	Bulgaria	20/08/2013
Cyprus	09/02/2015	Denmark	04/10/2012	Finland	14/08/2012	France	01/10/2012
Germany	02/07/2012	Greece	11/09/2012	Hungary	19/02/2016	Iceland	20/08/2012
Ireland	03/04/2013	Israel	27/03/2014	Italy	28/11/2012	Lithuania	03/10/2012
Malta	28/07/2012	Netherlands	13/08/2012	Norway	08/11/2012	Poland	16/07/2012
Portugal	19/09/2012	Romania	07/09/2012	Serbia	25/07/2013	Spain	16/08/2012
Sweden	20/09/2012	Switzerland	16/07/2012	Turkey	14/11/2012	United Kingdom	02/07/2012

Total: 28

Bulgaria

Prof Evelina SHIKOVA-LEKOVA
MC Member
National Center of Infectious and Parasitic Diseases14A General Stoletov blvd.1233 SofiaBulgaria

Prof Tatyana VLAYKOVA
MC Member
Trakia University, Medical Faculty, Stara Zagora11 Armeiska Str. 6000 Stara Zagora, Bulgaria

Dr Dimo DIMOV
MC Substitute
Medical Faculty, Trakia University, Stara ZagoraArmeiska 116000 Stara ZagoraBulgaria

Management Committee

Chair	Vice Chair
Prof Susanne KRAUSS-ETSCHMANN Research Center Borstel, Leibniz-Center for Medicine and Biosciences (FZB) Borstel, Germany	Prof John W. HOLLOWAY University of Southampton, Human Genetics, Southampton, United Kingdom

Научни групи на COST BM1201

- Working Group 1: „Развитие на белите дробове“ - Идентифициране на генетични, епигенетични и екологични рискови фактори за неблагоприятно развитие на белите дробове
  - Цел 1 – Разработване на нови инструменти за оценка на растежа на белите дробове в пре- и ранен постнатален период;
  - Цел 2 – Мета-анализ на връзката между антропометричните показатели при раждане и последващата белодробна функция и вероятността за влошаване на белодробната функция.
  - Цел 3 – Мета-анализ на ефекта на различни SNPs върху функцията на белите дробове при възрастни и връзката им с белодробните показатели на новородените и малки деца.

Научни групи на COST BM1201

- Working Group 2: „Белодробна морфогенеза”:
  - Цел 1 – Установяване в животински модели на ХББ на клетъчно-специфични маркери и регулатори на клетъчната съдба на клетъчните типове на белия дроб.
  - Цел 1 – Определяне на физиологичната роля на гени, ассоциирани с ХББ при геномните изследбания (GWAS) в развитието и функцията на белите дробове.

Научни групи на COST BM1201

- Working Group 3: „Пре- и постнатално развитие на белия дроб и връзката с ХББ”
  - Цел 1 – Уточняване на функционалните ефекти на екологичните и генетични фактори върху риска от развитие на ХББ в по-късен период (миши модели на астма, ХОББ, идиопатична пулмонарна фиброза, IPF).
  - Цел 2 – Идентифициране на отключващите механизми и фактори на патологичното развитие на белия дроб и ХББ.

Научни групи на COST BM1201

- Working Group 4: „Трансгенерационни животински модели на белодробни заболявания”
  - Цел 1 – Създаване и валидиране на трансгенерационни животински модели на ХББ
  - Цел 2 – Идентифициране на механизмите на трансгенерационния пренос на риска (молекулните пътища, клетъчни взаимодействия, епигенетични промени)

Exposure	*Assessment of disease risk in offspring*
Prenatal /early postnatal smoke	Asthma; COPD; IPF
Prenatal /early vitamin D	Asthma; COPD; IPF
Prenatal/early infections	Asthma; COPD; IPF
Genetic and allergen-induced models of maternal asthma	Asthma; COPD
Early postnatal allergen challenge	Course of asthma (neonatal vs. juvenile vs. adults)
Preterm/Neonatal ventilation	Airway hyperreactivity/remodelling; COPD

Инструменти на COST BM1201

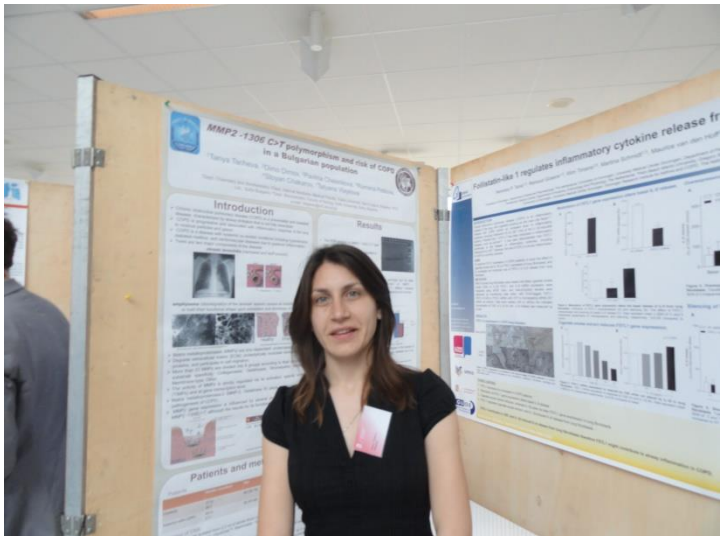
- Работни срещи (workshops) на членовете на управителния комитет (MC) от всички страни и институции, участващи в акцията.
- Ежегодни научни конференции (kick-off conference)
- Краткосрочни специализации (short term scientific missions, STSM)
- Междудисциплинарни училища (Cross-disciplinary Training Schools)

Участие на нашата научна група

2nd COST BM1201 Summer School
Molecular Mechanisms of Ageing

June 23-25
University of Groningen, the Netherlands

- **Доклад: ас. Таня Тачева** - *MMP-3 serum levels in children and adults suffering from Bronchial asthma* (Tanya Tacheva, Dimo Dimov, Ivan Chakarov, Petrana Chakarova, Tatyana Vlaykova)



Участие на нашата научна група

university of groningen

GRIAC Groningen

2nd COST BM1201 Conference
A Bird's eye view on the ageing lung
June 26-27
University of Groningen, the Netherlands

Постер: Tanya Tacheva, Dimo Dimov, Pavlina Chelenkova, Rumena Petkova, Stoyan Chakarov, Tatyana Vlaykova.
MMP2 -1306 C>T polymorphism and risk of COPD in a Bulgarian population

Участие на нашата научна група

Karolinska Institutet

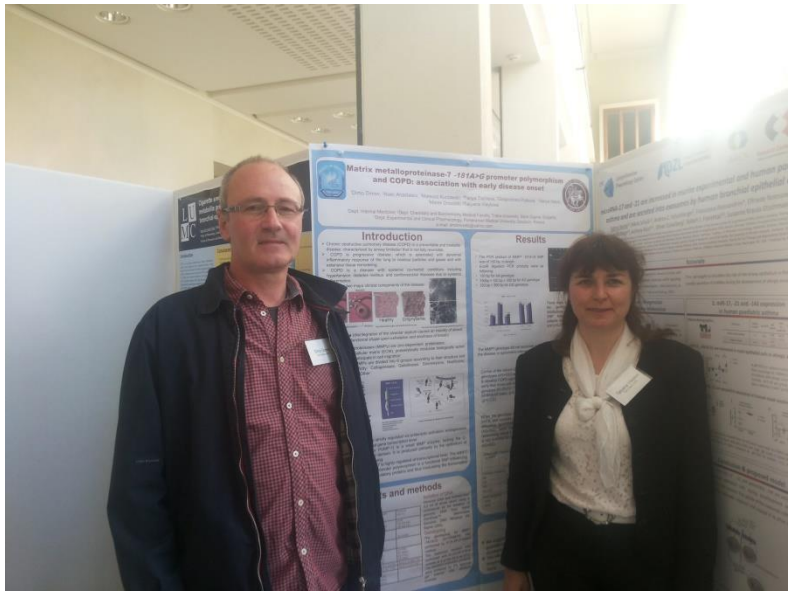
Programme version 23rd March 2015, page 1 of 2

Annual Meeting of COST BM 1201: Early Origins of Chronic Lung Disease

15-16th June 2015

Venue: Nobel Forum, Karolinska Institutet, Stockholm, Sweden

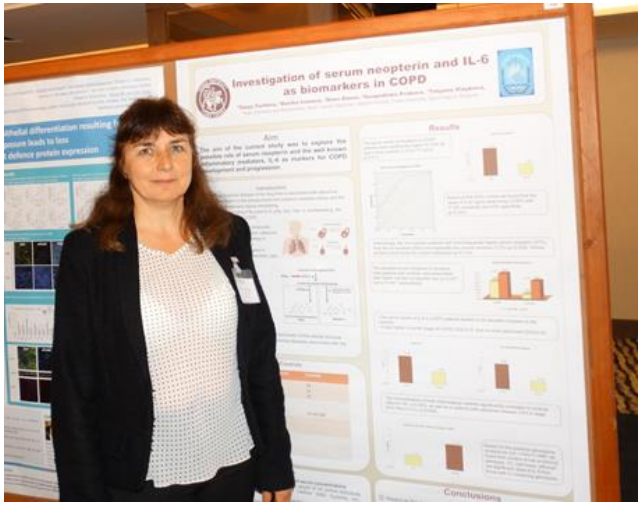
Постер: Dimo Dimov, Asen Anastasov, Mateusz Kurzawski, Tanya Tacheva, Gospodinka Prakova, Vanya Ilieva, Marek Drozdzik, Tatyana Vlaykova.
Matrix metalloproteinase-7 -181A>G promoter polymorphism and COPD: association with early disease onset



Final 4th Annual Meeting of COST BM 1201: Early Origins of Chronic Lung Disease: “The end of the beginning”. 3-4th of November 2016 Venue: Electra Metropolitan Hotel, Athens, Greec

Investigation of serum neopterin and IL-6 as biomarkers in COPD

[1]Tanya Tacheva, [2]Dimo Dimov, [1]Donika Ivanova, [2]Gospodinka Prakova**,**
[1]Tatyana Vlaykova,
[1]Dept. Chemistry and Biochemistry, [2]Dept. Internal Medicine I, Medical Faculty, Trakia University, Stara Zagora, Bulgaria, tvlaykova@abv.bg



Prof. Aage Haugen и Prof. Shan Zienolddiny
Section for Toxicology and Biological Work Environment, National Institute of Occupational Health, Oslo, Norway

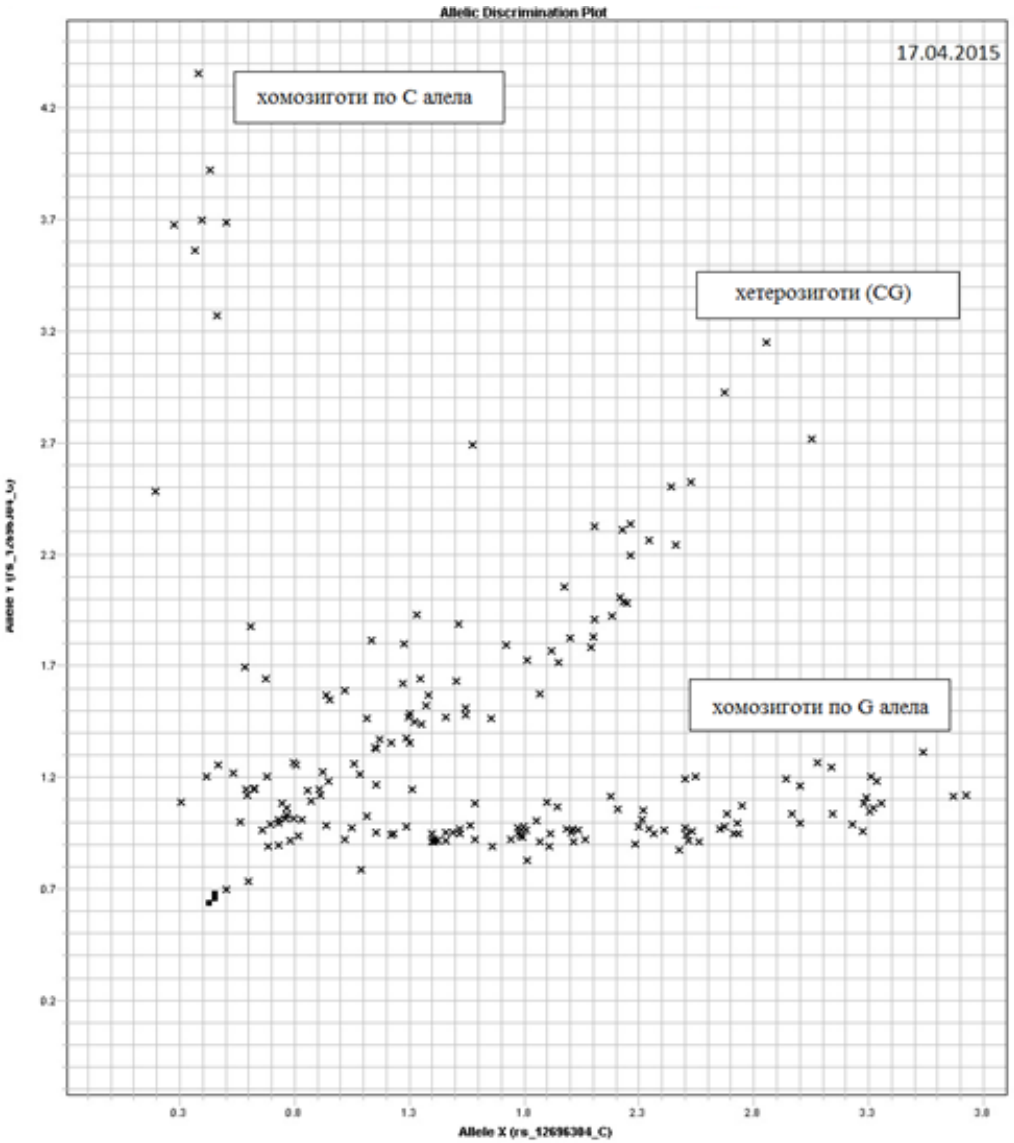
- **Ас. Таня Тачева** - **13.04 – 02.05.2015- 3-седмична** специализация по програма BG09 „Фонд за стипендии на Европейското икономическо пространство“ на МОН
- **Проф. Татяна Влайкова – август 2014 - едноседмична** специализация по програма BG09 „Фонд за стипендии на Европейското икономическо пространство“ на МОН
- **Проф. Татяна Влайкова – 05.06 – 25.06.2015 - 3-седмична** специализация по същата програма на МОН

Prof. Aage Haugen и Prof. Shan Zienolddiny
Section for Toxicology and Biological Work Environment, National Institute of Occupational Health, Oslo, Norway

Генотипиране по еднонуклеотидния полиморфизъм *TERC* C>G (rs12696304) и *TERC* C>T (rs10936599)

- Количествен Real-time PRC (q-PCR) при генотипиране по еднонуклеотидните полиморфизми TERC C>G и TERC C>T
- SYBR green-базиран qPCR метод при определяне дължината на теломерите

.

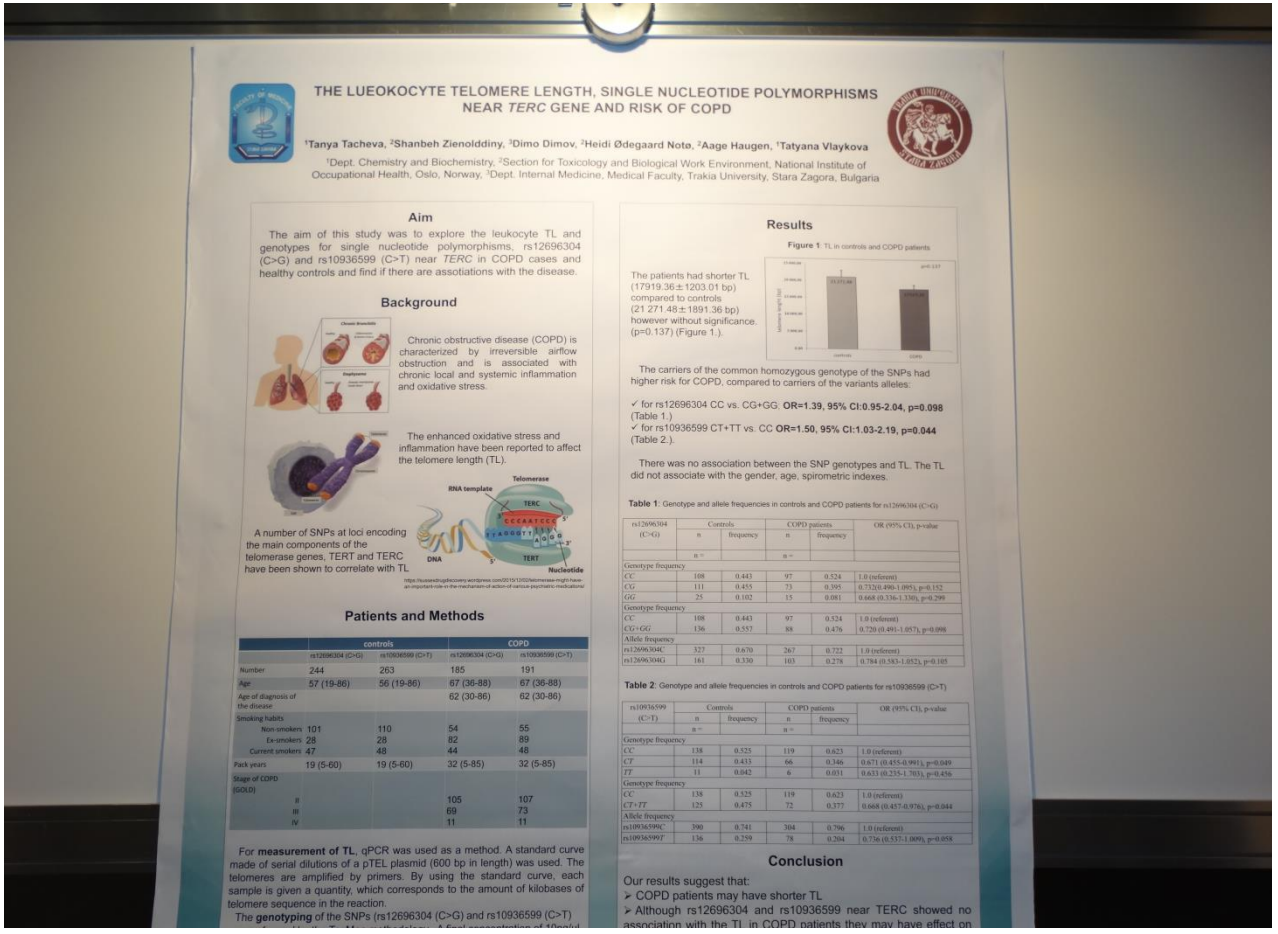


EUROPEAN RESPIRATORY *journal*
FLAGSHIP SCIENTIFIC JOURNAL OF ERS

The lueokocyte telomere length, single nucleotide polymorphisms near *TERC* gene and risk of COPD

Tanya Tacheva, Shanbeh Zienolddiny, Dimo Dimov, Heidi Ødegaard Notø, Aage Haugen, Tatyana Vlaykova

European Respiratory Journal 2016 48: PA894; **DOI:** 10.1183/13993003.congress-2016.PA894



THE LUEOKOCYTE TELOMERE LENGTH, SINGLE NUCLEOTIDE POLYMORPHISMS NEAR *TERC* GENE AND RISK OF COPD

[1]Tanya Tacheva, [2]Shanbeh Zienolddiny, [3]Dimo Dimov, [2]Heidi Ødegaard Notø, [2]Aage Haugen, [1]Tatyana Vlaykova

[1]Dept. Chemistry and Biochemistry, [2]Section for Toxicology and Biological Work Environment, National Institute of Occupational Health, Oslo, Norway, [3]Dept. Internal Medicine, Medical Faculty, Trakia University, Stara Zagora, Bulgaria

Aim

The aim of this study was to explore the leukocyte TL and genotypes for single nucleotide polymorphisms, rs12696304 (C>G) and rs10936599 (C>T) near *TERC* in COPD cases and healthy controls and find if there are assotiations with the disease.

Background

Chronic obstructive disease (COPD) is characterized by irreversible airflow obstruction and is associated with chronic local and systemic inflammation and oxidative stress.

The enhanced oxidative stress and inflammation have been reported to affect the telomere length (TL).

A number of SNPs at loci encoding the main components of the telomerase genes, TERT and TERC have been shown to correlate with TL

Patients and Methods

	controls		COPD	
	rs12696304 (C>G)	rs10936599 (C>T)	rs12696304 (C>G)	rs10936599 (C>T)
Number	244	263	185	191
Age	57 (19-86)	56 (19-86)	67 (36-88)	67 (36-88)
Age of diagnosis of the disease			62 (30-86)	62 (30-86)
Smoking habits				
Non-smokers	101	110	54	55
Ex-smokers	28	28	82	89
Current smokers	47	48	44	48
Pack years	19 (5-60)	19 (5-60)	32 (5-85)	32 (5-85)
Stage of COPD (GOLD)				
II			105	107
III			69	73
IV			11	11

For **measurement of TL**, qPCR was used as a method. A standard curve made of serial dilutions of a pTEL plasmid (600 bp in length) was used. The telomeres are amplified by primers. By using the standard curve, each sample is given a quantity, which corresponds to the amount of kilobases of telomere sequence in the reaction.

The **genotyping** of the SNPs (rs12696304 (C>G) and rs10936599 (C>T)

Results

Figure 1: TL in controls and COPD patients

The patients had shorter TL (17919.36±1203.01 bp) compared to controls (21 271.48±1891.36 bp) however without significance. (p=0.137) (Figure 1.).

The carriers of the common homozygous genotype of the SNPs had higher risk for COPD, compared to carriers of the variants alleles:

✓ for rs12696304 CC vs. CG+GG: **OR=1.39, 95% CI:0.95-2.04, p=0.098** (Table 1.)
✓ for rs10936599 CT+TT vs. CC **OR=1.50, 95% CI:1.03-2.19, p=0.044** (Table 2.).

There was no association between the SNP genotypes and TL. The TL did not associate with the gender, age, spirometric indexes.

Table 1: Genotype and allele frequencies in controls and COPD patients for rs12696304 (C>G)

rs12696304 (C>G)	Controls		COPD patients		OR (95% CI), p-value
	n	frequency	n	frequency	
	n =		n =		
Genotype frequency					
CC	108	0.443	97	0.524	1.0 (referent)
CG	111	0.455	73	0.395	0.732(0.490-1.095), p=0.152
GG	25	0.102	15	0.081	0.668 (0.336-1.330), p=0.299
Genotype frequency					
CC	108	0.443	97	0.524	1.0 (referent)
CG+GG	136	0.557	88	0.476	0.720 (0.491-1.057), p=0.098
Allele frequency					
rs12696304C	327	0.670	267	0.722	1.0 (referent)
rs12696304G	161	0.330	103	0.278	0.784 (0.583-1.052), p=0.105

Table 2: Genotype and allele frequencies in controls and COPD patients for rs10936599 (C>T)

rs10936599 (C>T)	Controls		COPD patients		OR (95% CI), p-value
	n	frequency	n	frequency	
	n =		n =		
Genotype frequency					
CC	138	0.525	119	0.623	1.0 (referent)
CT	114	0.433	66	0.346	0.671 (0.455-0.991), p=0.049
TT	11	0.042	6	0.031	0.633 (0.235-1.703), p=0.456
Genotype frequency					
CC	138	0.525	119	0.623	1.0 (referent)
CT+TT	125	0.475	72	0.377	0.668 (0.457-0.976), p=0.044
Allele frequency					
rs10936599C	390	0.741	304	0.796	1.0 (referent)
rs10936599T	136	0.259	78	0.204	0.756 (0.537-1.009), p=0.058

Conclusion

Our results suggest that:
- COPD patients may have shorter TL
- Although rs12696304 and rs10936599 near TERC showed no

БЛАГОДАРЯ ЗА ВНИМАНИЕТО!