Title: Telomere length in circulating leukocytes is associated with lung function and disease

Holger 8451 Schulz schulz@helmholtz-muenchen.de MD 24, Elina 10564 Sillanpää elina.x.sillanpaa@jyu.fi 2, Stefan 10565 Karrasch Stefan.Karrasch@med.uni-muenchen.de 3, Alexessander 10577 Couto Alves acoutoaal@imperial.ac.uk 4, Veryan 10580 Codd vc15@leicester.ac.uk 5,6, Iiris 10582 Hovatta iiris.hovatta@helsinki.fi 7,8, Jessica L. 10589 Buxton j.buxton@imperial.ac.uk 9, Christopher P. 10590 Nelson cn46@leicester.ac.uk 5,6, Linda 10904 Broer l.broer@erasmusmc.nl 10,11, Sara 10907 Hägg Sara.Hagg@ki.se 12, Massimo 10911 Mangino massimo.mangino@kcl.ac.uk 14, Gonneke 10916 Willemsen a.h.m.willemsen@vu.nl 15, Kirs H. 10920 Pietiläinen kirsipietilaainen@helsinki.fi 16,17, Manuel A.R. 10924 Ferreira Manuel.Ferreira@qimr.edu.au 18, Najaf 10931 Amin n.amin@erasmusmc.nl 11, Ben A. 10932 Oostra b.oostra@erasmusmc.nl 11, Heli M. 10936 Bäckmand heli.backmand@vantaa.fi 19,20, Markku 10937 Peltonen markku.peltonen@thl.fi 21, Seppo 10938 Sarna seppo.sarna@helsinki.fi 19, Taina 10942 Rantanen taina.rantanen@jyu.fi 2, Sarianna 10944 Sipila sarianna.sipila@jyu.fi 2, Tellervo 10951 Korhonen Tellervo.korhonen@helsinki.fi 19, Pamela A.F. 10952 Madden maddenp@wustl.edu 22, Christian 10956 Gieger christian.gieger@helmholtz-muenchen.de 1, Rudolf A. 10962 Jörres rudolf.joerres@med.uni-muenchen.de 3,23, Joachim 10973 Heinrich joachim.heinrich@helmholtz-muenchen.de 23,24, Jürgen 10975 Behr juergen.behr@med.uni-muenchen.de 23,25, Rudolf M. 10977 Huber Rudolf.Huber@med.uni-muenchen.de 23,26, Annette 10983 Peters peters@helmholtz-muenchen.de 27,28,29, Konstantin 10990 Strauch konstantin.strauch@helmholtz-muenchen.de 1,3, H.-Erich 10996 Wichmann wichmann@helmholtz-muenchen.de 24,31,32, Melanie 11002 Waldenberger waldenberger@helmholtz-muenchen.de 27, Alexandra I.F. 11003 Blakemore a.blakemore@imperial.ac.uk 9, Eco J.C. 11004 de Geus eco@psy.vu.nl 15, Nyholt 11005 Nyholt Dale.Nyholt@qimr.edu.au 18, Anjali K. 11008 Henders Anjali.Henders@qimr.edu.au 18, Päivi L. 11010 Piirilä Paivi.Piirila@hus.fi 33, Ida 11025 Surakka ida.surakka@thl.fi 17,34, Aila 11027 Rissanen aila.rissanen@medi.inet.fi 35, Patrik K.E. 11045 Magnusson Patrik.Magnusson@ki.se 12, Ana 11047 Vińuela ana.vinuela@kcl.ac.uk 14, Nicholas G. 11050 Martin Nick.Martin@qimr.edu.au 18, Nancy L. 11053 Pedersen Nancy.Pedersen@ki.se 12, Dorret I. 11055 Boomsma dorret@psy.vu.nl 15, Tim D. 11057 Spector tim.spector@kcl.ac.uk 14, Cornelia M. 11070 van Duijn c.vanduijn@erasmusmc.nl 10,11, Jaakko 11077 Kaprio jaakko.kaprio@helsinki.fi 7,17,19, Niles J. 11080 Samani njs@leicester.ac.uk 5,6, Marjo-Riitta 11088 Jarvelin m.jarvelin@imperial.ac.uk 4,36,37,38,39 and Eva 11097 Albrecht eva.albrecht@helmholtz-muenchen.de 1. 1 Institute of Genetic Epidemiology, Helmholtz Zentrum München - German Research Center for Environmental Health, Neuherberg/Munich, Germany ; 2 Gerontology Research Center and Department of Health Sciences, University of Jyväskylä, Jyväskylä, Finland ; 3 Institute and Outpatient Clinic for Occupational, Social and Environmental Medicine,
Body: Rationale: Telomere length is recognized as a marker of biological age. Previous studies reported decreased telomere length in patients with chronic obstructive pulmonary disease (COPD), suggesting premature aging due to environmental exposure and/or chronic inflammation. Since the lungs are continuously exposed to environmental hazards, lung function per se may be a surrogate marker for biological age in light of the large inter-individual variability observed. Objectives: We investigated the association of telomere length with respiratory disease (COPD and asthma), and spirometric indices: forced
expiratory volume in one second (FEV₁), forced vital capacity (FVC) and FEV₁/FVC. Methods: Our meta-analysis of 14 studies included 1,189 COPD cases with 16,115 controls, 2,834 asthma cases with 28,195 controls and spirometric parameters of 13,100 individuals. Associations were tested by linear regression, adjusting for age, sex, and smoking status. Measurements and Main Results: We observed negative associations between telomere length and COPD (β=-0.0676, p=0.018) as well as asthma (β=-0.0452, p=0.024) with stronger effects in women compared to men. The investigation of spirometric indices showed positive associations between telomere length and FEV₁ (p=1.62x10⁻⁷), FVC (p=2.38x10⁻⁴), and their ratio FEV₁/FVC (p=6.13x10⁻³). The associations were weaker in apparently healthy subjects compared to COPD or asthma patients. Conclusions: Our results indicate that lung function may reflect biological aging primarily due to intrinsic processes which are likely to be aggravated in lung diseases. Shortened telomeres in lung disease suggest that aging processes are involved in the pathogenesis of COPD and asthma.