

3rd Japan – Germany Symposium on Advanced Preventive Medicine 2021

Date: 4th-6th of March 2021

Place: Online







Table of Content

- page 3 Schedule for Thursday (4th of March)
- page 4 Schedule for Friday (5th of March)
- page 5 Schedule for Saturday (6th of March)
- page 7 Chairs and Speakers from Kanazawa University
- page 29 Chairs and Speakers from Chiba University
- page 32 Chairs and Speakers from Nagasaki University
- page 40 Chairs and Speakers from HHU / Düsseldorf University

3rd Japan-Germany Symposium on Advanced Preventive Medicine 2021

Date: 4th-6th of March 2021

Thursday, March	4 th				
Time Japan:	Opening remarks				
16:00~	Prof. Heiner FANGERAU (HHU)				
Time Germany: 8:00~	1 st Session: <u>Preventive Medicine and Health Promotion</u> Chair: Prof. Chisato MORI (Chiba)				
	1. Association between levels of PCB in maternal serum with birth weight of newborn in C-MACH study - Prof. Akifumi EGUCHI (15 min)				
	 2. The tumor microenvironment in hepatocellular carcinoma: Interaction with cancer stem cells and therapeutic targets Prof. Tatsuya YAMASHITA (15 min) 				
3. Walkable Design in Practice - Prof. Hiroaki YOSHIDA (15min)					
4. Association of FTO genotype with obesity and bone health - Xiao XU (15 min)					
Coffee Break					
	(15 min)				
	Special; Session: <u>Covid-19 and Prevention</u> Chair: Prof. Hiroshi ICHIMURA (Kanazawa) and Prof. Heiner FANGERAU (HHU)				
	1. Ethical aspects of public health measures against Covid-19 in Germany - Dr. Matthis KRISCHEL (25min)				
	 2. COVID-19 and Hygiene hypothesis - Prof. Masaharu TOKORO (25min) 				
	 3. How COVID-19 lockdown in China significantly influenced the air pollutants at the Wajima Air Monitoring Station of Japan - Hao ZHANG (15 min) 				
Closing remarks					
	Prof. Kiyoshi AOYAGI (Nagasaki)				

Eriday March 5th									
Friday, March 5									
1 ime Japan:	Opening remarks								
16:00~	Prof. Shuichi KANEKO (Kanazawa)								
Time Germany:	2nd Session:								
8:00~	Immunology and Infection Session								
	Chair: Prof. Atsushi KAWAKAMI (Nagasaki)								
	1. HTLV-1 infection and age-associated health problems - Dr. Hirotomo YAMANASHI (15 min)								
	2. A prospective cohort study of rheumatic disease in a residential health checkup-based healthy population: prediction of rheumatoid arthritis and IgG4-related disease development - Yoshika TSUJI (15min)								
	3. Current status and future prospects in the diagnosis and treatment of familial Mediterranean fever in Japan - Dr. Tomohiro KOGA (15min)								
	4. ISGylation and de-ISGylation in HIV infection and inflammation - Prof. Carsten MÜNK (25min)								
	Special Lecture of Diabetes and Metabolism Session - PART 1								
	Chain Drof Michael Dodon (DD7 / HHI) and Drof Tachineri TAKAMUDA								
	($U_{\text{resonance}}$)								
	(Kanazawa)								
	1. Air pollution and complications of diabetes - Prof. Christian HERDER (25min)								
	Coffee Break								
(15 min)									
(15 min)									
Special Lecture of Diabetes and Metabolism Session - PART 2									
Chair: Prof. Michael RODEN and Prof. Toshinari TAKAMURA									
	 2. Precision medicine in metabolic diseases - Identifying subgroups of diabetes - Prof. Michael RODEN (ca.25min) 								
	3. Association between chronic pain and serum 25-hydroxyvitamin D concentrations - Dr. Keita SUZUKI (25min)								
	4. Biomarkers of inflammation in novel subgroups of patients with recent- onset diabetes: German Diabetes Study - Dr. Haifa MAALMI (15min)								
	5. Using statutory health insurance data to evaluate patterns of healthcare utilization and associated factors of patients with diabetes in Germany - Ute LINNENKAMP (15min)								
Closing Remarks									
	Prof Michael RODEN (HHII)								

	۲th ا							
Saturday, March 6 th								
Time Japan:	Opening remarks							
16:00~	Dr. Tamara SCHIKOWSKI (IUF/HHU)							
T1 C								
Time Germany:	3rd Session:							
8:00~	Cell Biology and Immunology							
	Chair: Prof. Yuji NAGAYAMA (Nagasaki)							
	1. Genetic and functional diversity of leukocyte immunoglobulin-like receptor							
	family in humans							
	- Prof. Kouyuki HIRAYASU (20 min)							
	2. Transcription factor regulation of CD8 T cell differentiation							
	- Prof. Makoto KURACHI (20 min)							
	3. Circadian clocks in senescent cells: a possible strategy to fight aging							
	- Dr. Yasukazu NAKAHATA (15min)							
	Remark by the President of 4th Japan- Germany Symposium on Advanced							
	Preventive Medicine 2022							
	Prof. Yuji NAGAYAMA (Nagasaki)							
	Coffee Break							
	(15 min)							
	Createl Lastrona							
	Special Lecture:							
	Atmospheric Environment and Health Chain Duck Himmeli NAVAMUDA (Vencence) and Dr. Tennere							
	Chair: Prof. Hiroyuki NAKAMUKA (Kanazawa) and Dr. Tamara							
	1 Effect of starsenhouse nextinulate metters on acquiretons commuters in							
	1. Effect of atmospheric particulate matters on respiratory symptoms in							
	people with chronic cougn							
	- Akinori HARA (20min)							
	2. Gene-environment interaction effects on respiratory nearin							
	- Sara KRESS (20min)							
	5. Skin aging in indians living in highly polluted areas							
	- Pla JAHAN (TUIIIII)							
	4. The notential health offects of Temperature and Air Dellution interaction							
	4. The potential health effects of Temperature and Air Pohution Interaction							
	- ASILYII AREAL (1011111)							
	5. Air collution approxime and require tary health of office workers in approxim							
	S. All pollution exposure and respiratory health of office workers in current China: a pilot survey in a heavy polluted region							
	Yuan 7HANG (10min)							
	Special Session.							
	Atmospheric Environment and Menitering							
Atmospheric Environment and Monitoring Chain: Drof. Kagnichi UAVAKAWA (Kagagawa)								
Unair: Proi, Kazuichi HAYAKAWA (Kanazawa)								
1. The unique course of polycyclic exemptic hydrogenhang on the								
	1. The unique source of polycyclic aromatic hydrocarbons on the							
	northwestern nighland of Unina							
	- Luiu Znang (10min)							

2. ro	Characteristics of PM _{2.5} -bound polycyclic aromatic hydrocarbons at a adside air pollution monitoring station at Yamashina, Kanazawa from 2017
to	2020
	- Wanli XING (10min)
3. ni	Seasonal characteristic and health risks of PM _{2.5} -bound polycyclic and tro-polycyclic aromatic hydrocarbons in Shenyang, China - Pengchu BAI (10min)
4. (P tw	Atmospheric behavior comparison of polycyclic aromatic hydrocarbons AHs), Nitro-PAHs (NPAHs), and water-soluble inorganic ions (WSIIs) at to background sites in Japan - Lu YANG (10min)
5. so to	Analysis of compositional variation and source characteristics of Water- luble ions in TSP at a remote background site in Japan (Wajima) from 2005 2015 - Yan WANG (10min)
C	losing Remarks
D۲	of Atsushi TAIIMA (Kanazawa)

Kanazawa University

Hiroshi ICHIMURA, MD & PhD

Professor, Department of Viral Infection and International Health; Graduate School of Advanced Preventive Medical Sciences/ Graduate School of Medical Sciences, Kanazawa University E-mail: <u>ichimura@med.kanazawa-u.ac.jp</u> Web site: <u>http://virus.w3.kanazawa-u.ac.jp/</u>

Research projects:

- 1. Viral and host factors associated with disease progression in children with HIV infection
- 2. Impact of anti-retroviral therapy (ART) on the immune status and gut microbiota of HIV-infected children
- **3.** Viral and host factors associated with the virulence of enterovirus 71 that causes Hand-Foot-and-Mouth disease
- 4. Monitoring of neutralizing antibody in the convalescent patients with COVID-19

Key publications:

- 1. Newly emerged enterovirus-A71 C4 sublineage may be more virulent than B5 in the 2015–2016 hand-foot-and-mouth disease outbreak in northern Vietnam. *Sci Rep* 10:159, 2020.
- 2. Novel Hyaluronate Lyase Involved in Pathogenicity of Streptococcus dysgalactiae subsp. *Frontiers in Microbiology* 11:552418, 2020.
- 3. Extremely diversified haplotypes observed among assemblage B population of Giardia intestinalis in Kenya. *Parasitol Int* 75:102038, 2020.
- 4. Low concordance of oral and genital HPV infection among male patients with sexually transmitted infections in Vietnam. *BMC Infect Dis* 19(1):578, 2019.
- 5. Effects of Short-term Probiotic Ingestion on Immune Profiles and Microbial Translocation among HIV-1-Infected Vietnamese Children. *Int J Mol Sci 18*(10), 2185, 2017.
- 6. Discrepancies in prevalence trends for HIV, hepatitis B virus, and hepatitis C virus in Haiphong, Vietnam from 2007 to 2012. *PLoS One* 12(6):e0179616, 2017.
- 7. A functional polymorphism in the NKG2D gene modulates NK-cell cytotoxicity and is associated with susceptibility to Human Papilloma Virus-related cancers. *Sci Rep* 6:39231, 2016.
- 8. Impact of HIV infection and anti-retroviral therapy on the immune profile of and microbial translocation in HIV-infected children in Vietnam. *Int J Mol Sci* 17: 1245, 2016.
- 9. Positive correlation of HIV infection with Giardia intestinalis assemblage B but not with assemblage A in asymptomatic Kenyan children. *AIDS* 30(15):2385-87, 2016.
- 10. Lower prevalence of *Entamoeba* species in children with vertically transmitted HIV infection in Western Kenya. *AIDS* 30(5):803-805, 2016.
- 11. Comparison of HIV-1 *nef* and *gag* Variations and Host HLA Characteristics as Determinants of Disease Progression among HIV-1 Vertically Infected Kenyan Children. *PLoS One* 10(8):e0137140, 2015.
- 12. Geographic and Temporal Trends in the Molecular Epidemiology and Genetic Mechanisms of Transmitted HIV-1 Drug Resistance: an Individual Patient and Sequence-level Meta-Analysis. *PLoS Medicine* 12(6):e1001845, 2015.



Educational background & professional experience:

1974-1980	Yamaguchi University School of Medicine. License of Medical Doctor (No. 251554).				
1980-1984	Tottori University Graduate School of Medical Sciences, Doctor of Medical Science.				
1985-1987	Research Associate, Department of Biochemical Virology, Baylor College of Medicine, USA.				
1991-1992	International Scholarship Doctor for 1991 of the Japan Ministry of Health, Labor and Welfare;				
	Cancer Research Institute, University of California, San Francisco, School of Medicine, USA.				
1994–1994	Assistant Professor, Department of Microbiology, Kyoto Prefectural University of Medicine.				
1994-1999	Associate Professor, Department of Microbiology, Kyoto Prefectural University of Medicine.				
1999-	Professor, Department of Viral Infection and International Health, School of Medicine,				
	Kanazawa University				
2018-2020	Dean, Graduate School of Advanced Preventive Medical Sciences, Kanazawa University.				
Award:	2016 "Medal for People's Health" from the Ministry of Health, Vietnam.				
	2011 Honorary Professor of Hanoi Medical University, Vietnam (No. 156/QD-DHYHN)				

2012 Honorary Professor of Hai Phong Medical University, Vietnam (No. 720/QD-DHYHP)



Fig. Epidemiology for life-style related diseases in Shika town in Japan

Research projects:

- 1. Basic and epidemiologic research on the effects of ambient chemicals on allergic diseases
- 2. Epidemiology on the effects of lifestyles on non-communicable disease including obesity, diabetes,
- vertebral and cardiovascular, renal, and respiratory diseases and musculoskeletal systems
- **3.** Effects of physical and chemicals and stress assessment in workplaces

Key publications:

- 1) Suzuki F et al., PLoS One. 2021Feb 26;16(2)
- 2) Suzuki K et al., J Pain Res. 2020 Nov 19;13:2987-2996
- 3) Noguchi-Shinohara M et al, PLoS One. 2020 Oct 23;15(10)
- 4) Hara A et al, Biomarkers. 2020 Nov;25(7):587-593
- 5) Miyagi S et al, J Diabetes Investig. 2020 Sep 10
- 6) Tsujiguchi H et al, Nutrients. 2020 Jul 28;12(8)
- 7) Mitsui-Iwama M et al, Asia Pac Allergy. 2019 Jan 21;9(1):e5.
- 8) Nakamura H et al, Nutrients. 2019 Apr 23;11(4)

- 9) Tsujiguchi H et al, Nutrients. 2019 Apr 3;11(4)
- 10) Thi Thu Nguyen T et al, Nutrients. 2019 Feb 13;11(2)
- 11) Hirota R et al,. Allergy. 2019 May;74(5):996-999
- 12) Nakamura H et al, Nutrition. 2018 26;61:8-15
- 13) Nakamura H, et al Nutrients. 2018 24;10(12)
- 14) Shimizu Y, et al. J-Multidisciplinary Scientific Journal 2018, 1, 148-155
- 15) Anyenda EO et al, 2016 Int J Environ Res Public Health. 13(8)
- 16) Anyenda EO et al, 2016 Atmospheric Environment. 140, 34-41
- 17) Nguyen TTT et al, 2016 Int J Environ Res Public Health. 13 (1)
- 18) Ogino K et al, 2016 Free Radic Res. 50 (11) 1165-1172
- 19) Watanabe T et al, 2016 PLoS One 23;11(3)
- 20) Fukutomi Y et al, 2014 Allergy. 69 (10) 1405-11
- 21) Higashi T et al, 2014 Atmospheric Environment. 92, 506-513
- 22) Higashia T et al,. 2014 Atmospheric Environment. 97, 537-543
- 23) Tanaka T, et al, Allergol Int. 2012;61(1):57-63
- 24) Fukutomi Y, et al, Clin Exp Allergy. 2012, 42(5):738-46
- 25) Fukutomi Y, et al, J Allergy Clin Immunol. 2012,129(3):860-863.e3
- 26) Nakamura H et al, Int Arch Allergy Immunol. 2007;142(4):329-34
- 27) Nakamura H et al, Int Arch Allergy Immunol. 2004, 135(1):40-3
- 28) Nakamura H et al, J Allergy Clin Immunol. 2003, 112(6):1127-31.

Educational background & professional experience:

- 1985 Graduate from Kanazawa University School of Medicine
- 1988-86 Researcher at Johannes Gutenberg-Universität Mainz. FRG
- 1989 Graduated from Kanazawa University Graduate School of Medicine (PhD)
- 2003-07 Professor of Kochi University School of Medicine (Department of Environmental Medicine)
- 2007- Professor of Kanazawa University School of Medicine (Department of Environmental and Preventive Medicine
- 2016-18 Dean, Graduate School of Advanced Preventive Medical Sciences, Kanazawa University
- 2017- Director of Center of Advanced Preventive Medical Sciences, Kanazawa University
- 2018- Dean, School of Medical, Pharmaceutical and Health Sciences, Kanazawa University

Awards:

- 1991: Incentive Award from Japanese Hygiene Society
- 2004: Prize of the Society of Fitness, Nutrition and Immunity

Toshinari TAKAMURA, MD & PhD

Professor, Department of Endocrinology and Metabolism, Kanazawa University Graduate School of Medical Sciences E-mail ttakamura@med.kanazawa-u.ac.jp

Web site https://metabology.w3.kanazawa-u.ac.jp/english/



Research projects:

- 1. Basic and clinical research on pathophysiology and treatment of diabetes, obesity, and their complications
- 2. Pathological trajectories of non-alcoholic fatty liver disease
- 3. Hepatokine-mediated inter-organ networks in diabetes and obesity

Key publications:

- 1. Cell Host Microbe 25:588-601.e7, 2019
- 2. Sci Rep 8:16727, 2018
- 3. PLoS One 13:e0194798, 2018
- 4. Nat Commun 8:1658, 2017
- 5. Nat Med 23:508-16, 2017
- 6. J Biol Chem 292:10791-800, 2017
- 7. *Diabetes* 63:1649-64, 2014
- 8. Diabetologia 57:1968-76, 2014
- 9. PLoS ONE 9:e92170, 2014
- 10. Diabetologia 57:878-90, 2014
- 11. Diabetes 62:811-24, 2013
- 12. Endocr J 59:745-63, 2012 (Review).
- 13. Cell Metab 12:483-95, 2010
- 14. Obesity (Silver Spring). 16:2601-9, 2008
- 15. Hepatology 46:1392-1403, 2007
- 16. Diabetologia 50:268-277, 2007
- 17. Diabetologia 47:638-647, 2004



Figure: The hepatokine selenoprotein P causes multi-signal resistances via reductive stress leading to pathology of type 2 diabetes such as insulin resistance, angiogenesis resistance, exercise resistance, and insulin secretory failure.

Educational background & professional experience:

- 1988~ Kanazawa University Graduate School of Medical Science
- **1992** Awarded the degree of PhD in Internal Medicine)
- 1993~ Department of Biochemistry, Tohoku University (Prof. Hiroshi Okamoto)
- 1994~ Special Researcher, Japan Society for the Promotion of Science
- 1997~ Assistant Professor, Department of Endocrinology and Metabolism, Kanazawa University Hospital
- 2001~ Associate Professor
- 2014~ Professor, Department of Endocrinology and Metabolism, Kanazawa University Graduate School of Medical Sciences

Award: 2018 Commendation for Science and Technology by the Minister of Education, Culture, Sports, Science and Technology

Shuichi Kaneko, MD

Professor, Department of system biology,

Kanazawa University Graduate School of Medical Sciences

Director, WHO Collaborating Center for Chronic Hepatitis and Liver Cancer

E-mail: skaneko@med.kanazawa-u.ac.jp

Web site: http://www.m-kanazawa.jp/ichinai/english/index.html

Research projects:

- Research on clinical epidemiology of hepatitis and HCC. 1.
- 2. Understanding of carcinogenesis of HCC.
- 3. Development of new diagnosis and treatment for HCC.

Key publications:

- Nat Commun 11(1):1557, 2020.
- 1. 2. 3. Hepatology 70(1):25-39, 2019.
- Hepatology 69(2):653-665, 2019.
- 4. Nat Commun 9(1):30, 2018.
- 5. Gastroenterology 152(6):1395-1406, 2017.
- 6. Nature Med 23(4):508-516, 2017.
- 7. Hepatology 61(4):1343-56, 2015.
- 8. Hepatology 60(5):1519-30, 2014.
- 9. Hepatology 60(5):1674-85, 2014.
- 10. Hepatology 59(3):828-38, 2014.
- Nat Med 19(11):1542-6, 2013. 11.
- 12. Hepatology 58(3):1133-42, 2013.
- 13. Hepatology 57(4):1484-97, 2013.
- 14. Hepatology 57(4):1448-57, 2013.
- 15. Hepatology 56(5):1792-803, 2012.
- 16. Gastroenterology 141(1):128-140, 2011.
- 17. Hepatology 53(4):1206-16, 2011.
- 18. Cell Metab 12(5):483-95, 2010.

Education:

1982	Graduate from Kanazawa University School of Medicine (MD)				
Honors:					
2004	Industry-Academia-Government Collaboration Service Award from Minister				
2014	Science and Technology Award from Japanese Ministry of Education, Culture,				
	Sports, Science and Technology				
2015	The "Khubilai Khan" Gold Medal of the Mongolian Academy of Sciences				
2015	Industry-Academia-Government Collaboration Service Award Minister Award				
	Japanese Ministry of Economy, Trade and Industry				



of

COVID-19 and Hygiene hypothesis

Masaharu TOKORO, MD & PhD

Associate Professor and Chief, Department of Parasitology, Graduate School of Medical Sciences, and Director, International Preventive Medicine Section, Advanced Preventive Medical Sciences Research Center, Kanazawa University.

E-Mail: tokoro@med.kanazawa-u.ac.jp Web site: https://www.parasitology.jp/



It is worth mentioning that parasites might be one of the candidates representing low-hygiene condition. The hygiene hypothesis, especially the notion of lost friends theory, is quite convincing to parasitologists, because the widespread presence of various parasites among humans and animals is a typical landscape of rural areas in developing countries. Such old friends may have constituted an essential initial immunological stimulus for the maturation of the human immune system, and in this regard, the immaturity, that is common in those industrialized areas, seems to allow the cytokine storm by COVID-19.

In this presentation, I would like to discuss the potential therapeutic applications using parasites to control the development of cytokine storm by COVID-19.



Fig. 1 Higher mortality rates of COVID-19 observed among people in higher-GDP countries.

Nominal GDP per capita (2018) vs. COVID-19 mortality rates per 1 million population (2020.9.24) are linearly related. The countries more than 20 million population were included for this analysis.

The countries were categorized to following four groups. Group I: high GDP and high mortality countries. Group II: high-mid GDP and mid-low mortality countries. Group III: mid GDP and high mortality countries. Group IV: low GDP and mid-low mortality countries. No country with low income and high mortality was found.

Current research focuses: As an expert of *PARASITOLOGY*, I've been engaged in the studies regarding molecula evolution and taxonomy of human-related protozoan parasites. Molecular epidemiological investigations targetin various pathogenic and commensal parasites in human population have been conducted in Kenya and Indonesia. Currently my research focus is further extended to the roles of commensal protozoans in human gut microbiota. The potential therapeutic utility of parasites for autoimmune and allergic diseases is pursued through re-evaluati of the "pathogenicity" of parasites to those residents living under parasites-endemic status. Representative publications related to the hygiene hypothesis:

- Matey EJ *et al.* Lower prevalence of *Entamoeba* species in children with vertically transmitted HIV infection in Western Kenya. AIDS. 2016 Mar 13;30(5):803-5.
- Matsumura T *et al.* Possible pathogenicity of commensal *Entamoeba hartmanni* revealed by molecular screening of healthy school children in Indonesia. Trop Med Health. 2019 Jan 15;47:7.

Atsushi Tajima, PhD

Dean, Graduate School of Advanced Preventive Medical Sciences, Kanazawa University

Professor, Department of Bioinformatics and Genomics,

Graduate School of Advanced Preventive Medical Sciences, Kanazawa University

E-mail: atajima@med.kanazawa-u.ac.jp

Web site: http://big.w3.kanazawa-u.ac.jp/

Research projects:

- 1. Genetics and genomics research to identify novel factors that contribute to inter-individual differences in disease susceptibility and quantitative traits in humans
- 2. Research on AI-related technologies for outcome predictions, identification of high-risk individuals and prediction of disease onset and severity for the realization of precision medicine

Recent publications (selected):

- 1. J Hum Genet 65(8):683-691, 2020
- 2. J Dent Res 99(3):271-276, 2020
- 3. Commun Biol 2(1):468, 2019
- 4. *Haematologica* 104(10):e447-e450, 2019
- 5. Science 361(6397):88-92, 2018
- 6. J Med Genet 55(6):415-421, 2018
- 7. Clin Cancer Res 24(10):2357-2369, 2018
- 8. Cell Rep 20(9):2131-2143, 2017
- 9. Blood 129(21):2908-2916, 2017
- 10. Endocr J 64(4):463-475, 2017
- 11. J Hum Genet 61(11):911-915, 2016
- 12. J Neurol Neurosurg Psychiatry 87(6):656-662, 2016

Education:

1990	B.Pharm., Faculty of Pharmaceutical Sciences, Kyoto University, Japan
1992	M.Pharm., Department of Pharmacology, Kyoto University, Japan
2002	Ph.D., Department of Biosystems Sciences, The Graduate University for Advanced Studies
	(SOKENDAI), Japan

Professional experience:

1992 - 1999	Researcher, Toray Industries, Inc., Japan
2002 - 2004	Postdoctoral Fellow, The Graduate University for Advanced Studies (SOKENDAI), Japan
2004 - 2006	Project Research Associate, Institute of Medical Science, The University of Tokyo, Japan
2006 - 2007	Project Research Associate, School of Medicine, Tokai University, Japan
2007 - 2009	Research Associate, School of Medicine, Tokai University
2009 - 2010	Lecturer, School of Medicine, Tokai University
2010 - 2014	Associate Professor, Department of Human Genetics, Institute of Health Biosciences,
	The University of Tokushima Graduate School, Japan
2014 -	Professor, Department of Bioinformatics and Genomics, Graduate School of Advanced
	Preventive Medical Sciences, Kanazawa University, Japan
2020 -	Dean, Graduate School of Advanced Preventive Medical Sciences, Kanazawa University

Tatsuya Yamashita, MD, and PhD

Associate Professor, Advanced preventive medical sciences research center, Kanazawa University

Department of Gastroenterology, Kanazawa University Hospital WHO Collaborating Center for Chronic Hepatitis and Liver Cancer

E-mail; ytatsuya@m-kanazawa.jp Website: <u>https://cellmeta.w3.kanazawa-u.ac.jp/</u>



Area of interest:

1. Diagnosis and Treatment of Hepatocellular carcinoma

2. Diagnosis and Treatment of Viral Hepatitis

Education:

1993 Graduate from Kanazawa University School of Medicine (MD)

1998 Graduate from Graduate School of Medicine, Kanazawa University (PhD)

Career Experiences:

January 2018: Associate Professor, Advanced preventive medical sciences research center

April 2016: Lecture, Department of Gastroenterology, Kanazawa University Hospital

April 2009: Research Professor, Center for Education in Community Medicine, Kanazawa University Hospital

June 2014: Secondment, Global Hepatitis Programme, Department of HIV, World Health Organization

April 2001: Assistant Professor, Department of Gastroenterology, Kanazawa University Hospital

October 1: Medical staff, Department of Gastroenterology, Kanazawa University Hospital

1st Session: Preventive Medicine

Title: The tumor microenvironment in hepatocellular carcinoma: Interaction with cancer stem cells and therapeutic targets

Tatsuya Yamashita^{1,2}, Kouki Nio², Kazuki Nagai², Taro Yamashita², Shuichi Kaneko² 1 Advanced preventive medical sciences research center, Kanazawa University 2 Department of Gastroenterology, Kanazawa University Hospital

Abstract:

We have isolated, and identified cancer stem cells (CSCs), which have played an essential role in the development, proliferation, and distant metastasis of hepatocellular carcinoma (HCC) and have identified the relationship between the diversity of CSCs and malignant progression in HCC. CSCs are present in the invasion frontier and are associated with a variety of stromal cells. It is believed that this tumor microenvironment is created to respond to external and internal stresses such as cancer immunity or anticancer drugs. This study aims to elucidate the tumor microenvironment induced by CSCs and identify new therapeutic targets in HCC. Since chemokines play an essential role in cancer immunosuppression induced by CSCs and chemokines. We found chemokine (C-C motif) ligand 20 (CCL20) as one of the cytokines through stem-cell-related gene expression analysis in the human HCC tissues. Serum CCL20 was related to prognosis, suggesting that it could be a biomarker. In the tissue immunostaining, the CCL20 receptor, CCR6, was expressed in the tumor's stroma cells. High CCL20 expression was related to the tumor microenvironment to promote cancer progression in HCC. The CCL20-CCR6 axis is related to the tumor microenvironment to promote cancer progression in HCC. The CCL20-CCR6 axis could be a potential therapeutic target.



CCL20 neutralizing antibody suppresses HCC tumor growth.

Transcription factor regulation of CD8 T cell differentiation

Makoto Kurachi, MD & PhD

Professor, Department of Molecular Genetics, Kanazawa University Graduate School of Medical Sciences E-mail <u>kurachi@med.kanazawa-u.ac.jp</u> Web site http://molgenet.w3.kanazawa-u.ac.jp/wordpress/



Abstract:

Several transcription factors (TFs) including T-bet, Eomes, Runx3, Id2 and Blimp-1 are known to regulate the expression of genes essential for CD8⁺ effector T cells such as IFN-γ and perforin. However, CD8⁺ T cells that lack T-bet, Eomes, Id2 or Blimp-1 acquire many features of normal effector T cells and are competent to form T cell memory. One interpretation of these relatively mild defects in single transcription factor (TF)-deficient settings is that functional redundancy exists between TFs known to be involved in CD8⁺ effector differentiation. Alternatively, or in addition, other TFs may exist that are upstream and/or more fundamental to the regulation of CD8⁺ T cell differentiation.

The transcription factor BATF is required for interleukin 17 (IL-17)-producing helper T cell (TH17) and follicular helper T cell (TFH) differentiation. Here, we show that BATF also has a fundamental role in regulating effector CD8⁺ T cell differentiation. BATF-deficient CD8⁺ T cells show profound defects in effector expansion and undergo proliferative and metabolic catastrophe early after antigen encounter. BATF, together with IRF4 and Jun proteins, binds to and promotes early expression of genes encoding lineage-specific transcription-factors (T-bet and Blimp-1) and cytokine receptors, while paradoxically repressing genes encoding effector molecules (IFN-γ and granzyme B). Thus, BATF amplifies TCR-dependent transcription factor expression and augments inflammatory signal propagation but restrains effector gene expression. This checkpoint prevents irreversible commitment to an effector fate until a critical threshold of downstream transcriptional activity has been achieved.

Research interests:

- 1. Molecular mechanisms of CD8 T cell differentiation (effector, memory and exhaustion)
- 2. Interaction of transcription factors
- 3. Anti-virus and awnti-tumor immunity provided by CD8 T cells

Key publications:

- 1. Sci Immunol. Jan 15;6(55):eabe3702, 2021
- 2. Sci Rep. Nov 27;10(1):20763, 2020
- 3. *Immunity*. May 19;52(5):825-841.e8, 2020
- 4. J Exp Med. May 4;217(5):e20190888, 2020
- 5. Immunity. Oct 15;51(4):591-592, 2019
- 6. Nat. protoc. 12(9): 1980-1998, 2017
- 7. Nat. Immunol. 15(4): 373-383, 2014

Educati	ional back	ground & professional experience:		
1997	M.D.	Kanazawa University, Faculty of Medicine		
2002	2002 Ph.D. Kanazawa University, Graduate School of Medicine			
2000~2011		Department of Molecular Preventive Medicine, The University of Tokyo (Prof. Kouji		
	Ν	Aatsushima)		
2011~20)18	Post-doc and research associate, University of Pennsylvania (Prof. John Wherry)		
2018~		Professor, Department of Molecular Genetics, Kanazawa University Graduate School of		
	Ν	Aedical Sciences		

Keita Suzuki

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Abstract: We aim to elucidate the association between lifestyles and the development of many kinds of diseases using epidemiological methods. We have held a cohort

study in Shika town that is a rural area located in Noto peninsula, Ishikawa. In particular, we have been trying to elucidate risk factors associated with the development of chronic pain. Although the effects of vitamin D on chronic pain have been investigated in many previous studies, it remains debated. Therefore, we assessed the association between chronic pain and serum 25-hydroxyvitamin D concentrations with the stratification of subjects by factors considered to affect the association. The results showed that the association between deficiency of serum 25-hydroxyvitamin D and prevalence of chronic pain was observed in subjects with drinking habits. Our findings will contribute to the development of tailored treatment for chronic pain. We also take part in a national cohort study called the Japan Diabetes and Obesity Study. This study included more than 700 patients with type 2 diabetes or obesity across Japan and had investigated the development of cardiovascular disease and chronic kidney disease for 5 years. Zaharia OP and colleagues from German Diabetes Center have reported novel subgroups of type 2 diabetes. Therefore, we also divided the Japanese patients of the cohort using clustering analysis that is the same method as the previous study. Then, the characteristics of each cluster of the Japanese cohort were compared with those of the German cohort. Furthermore, our group is developing a collaboration study with professor Michael Roden and professor Cristian Herder groups. We are going to exam the effects of several genes reported to be altered methylation 52 weeks after a metabolic surgery on muscle insulin sensitivity. We will demonstrate the tentative study plan.

Research projects:

- 1. Epidemiological study on the effects of lifestyles on chronic pain
- 2. National cohort study of patients with obesity and metabolic syndrome
- 3. Basic research on pathophysiology of diabetes

Key publications:

- 1. J Pain Res 13:2987-2996, 2020
- 2. J Diabetes Investig:jdi.13402, 2020
- 3. Biomarkers 25:587-593, 2020
- 4. Nutrients 12:nu12082258, 2020
- 5. Prog Rehabil Med:prm.20200008, 2020
- 6. Nutrients 11:nu11040911, 2019
- 7. Nutrients 11:nu11020389, 2019
- 8. Nutrients 10:nu10121825, 2018
- 9. Jpn J Compr Rehabil Sci 6:56-63, 2015

Educational background & professional experience:

2018 - present	Department of Public Health, Graduate School of Advanced Preventive Medical Sciences	,
	Kanazawa University	

- 2015 2018 Assistant Professor, Department of Rehabilitation, Faculty of Health Science and Technology, Kawasaki University of Medical Welfare
- 2013 2015 Master's Program in Rehabilitation, Graduate School of Health Science and Technology, Kawasaki University of Medical Welfare
- 2009 2013 Department of Rehabilitation, Faculty of Health Science and Technology, Kawasaki University of Medical Welfare

Effect of atmospheric particulate matters on respiratory symptoms in people with chronic cough

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Web site http://publichealth.w3.kanazawa-u.ac.jp/index-en.html

Abstract:

To clarify the relationship between particulate matters (PM) and their components and respiratory diseases with chronic cough, epidemiological studies in combination with the measurement of PM components, especially polycyclic aromatic hydrocarbons, are under conducted. Through these studies, standards of the atmospheric concentration for PM components are expected to be revised to prevent the development and progression of diseases with chronic cough, especially in health-vulnerable populations.

Research projects:

- 1. Biochemical and epidemiological research on the causal relationship between PM elements and respiratory diseases with chronic cough
- 2. Prospective cohort study on lifestyle-related diseases in a Japanese rural area
- 3. Analysis of gene-environment interactions in lifestyle-related diseases

Related publications in the present topic:

- 1. Higashi T, et al. Effects of Asian dust on daily cough occurrence in patients with chronic cough: A panel study. Atmos Environ 2014;92:506-513
- 2. Higashi T, et al. Exacerbation of daily cough and allergic symptoms in adult patients with chronic cough by Asian dust: A hospital-based study in Kanazawa. Atmos Environ 2014;97:537-543
- 3. Anyenda EO, et al. Associations of Cough Prevalence with Ambient Polycyclic Aromatic Hydrocarbons, Nitrogen and Sulphur Dioxide: A Longitudinal Study. Int J Environ Res Public Health 2016;13:800
- 4. Nguyen TT, et al. A Longitudinal Study of Association between Heavy Metals and Itchy Eyes, Coughing in Chronic Cough Patients: Related with Non-Immunoglobulin E Mediated Mechanism. Int J Environ Res Public Health. 2016;13:110

Educational background & professional experience:

- 2000~ Kanazawa University Graduate School of Medical Science
- 2006 Awarded the degree of PhD in Internal Medicine
- 2010~ Assistant Professor, Section of Emergency Medicine, Kanazawa University Hospital
- 2012~ Assistant Director, Health Policy Bureau, Ministry of Health, Labour and Welfare
- 2014~ Associate Professor, Kanazawa University

Genetic and functional diversity of leukocyte immunoglobulin-like receptor family in humans

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Abstract: Genes of the leukocyte immunoglobulin (Ig)-like receptor (LILR) family are located on human chromosome 19q13.4, within the leukocyte receptor complex (LRC) region, which includes the genes encoding a number of immunoglobulin superfamily receptors, such as leukocyte associated Ig-like receptors and killer Ig-like receptors (KIRs). The LILR gene cluster differs greatly in the number of genes and amino acid sequences among species, owing to their species-specific evolution. Human LILRs comprise 11 protein-coding genes and two pseudogenes, comprising five inhibitory receptors, five activating receptors, and one soluble form. LILR genes show high genetic diversity, including copy number variations and functional SNPs, resulting in large inter-individual differences. It is still unclear why the LILR family shows such remarkable genetic diversity. In general, inhibitory LILRs are involved in immune regulation by recognizing self-molecules such as HLA class I molecules. However, our recent studies have revealed that some pathogenic microorganisms and tumor cells use inhibitory LILRs to escape from host immunity. In contrast, the activating receptors of the LILR family play a role in defense against pathogenic microorganisms. These data suggest that the LILR family has co-evolved with microbial pathogens, which have diversified their functions in humans. In this symposium, I will introduce the genetic and functional diversity of the LILR family in humans.

Research projects:

- 4. Host-microbe interaction through leukocyte receptor complex
- 5. Genetic association study of leukocyte receptor complex
- 6. Immune evasion mechanism that targets host inhibitory receptors

Key publications:

- 10. J Hum Genet. 2021 (Online ahead of print)
- 11. J Biol Chem. 295:9531-41, 2020
- 12. Nature. 562:605-9, 2018
- 13. Nature. 552:101-5, 2017
- 14. Nat Microbiol. 1:16054, 2016
- 15. Blood. 124:924-35, 2014
- 16. PLoS Pathog. 8:e1002565, 2012
- 17. Am J Hum Genet. 82:1075-83, 2008

Educational background & professional experience:

- **2004 B.S.**, The University of Tokyo
- 2006 M.S., The University of Tokyo
- 2008~ JSPS Research Fellow
- 2009 Ph.D., The University of Tokyo
- 2010~ Postdoctoral Fellow, WPI Immunology Frontier Research Center, Osaka University
- 2012~ Assistant Professor, WPI Immunology Frontier Research Center, Osaka University
- 2018- Associate Professor, Advanced Preventive Medical Sciences Research Center, Kanazawa University

Award: 2019 The Young Scientists' Award, the Commendation for Science and Technology by the Minister of Education, Culture, Sports, Science and Technology



Atmospheric behavior comparison of polycyclic aromatic hydrocarbons (PAHs), Nitro-PAHs (NPAHs), and water-soluble inorganic ions (WSIIs) at two background sites in Japan

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[Objective] Among air pollutants, PM_{2.5} consists of a variety of organic and inorganic compounds. Polycyclic aromatic hydrocarbons (PAHs) and nitro-PAHs (NPAHs) are both well-known environmental pollutants due to their carcinogenicity and mutagenicity. Water-soluble inorganic ions (WSIIs) are some of the dominant chemical components of PM_{2.5} that can affect the size, composition, and lifetime of particles, and they play a key role in the formation of severe pollution events such as haze. Japan is located on the leeward side of the East Asian winter monsoon. PM_{2.5} in Japan is not only domestically produced but is also produced on the Asian continent and reaches Japan via long-range transport. Daily PM_{2.5} samples were simultaneously collected at Kanazawa University Wajima Air Monitoring Station (WAMS) and Fukue-Jima Atmosphere and Aerosol Monitoring Station (FAMS) in Japan, to compare the characteristics of air pollutants among different regions and to determine the possible variation during the long-range transport process.

[Methods] PM_{2.5} sampling was simultaneously performed at WAMS and FAMS using high-volume air samplers at a flow rate of 1000 L/min that were equipped with quartz fibre filters. Filters were changed every 24 hours in the winter monsoon period (Period 1) in April 2017 and in the summer monsoon period (Period 2) in June 2019. After filter pretreatment, nine PAHs and three NPAHs including fluoranthene, pyrene, benz[*a*]anthracene, chrysene, benzo[*b*]fluoranthrene, benzo[*k*]fluoranthrene, benzo[*a*]pyrene, benzo[*ghi*]perylene, indeno[1,2,3-*cd*]pyrene, 1-, 2-nitropyrenes, and 2-nitrofluoranthene were determined by using HPLC with fluorescence detection. Nine WSIIs including sodium, ammonium, potassium, calcium, magnesium, chloride, sulfate, nitrate, and bromine were determined by using ion chromatography.

[Results] In Period 1, the daily average PM_{2.5} concentrations at FAMS was 23.2 μ g/m³ (8.90 - 78.5 μ g/m³) that mostly higher than 8.62 μ g/m³ (2.33 - 21.2 μ g/m³) which observed at WAMS, but the opposite trend was observed in the Period 2. The average concentrations of Σ PAHs, Σ NPAHs, and Σ WSIIs were similar between two sites both in the two periods. The results revealed that the air pressure and coexistence reactants are the main causes, which result in the differences in the composition of air pollutants in long-range transportation receptor areas.

Key publications:

- 1. <u>Yang L., et al., Int. J. Environ. Res. Public Health, accepted (Review)</u>
- 2. Yang, L., et al., Int. J. Environ. Res. Public Health, 18, 688, 2021
- 3. Yang, L., et al., Int. J. Environ. Res. Public Health, 17, 8224, 2020
- 4. Yang, L., et al., J. Environ. Sci., 99, 72-79, 2020
- 5. Yang, L., et al., Int. J. Environ. Res. Public Health, 16, 2817, 2019
- 6. Yang, L., et al., Asian J. Atmos. Environ., 12, 369-376, 2018

Educational background:

2016 ~ Graduate School of Natural Science and Technology, Kanazawa University (Awarded the degree of Master)

2018 ~ Graduate School of Medical Sciences, Kanazawa University (PhD Student) Award:

2017.10 Joint International Symposium of Institute of Nature and Environmental Technology, Kanazawa University (*The Best Poster Award*)

The unique source of polycyclic aromatic hydrocarbons on the northwestern highland of China

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Abstract: Lanzhou is an important heavy industry city in northwestern China. In the study, polycyclic aromatic hydrocarbons (PAHs) and nitro-PAHs (NPAHs) in PM_{2.5} were first observed at a background site, the Semi-Arid Climate and **Environment Observation Station of Lanzhou University** (SACOL), in Lanzhou in five seasonal campaigns. The results show that the PAH and NPAH concentrations peaked in the winter campaigns, which were approximately a dozen times higher than those in the spring, summer, and fall campaigns. The enhancement in the PAH and NPAH pollution would increase the toxic potential of PM_{2.5}. In addition, the diagnostic ratios indicate that vehicle emissions were the primary source of the PAHs throughout the five campaigns, and coal and biomass combustion also contributed during the winter, summer, and fall campaigns. Among NPAHs, 2nitrofluoranthene and 2-nitropyrene were generated through OH radical-initiated reactions during atmospheric transport, while 1nitropyrene came from combustion sources. Moreover, it is noticed that the ratio between pyrene and fluoranthene increased abnormally in the spring and fall campaigns, which is presumably caused by the burning of Tibetan barley straw in the northwestern highlands. This finding underscores that air pollution, such as PAHs, derived from traditional habits in the northwestern highlands gives a unique and prospective clue to the atmospheric transport network in East Asia. Therefore, it is requested that



Fig. 1. Location of the sampling site. SACOL is located in Yuzhong County in Lanzhou.

research involving endemic emissions and tracers in the northwestern highlands in China be carried out. For more details, please check out the full article (Zhang L.L. et al., *Environ. Pollut.*, 2021).

Lulu ZHANG, Ph.D.

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Key Publications

- 1. Environ. Pollut. 274: 116527, 2021
- 2. Aerosol Air Qual. Res. 20: 2035-2046, 2020
- 3. Environ. Pollut. 263: 114454, 2020
- 4. Sci. Total Environ. 705: 135840, 2020
- 5. J. Sci. Environ. 88: 370-384, 2020
- 6. Asian J. Atmos. Environ. 13: 266-275, 2019
- 7. Environ. Pollut. 255: 113147, 2019

Educational background

2017~2020: Ph.D., Graduate School of Medical Sciences, Kanazawa University

Characteristics of $PM_{2.5}$ -bound polycyclic aromatic hydrocarbons at a roadside air pollution monitoring station at Yamashina, Kanazawa from 2017 to 2020

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[Introduction] Ambient particulate matter (PM) is a well-known atmospheric pollutant. PM greatly influences air quality, climate, and human health. Especially, fine particulates (PM2.5) is more harmful because it can be enriched in more toxic components and penetrate into the human lungs deeply. On PM2.5, polycyclic aromatic hydrocarbons (PAHs) are a group of ubiquitous organic pollutants composed of multiple aromatic rings. PAHs are mainly originated from incomplete combustion processes and have been widely researched due to their carcinogenicity and mutagenicity. In the urban area, traffic emission is recognized as a major source of PAHs. In Japan, since the 1980s, traffic emission has gradually become the main source of air pollution in commercial cities. Among these cities, Kanazawa is the capital city of Ishikawa Prefecture and the largest city in the Hokuriku region of Japan. It is a tourist city with no significant industrial or agricultural activities and does not use coal for winter heating. Moreover, based on the data from Automobile Inspection & Registration Information Association, in Kanazawa, per 1000 inhabitants owned an average of 1489 vehicles until March 2016 ranking 13th among cities in Japan. The monitoring of traffic emission in Kanazawa is particularly important. Therefore, several air pollution monitoring stations were set up where the traffic emission is most obvious to monitor the traffic-related pollutants. In this study, a four-year sampling campaign was conducted at one of these stations at a heavily trafficked road in Yamashina, Kanazawa. We aimed to have a better understand on the characteristics of traffic-related PAHs and were hoping to provide data basic for more accurate health risk assessment and the formulation of traffic emission policy.

[Materials and Methods] Sampling was conducted at a roadside air pollution monitoring station in Yamagawa loop road in Yamashina, Kanazawa for one or two weeks in four seasons from April 2017 to February 2020 (spring: April 2017, 2018 and 2019; summer: August 2017, 2018 and 2019; autumn: November 2017, 2018 and 2019; winter: February 2018, 2019 and 2020). Twenty-four hour PM_{2.5} samples were collected on quartz fiber filters using a high-volume air sampler at a flow rate of 1000 L/min. Nine PAHs include fluoranthene (FR), pyrene (Pyr), benz[a]anthracene (BaA), chrysene (Chr), benzo[b]fluoranthene (BbF), benzo[k]fluoranthene (BkF), benzo[a]pyrene (BaP), benzo[ghi]perylene (BgPe) and indeno[1,2,3-cd]pyrene (IDP) were analyzed by HPLC with a fluorescence detector.

[Results and Discussion] **During the sampling campaign, the** PM_{2.5} level in most days (over 90%) were lower than the 24-hour standard (35 µg/m³) which indicated that air pollution was not serious in the roadside environment of Yamashina. The PAHs concentration presents a similar seasonal variation trend. Higher concentrations were observed in the winter campaigns (1004 ± 260 pg/m³ in 2018, 1069 ± 450 pg/m³ in 2018 and 566 ± 256 pg/m³ in 2019), while lower concentrations were in the summer campaigns (298 ± 90.7 pg/m³ in 2017, 202 ± 84.6 pg/m³ in 2018 and 259 ± 154 pg/m³ in 2019). Possible reasons for the seasonal variations were that high temperature could cause vaporization of semivolatile PAHs from the particle to the gas phase and enhanced photochemical degradation of PAHs in summer. FR, Pyr, BgPe and BbF predominantly contributed to the total PAHs. The proportion of PAHs exhibited variations but with no significance (p < 0.05). These variations might be associated with the variations of weather conditions, etc. Among these variations, [BbF]/([BbF] + [BkF]) and [IDP]/([BgPe] + [IDP]) remained at the range of 0.47 to 0.83 and 0.28 to 0.49, respectively. And these ranges were different with the ranges for identifying other PAHs emission sources. These two ratios seemed to be good indicators for identifying the traffic emission sources.

Key publication:

1. Int. J. Environ. Res. Public. Health. 17, 805, 2020.

Educational background & professional experience:

2019~ Division of Pharmacy and Division of Pharmaceutical Sciences, Graduate School of Medical Sciences, Kanazawa university (Master student).

Seasonal characteristic and health risks of PM_{2.5}-bound polycyclic aromatic hydrocarbons and nitro-polycyclic aromatic hydrocarbons in Shenyang, China

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- ² School of Pharmaceutical Sciences, Liaoning University, Shenyang, China
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- ⁴ Institute of Nature and Environmental Technology, Kanazawa University, Kanazawa, Japan.
- ⁵ School of Pharmaceutical Sciences, Nagasaki University, Nagasaki, Japan.

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[Objective]

Polycyclic aromatic hydrocarbons (PAHs) and nitro-PAHs (NPAHs) are some of the most harmful organic compounds in fine particles ($PM_{2.5}$), which are well-known for their carcinogenicity and mutagenicity. PAHs and some NPAHs in the urban atmosphere released from man-made sources such as traffic emission and coal combustion. Shenyang is the largest city in northeast China, also is the industrial and transported center, those factory activities and crowded roads can largely increase the direct emission of PAHs and NPAHs, severely affected the air quality and human health. Moreover, some other NPAHs can secondarily formed by the atmospheric reaction, occupied a large proportion of total NPAHs in the atmosphere. Therefore, this study collected $PM_{2.5}$ samples in Shenyang in four seasons from 2018 to 2019 to clarify the characteristics of $PM_{2.5}$ -bound PAHs and NPAHs in Shenyang, as well as the health risks.

[Methods]

PM_{2.5} samples were collected at the School of Pharmaceutical Sciences, Liaoning University in Shenyang by using a low-volume air sampler (3 L/min), equipped with quartz fiber filters. Filters were changed every 48 h in summer (2017/07/25 - 08/06), winter (2018/01/05 - 01/17), and autumn (2018/11/15 -11/27), every 24 h in spring (2019/03/20 - 03/27), respectively. After pretreatment, 9 kinds of PAHs and 3 kinds of NPAHs including fluoranthene (FR), pyrene (Pyr), benz[*a*]anthracene, chrysene, benzo[*b*]fluoranthene, benzo[*a*]pyrene (BaP), benzo[*k*]fluoranthene, benzo[*ghi*]perylene, indeno[1,2,3*cd*]pyrene, 1-, 2-nitropyrenes (1-, 2-NP), 2-nitrofluoranthene (2-NFR) were detected by using HPLC system with fluorescence detector.

[Results and discussion]

The concentration of $PM_{2.5}$ -bound PAHs was highest in winter (49.67 ± 21.75 ng/m³) and lowest in summer (3.72 ± 1.92 ng/m³). The concentration of NPAHs was highest in winter (260.32 ± 159.93 pg/m³) and lowest in spring (95.36 ± 111.61 pg/m³). The concentration of NPAHs was significantly lower than PAHs and the seasonal characteristics were different. By using diagnostic ratio, the result of [FR]/([FR] + [Pyr]) indicated that PAHs were mainly affected by traffic emission in summer and coal combustion in winter. The NPAHs diagnostic ratios ([2-NFR]/[1-NP]) showed that NPAHs in winter mainly generated from local emission, which differed from other seasons. The potential health risks of PAHs calculated by BaP-equivalent concentration were highest in winter, showed a serious health risks on human.

Educational background

2019 Faculty of Water Resources and Hydroelectric Engineering, Environmental Engineering, Xi'an University of Technology (bachelor's degree)

2020~ Graduate School of Medical Sciences, Kanazawa University (Master student)

How COVID-19 lockdown in China significantly influenced the air pollutants at the Wajima Air Monitoring Station of Japan?

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[Introduction]

Air pollution as a global problem has attracted considerable attention, health studies from many researchers had already proved the damage of air pollution to human. Particulate matter (PM) including PM₁ (aerodynamic diameter <1 mm) and PM_{2.5} are deliberate as the air pollutant. Both PM₁ and PM_{2.5} will then turn into lung cells (alveolar macrophages and epithelial cells, etc.) after inhaling, which leads to oxidative stress. Carbonaceous aerosol such as elemental carbon (EC) and organic carbon (OC) also plays a significant role in the pollution of atmospheric aerosol, which attracted many attentions by the researchers. The Kanazawa University Wajima Air Monitoring Station (KUWAMS) in Japan is a monitoring station for studying long-range transport of air pollution from East Asia. Previous researches had found the air pollutants that emission from combustion in northeast China can strongly affect KUWAMS in the cold season. During the period of COVID-19, most factories, transportation, work and even schooling were prohibited, the cease leads to the significant decreasing of the intensity of air pollution level. The impact of anti-epidemic measurements implemented by China during COVID-19 on the longrange transport of air pollutants from East Asia to KUWAMS was documented and analyzed in this study. [Method] With the surrounding of dense forest, KUWAMS located at the north western coast of Noto Peninsula, 2.1 kilometres south of the Sea of Japan. There was nearly no sever artificial industrial emissions around the site. The concentration of PM1, PM2.5, OC, EC and meteorological conditions was measured online during December 2019 to April 2020. The back-trajectory analysis was used to analyze the orbit of air mass to track the source of air pollutants.

[Result and Discussion]

The mean concentration of PM₁, PM_{2.5}, OC and EC were $4.46 \pm 2.17 \ (\mu g \text{ m}^{-3})$, $11.49 \pm 4.24 \ (\mu g \text{ m}^{-3})$, $0.64 \pm 0.42 \ (\mu g \text{ m}^{-3})$ and $0.10 \pm 0.06 \ (\mu g \text{ m}^{-3})$, respectively. Comparing with the same period of 2019, the concentration of all pollutants shows a significant decrease in the COVID-19 period. This might due to the curbing of disease transmission by adopting drastic containment measures in China. Also, the year to year contrast of the concentration of PM_{2.5} in KUWAMS with other cities in China shows a similar tendency during the lockdown. Overall, the decrease of artificial air pollution emissions during the epidemic in Northeast China caused a major reduction in the pollution at KUWAMS after long-range transportation. This study also demonstrated the sensitivity of KUWAMS sampling point to long-range transportation of air pollutants from East Asia continent.

Key publications:

1. Chem. Pharm. Bull., 2021. (In press)

Educational background:

Department of Chemistry, Loughborough University (Awarded the degree of Master of Science) Graduate School of Medical Sciences, Kanazawa University (PhD Student) Analysis of compositional variation and source characteristics of Water-soluble ions in TSP at a remote

background site in Japan (Wajima) from 2005 to 2015.

Y. Wang¹, Q.Y. Zhou¹, L. Yang¹, H. Zhang¹, X. Zhang¹, W.L. Xing¹, P.C.Bai¹, L.L.Zhang², K. Hayakawa², N. Tang ^{2,3}

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Introduction

Atmospheric particulate matter has a wide range of sources and multiple compositions and is an important pollutant affecting air quality, climate change, and human health. Wajima in Japan is a typical remote background site facing the Sea of Japan, located in the East Asian monsoon region. During winter and spring, the Wajima area mostly receives the Asian continent air masses with the East Asian winter monsoon before crossing Japan to the North Pacific Ocean which provides the possibility for long-term studies of long-range transport in such a unique geographic location. In this study, total suspended particulate (TSP) was consecutively collected at Kanazawa University Wajima Air Monitoring Station (KUWAMS) from 2005 to 2015, and water-soluble inorganic ions (WSIIs) were determined. Our purpose is to understand the composition characteristics; analyze research time trends and sources of the generation of WSIIs and the impact of the marine and anthropogenic sources during the short- and long-range transportation from other areas.

Methods

TSP samples were collected with a high-volume air sampler with a quartz fiber filter at a flow rate of 700 L/min every seven consecutive days, from January 7, 2005, to December 18, 2015. The filter samples were analyzed with an ion chromatograph to determine the concentrations of water-soluble inorganic ions (WSIIs), including Cl⁻, NO₃⁻, SO₄²⁻, Na⁺, NH₄⁺, K⁺, Mg²⁺, and Ca²⁺.

Results and Conclusion

The average TSP concentration was $19.91 \pm 11.33 \mu g/m^3$. The average total WSIIs concentration was $7.93 \pm 3.93 \mu g/m^3$, accounting for 42.3 % of TSP mass, ranged from 11.4 to 93.9 %. SO₄²⁻ is the most abundant ion, contributing a total WSII mass from 18.0 to 79.8 %, and non-sea-salt (nss-) SO₄²⁻ contributed from 63.6 % - 99.6 % of total SO₄²⁻, which was related to human activities on the Asian continent and the effects of marine precursors in spring and summer, respectively. NO₃⁻ and NH₄⁺ contribute 6.3 and 7.4 % of the total WSIIs and were affected by long-range transport and local sources as well. The representative ions of sea salt, Na⁺ and Cl⁻, with the lowest concentration. K⁺ is mainly produced from biomass burning with a stable seasonal variation, Ca²⁺ as the characteristic ion of dust has the highest concentration in spring. Mg²⁺ comes from minerals and marine sources during spring and summer, respectively.

This work describes in detail the annual change trend of the WSIIs of atmospheric particles in the Wajima area (KUWAMS), seasonal characteristics, and source contributions, provide a comprehensive understanding of long-term variation in atmospheric particulate.

Educational background

2015 ¬ 2019: Graduate School of Food Science and Engineering, Dailian Ocean University

2019 ¬ present: Graduate School of Medical Sciences, Kanazawa University

Air pollution exposure and respiratory health of office workers in current China: a pilot survey in a heavy-polluted region

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⁴Chinese Research Academy of Environment Sciences, China.

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[Introduction]

Air pollution is a silent killer for human health. Exposure to air pollution is associated with multiple health outcomes, especially to respiratory system. Fine particulate matter (PM_{2.5}), nitrogen oxides (NO₂, NO), ozone (O₃) and sulfur dioxide (SO₂) are typical pollutants with wide distribution resulting to extensive human health risk. Polycyclic aromatic hydrocarbons (PAHs) are a group of ubiquitous organic pollutants enhancing the health hazard of air pollution. As a rapidly developing country with the largest population, China is facing severe air quality and undertaking active measures to control air pollution. The population number of indoor work force in China has increased due to rapid urbanization and modernization, especially in economically active but heavy-polluted Beijing-Tianjin-Hebei region. Thus, it is significant and urgent to evaluate the air pollution exposure and respiratory health on office workers residing in this region.

[Methods]

Fourteen healthy office workers were recruited in the urban Beijing and Baoding. During the periods of eleven continuous days in each of summer, autumn and winter in 2019, daily personal sampling was conducted for various air pollutants including PM_{2.5}, PM_{2.5}-bound PAHs, NO₂, NO, O₃ and SO₂. The concurrent ambient air pollutants data were obtained from the national air monitoring stations which were nearest to the subjects. Simultaneously, repeated measurements on lung function index were performed including forced expiratory volume in the first second (FEV₁) and peak expiratory flow (PEF). Additionally, time-activity diary was recorded by each subject. A mixed linear model was utilized to explore the relationship between air pollution exposure and lung function changes. Inhalation cancer risk due to PM_{2.5}-bound PAHs exposure was calculated based on a well-known carcinogenic PAH, Benzo[*a*]pyrene (BaP).

[Results and discussion]

During the entire sampling period, the major exposure pollutants were $PM_{2.5}$, NO_2 and $PM_{2.5}$ -PAHs with a mean concentration of 38.5 ± 27.1 , 46.41 ± 39.29 , $114.0 \pm 121.6 \mu g/m^3$, and $26.6 \pm 27.0 ng/m^3$, respectively. A significant seasonal order was shown in above pollutants as winter > autumn > summer, except for $PM_{2.5}$ (autumn > winter). Moreover, there were 8% of $PM_{2.5}$, 17% of NO_2 and 25% of BaP measurements higher than the respective Chinese standards, especially in autumn and winter, indicating an elevated health risk.

No significant adverse effect was shown in pulmonary function in the short-term air pollution exposure, which might result from a good lung health status of these subjects with an average FEV₁ and PEF higher than the respective standard limits. Notably, the lifetime cancer risk of exposure to PM_{2.5}-bound PAHs was 1.69 × 10^{-5} for the office workers in Beijing and Baoding, which was higher than the acceptable level of 10^{-6} suggested by the U.S. Environmental Protection Agency, indicating the urgency to improve the air quality and protect respiratory health for the office workers.

On the other hand, individual exposed pollutants depicted great difference with those measured in ambient monitoring station in the concentration level and seasonal variation, indicating that ambient air pollution data can't characterize personal exposure accurately. Furthermore, based on the stable time-location features of the office workers, a feasible estimation approach monitoring was found to estimate human exposure based on microenvironmental exposure model, which will be researched and utilized in the further investigation.

Key publications:

13. Int. J. Environ. Res. Public Health. 17, 957, 2020.

Educational background & professional experience:

- 2014~ Department of Pharmaceutical Engineering and Environmental Sciences, School of Pharmaceutical Engineering, Shenyang Pharmaceutical University
- 2019~ Division of Pharmacy and Division of Pharmaceutical Sciences, Graduate School of Medical Sciences, Kanazawa University

Chisato MORI, MD & PhD

Professor, Department of Bioenvironmental Medicine, Graduate School of Medicine, Chiba University Director, Center for Preventive Medical Sciences, Chiba University

E-mail cmori@faculty.chiba-u.jp

Web site https://cpms.chiba-u.jp

Research projects:

- 1. Environmental Medicine
- 2. Public Health
- 3. Developmental Medicine

Key publications:

- 1. Environ Sci Pollut Res Int. 2019
- 2. PLoS One. 2019
- 3. J Dev Orig Health Dis. 2019
- 4. J Epidemiol. 2018
- 5. J Diabetes Investig .2018
- 6. Environmental Pollution.2018
- 7. J Epidemiol Community Health. 2017
- 8. J Hum Genet. 2016
- 9. J Toxicol Sci. 2016
- 10. Indoor and Built Environment 2014
- 11. Anat Sci Int. 2014
- 12. Chemosphere. 2014
- 13. Nature. 1995

Educational background & professional experience:

- 1984 Doctor of Medicine (M.D.), Asahikawa Medical College
- 1989 Doctor of Medical Science (D.Med.Sc; Ph.D) Kyoto University

1984-1992 Research Associate, Department of Anatomy, Faculty of Medicine, Kyoto University

1990-1992 Visiting Associate, National Institute of Environmental Health Sciences, National Institutes of

Health (NIEHS/NIH), Research Triangle Park, North Carolina, U.S.A.

1992-2000 Associate Professor, Department of Anatomy and Developmental Biology, Faculty of Medicine, Kyoto University

2000-2001 Professor, Department of Anatomy and Cell Biology, School of Medicine, Chiba University,

- 2001- Professor, Department of Bioenvironmental Medicine, Graduate School of Medicine, Chiba University
- 2006-2008 Adjunct Professor, Division of Environmental Health Sciences University of Minnesota, School of Public Health, USA
- 2008- Director, Center for Preventive Medical Sciences, Chiba University
- 2009-2013 Adjunct Professor, College of Medicine, Inje University, Korea

Award: 1995 Young Investigator Award of the Japanese Association of Anatomists

Walkable Design in Practice

Hiroaki Yoshida

Project Assistant Professor, Center for Preventive Medical Sciences, Chiba University E-mail: hiroaki.yoshida@chiba-u.jp Website: https://hpd.cpms.chiba-u.jp/



Abstract:

In recent years, there is an increase in the number of reports showing the influence of the built environment on human health. The research theme of our group is to characterize the relationship between health and the built environment from an engineering perspective. We aim to construct useful objects and comfortable environments for public safety, health, and welfare, and to translate our research findings into sustainable urban development practices.

Specifically, we focus on the following two areas:

- Characterizing the relationship between health and the built environment.
- Implementing healthy urban development in collaboration with various stakeholders.

Research projects:

- 1. Relationship between health and the built environment
- 2. Walkability and walkable design implementation
- 3. Tool design for healthy community development

Educational background & professional experience:

- 2002~ Bachelor of science, Department of Mathematical Sciences, Ritsumeikan University, Japan.
- 2007~ Bachelor of Engineering, Department of Architecture, Chiba University, Japan.
- 2011~ Technical assistant, Graduate of Architecture, Chiba University
- 2013~ Design Department, Nikken Sekkei Ltd.
- 2014~ Project Researcher, Campus Planning Office, Chiba University, Japan
- 2015~ Design intern, Ashton Porter Architects, London
- 2016~ Technical assistant, Center for Preventive Medical Sciences, Chiba University, Japan
- 2019~ Project Assistant Professor, Center for Preventive Medical Sciences, Chiba University, Japan

Association between levels of PCB in maternal serum with birth weight of newborn in C-MACH study

Akifumi Eguchi¹, Kenichi Sakurai¹, Midori Yamamoto¹, Masahiro Watanabe¹, Aya Hisada¹, Tomoko Takahashi¹, Emiko Todaka¹, Chisato Mori^{1, 2}

¹Center for Preventive Medical Sciences, Chiba University, Japan. ²Department of Bioenvironmental Medicine, Graduate school of Medicine, Chiba University, Japan

Background and Purpose:

In our previous studies, it was reported that maternal exposure to polychlorinated biphenyls (PCBs) was negatively correlated with birth weight of newborns in part of C-MACH cohort. However, congener specific effect and mixture effect of PCB congeners were not well determined. Therefore, in the present study, we used all maternal serum samples collected at 32 weeks of gestational age in the C-MACH cohort to examine the relationship between newborn birth weight and the individual PCB congener in maternal serum to analyze the individual and synergistic effects of PCB exposure.

Methods:

Informed consents were obtained from all the participants. Human serum samples (291 maternal sera) were collected from the participants in Chiba and Saitama Prefecture, Japan. Thirteen congeners of PCB in maternal serum were analyzed using the gas chromatography electron capture negative ionization quadrupole mass spectrometry. Effects of mixture and individual PCB congener (13 congeners: CB74, 118, 126, 138, 146, 153, 156, 170, 177, 178, 180, 183 and 187) were analyzed by generalized weighted quantile sum regression (gWQS) model with multiple imputation. This study was approved by the Biomedical Research Ethics Committee of the Graduate School of Medicine, Chiba University.

Results and Discussion

The mean concentration of total PCBs in maternal sera was 410 pg g⁻¹ wet weight. Individual congener levels of PCBs were highly correlated each other (R = 0.63 - 0.99), however, these levels were not significantly correlated with birth weight of newborns. Birth weight of newborns were significantly associated with exposure of mixture PCB in gWQS model. The results suggest that exposure to mixture PCB were associated with birth weight of newborns. However, specific effects of individual PCB congeners were not shown, indicated the possibility that a single PCB congerners may have special effects was not observed in this study.

Nagasaki University



Department of Molecular Medicine *Yuji Nagayama* E-mail: nagayama@nagasaki-u.ac.jp TEL: +81-95-819-7173 FAX: +81-95-819-7175

Aims of Study

The research object is to elucidate the pathogenesis of thyroid cancer, through the basic research using cultured cells and animal models.

Research Projects

- 1. Generation of mouse models and elucidation of pathophysiology of thyroid cancer
- 2. Study on relationship between autophagy and thyroid morphology/function/carcinogenesis
- 3. Study on relationship between mitophagy and thyroid morphology/function/carcinogenesis
- 4. Identification and functional analysis of thyroid cancer stem cells

Status and Prospects

- 1. By crossing the conditional knock-in (KI) mice that express BRAF^{V600E} in the presence of Cre DNA recombinase (Braf^{CA}) and adenovirus expressing Cre in the thyroid, the new mouse model of thyroid cancer was established. These mice are now combined with the PTEN knockout (KO) mice or the conditional TGFβ KI mice. In addition, the conditional KI mice for ATM is also being used.
- 2. By crossing the conditional KI mice that lose Atg5 gene expression in the presence of Cre (Atg5^{f/f}) and thyroid-specific Cre expressing transgenic mice (TPO-Cre), the morphological and functional significance of autophagy in the thyroid is now being studied.
- 3. Two KO mice that lack expression of PARK2, a component of canonical mitophagy, or MIEAP, a component of non-canonical mitophagy are being used to study the relationship quality control of mitochondria and carcinogenesis. Thyroid Hurthle cell cancer line, XTC.UC1, is also being used

The functional significance of ALDH and ROS as a marker for thyroid cancer stem cells is being studied.



Atsushi Kawakami, MD & PhD Dean, Nagasaki University Graduate School of Biomedical Sciences Professor and Chairman, Department of Immunology and Rheumatology, Division of Advanced Preventive Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences E-mail atsushik@nagasaki-u.ac.jp Web site http://www.med.nagasaki-u.ac.jp/intmed-1/

Research projects:

- 1. Inflammatory arthritis: Genetic, environmental, immunological and imaging analysis
- 2. Autoinflammatory diseases: Genetic and inflammasome analysis leading to drug discovery
- 3. Sjögren's syndrome: Pathological analysis especially the role of HTLV-1
- 4. Systemic lupus erythematosus: Pathological analysis especially identification of autoantigen
- 5. Immuno-related adverse events: Identification of susceptibility through whole-genome analysis

Key publications:

- 1. J Intern Med 289(2):206-220, 2021
- 2. Ann Rheum Dis 78(10):1320-1332, 2019
- 3. Virus Res 269:197643, 2019
- 4. Arthritis Rheumatol 71(5):766-772, 2019
- 5. Ann Rheum Dis 77(4):602-611, 2018
- 6. Arthritis Care Res 26,2018
- 7. Frontiers in Immunology 8;8: 1958, 2018
- 8. Arthritis <u>Rheumatol</u> 70(7):1014-1021, 2018
- 9. Clin Infect Dis 2;67(2):291-294, 2018
- 10. *Rheumatology* 1;57(4):718-726, 2018
- 11. Arthritis Res Ther 25;19(1):108, 2017
- 12. Arthritis Rheumatol 68(8):1981-8, 2016
- 13. Arthritis Rheumatol 67(4):1096-106, 2015
- 14. Blood 1;94(11):3847-54, 1999

Educational background & professional experience:

- 1985 First Department of Internal Medicine, Nagasaki University School of Medicine
- 1987~1991 Department of Immunology and Rheumatology, Nagasaki University Graduate School of Biomedical Sciences
- 1991~1993 Post-Doctoral Fellow, Division of Tumor Immunology, Dana-Farber Cancer Institute, Boston (Supervised by Prof. Paul Anderson)
- 1991~1993 Post-Doctoral Fellow, Division of Tumor Immunology, Dana-Farber Cancer Institute, Boston (Supervised by Prof. Paul Anderson)
- 2000 Assistant Professor, Unit of Translational Medicine, Department of Immunology and Rheumatology, Nagasaki University Graduate School of Biomedical Sciences
- 2009 Associate Professor
- 2010 Professor and Chairman
- 2016 Professor and Chairman, Department of Immunology and Rheumatology, Unit of Advanced Preventive Medical Sciences, Division of Advanced Preventive Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences
- 2017 Professor and Chairman, Department of Immunology and Rheumatology, Division of Advanced Preventive Medical Sciences, Nagasaki University Graduate School of Biomedical Sciences
- 2019 Dean, Nagasaki University Graduate School of Biomedical Science

Awards:

- 2000 Japan College of Rheumatology Scientific Award
- 2001 7th The Japanese Society of Inflammation and Regeneration Promotion Award
- 2004 32th Japan Clinical Immunology Society of the General Assembly Best Poster Award

How to identify preclinical phase, onset and

progression of RA?



Kiyoshi AOYAGI, MD & PhD

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Nagasaki University Graduate School of Biomedical Sciences

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Research projects:

- 7. Epidemiology on musculoskeletal health
- 8. The Japan Public Health Center-based Prospective Study for the Next Generation

Key publications:

- 1. BMC Geriatr. 2020 Nov 11;20(1):466.
- 2. J Physiol Anthropol. 2020 Apr 10;39(1):9.
- 3. J Epidemiol. 2020 Sep 5;30(9):396-403.
- 4. J Epidemiol. 2020 Jan 5;30(1):46-54.
- 5. Medicine (Baltimore). 2018 Jan;97(4):e9721.
- 6. BMC Musculoskelet Disord. 2017 Apr 28;18(1):176.
- 7. BMC Musculoskelet Disord. 2016 Dec 1;17(1):493.
- 8. Osteoporos Int. 2014 Jun;25(6):1727-34.
- 9. Geriatr Gerontol Int. 2013 Oct;13(4):881-6.
- 10. Osteoporos Int. 2013 Mar;24(3):907-15.
- 11. Osteoporos Int. 2011 Apr;22(4):1167-73.
- 12. Osteoporos Int. 2002 Sep;13(9):723-30.
- 13. J Rheumatol. 2002 Jul;29(7):1454-8.
- 14. BMC Geriatr. 2001;1:3.
- 15. Calcif Tissue Int. 2000 Aug;67(2):106-10.
- 16. Ann Rheum Dis. 1999 May;58(5):315-9.
- 17. J Bone Miner Res. 1998 Sep;13(9):1468-74.

Educational background & professional experience:

- 1985 MD, Nagasaki University School of Medicine
- 1989 Ph.D. received from Nagasaki University Graduate School of Biomedical Sciences
- 1989 Department of Orthopedic Surgery, Nagasaki University
- 1995-96 Research Fellow, Hawaii Osteoporosis Center, USA
- 1997 Assistant Professor, Department of Public Health, Nagasaki University School of Medicine
- 2000 Associate Professor, Department of Public Health, Nagasaki University School of Medicine
- 2002 Professor, Department of Public Health, Nagasaki University Graduate School of Biomedical Sciences

Award: 2019 Japan Society of Physiological Anthropology

Current status and future prospects in the diagnosis and treatment of familial Mediterranean fever in Japan Tomohiro KOGA, M.D., Ph.D.

Center for Bioinformatics and Molecular Medicine, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan



Abstract:

Familial Mediterranean fever (FMF) is a common inherited autoinflammatory disease associated with periodic fevers, arthritis, and serositis. The therapeutic goals of FMF are to prevent febrile attacks, minimize subclinical inflammation during attacks, and prevent the development and progression of amyloidosis. Canakinumab, a monoclonal antibody against IL-1 β , is expected to be effective in such cases of colchicine invalidity and intolerance, but there is not sufficient evidence in Japan. With the pandemic of COVID-19, the importance of appropriate management of patients with periodic fevers has increased. In this lecture, we will discuss the actual treatment of familial Mediterranean fever, the latest evidence for treatment in Japan, COVID-19 infection, and autoinflammatory diseases.

Reference:

1. Endo Y, Koga T, et al., Clin Exp Rheumatol. 2020 Sep-Oct;38 Suppl 127(5):49-52.

2. Koga T et al., Clin Exp Rheumatol. 2020 Sep-Oct;38 Suppl 127(5):35-41.

3. Hara K, Koga T, et al., Mod Rheumatol. 2020:1-2. doi: 10.1080/14397595.2020.1800558.

4. Koga T et al., Immunol Med. 2018 Dec;41(4):177-180. doi: 10.1080/25785826.2018.1524105.

5. Koga T et al., Rheumatology (Oxford). 2018;57(4):718-726. doi: 10.1093/rheumatology/kex451.

6. Koga T et al., Medicine (Baltimore). 2016;95(16):e3449. doi: 10.1097/MD.00000000003449.

Educational background & professional experience:

2005 M.D. Oita University School of Medicine, Japan.

2011 Ph.D. received from Graduate School of Biomedical Sciences, Nagasaki University, Japan.

2011-2014 Post-Doc. Department of Medicine, Division of Rheumatology, Beth Israel Deaconess Medical Center (Tsokos Lab), Harvard Medical University, Boston, USA.

2014-2016 Assistant prof. Medical Education Development Center, Nagasaki University, Japan.

2016-present Assistant prof. Graduate School of Biomedical Sciences, Nagasaki University, Japan.

(2016-present Leading Initiative for Excellent Young Researchers of the Ministry of Education, Culture, Sports, Science and Technology, Japan.)

Circadian clocks in senescent cells: a possible strategy to fight aging

Yasukazu NAKAHATA, Ph.D.

Center for Bioinformatics and Molecular Medicine, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan



Abstract:

Our research goal is to reveal molecular mechanisms connecting circadian clocks and aging process and contribute to extend healthy aging. To address this goal, we have first investigated at cellular level. So far, we have found that cellular senescence, aging at cellular level, triggers altered circadian clocks with a prolonged period and delayed phase [1,2]. We have also found that intracellular NAD⁺ amount decreases with cellular senescence, furthermore, the onset of cellular senescence delays when NAMPT, which is the rate-limiting enzyme in NAD⁺ salvage pathway, is overexpressed [3]. Our previous study that circadian clock and NAD⁺ salvage pathway are mutually regulated via NAD⁺/SIRT1 axis [4-6] prompted us to investigate whether the boost of NAD⁺ in senescent cells recover the alteration of circadian clock properties. The answer was "yes", circadian period was shortened in NAD⁺-boosted senescent cells and even aged mice [unpublished data]. Now we have been struggling to reveal molecular mechanisms of how NAD⁺ influences circadian clocks. We have also started to find out other molecules which recover the alteration of circadian clock properties in senescent cells to understand how circadian clock regulates aging process and contribute to extend healthy aging.

Reference:

1. Ahmed et al., Front Neurosci. 15:638122, 2021 doi: 10.3389/fnins.2021.638122

2. Ahmed et al., Aging (Albany NY) 11(3):950-973, 2019 doi: 10.18632/aging.101794

3. Khaidizar et al., Genes cells 22(12):982-992, 2017 doi: 10.1111/gtc.12542

4. Nakahata and Bessho, Biomed Res Int. 2016:3208429, 2016 doi: 10.1155/2016/3208429

5. Nakahata et al., Science 324(5927):654-657, 2009 doi: 10.1126/science.1170803

6. Nakahata et al., Cell 134(2):329-40, 2008 doi: 10.1016/j.cell.2008.07.00

Educational background & professional experience:

2002 Ph.D. received from Osaka University Graduate School of Scince, Japan

2002-2005 Post-Doc. Osaka Bioscience Institute, Japan

2005-2006 Post-Doc. Institut de Génétique et de Biologie Moléculaire et Cellulaire (IGBMC), France

2006-2009 Post-Doc. University of California, Irvine, USA

(2008-2009, supported by Postdoctoral Fellowship for Research Abroad of Japan Society for the Promotion of Science)

2009-2019 Assistant prof. Nara Institute of Science and Technology (NAIST), Japan 2019-present Associate prof. Nagasaki University, Japan

A prospective cohort study of rheumatic disease in a residential health checkup-based healthy population:prediction of rheumatoid arthritis and IgG4-related disease development.

Yoshika TSUJI, M.D.



Graduate School of Biomedical Sciences, Division of Advanced Preventive Medical Sciences, Nagasaki University, Japan

Abstract:

Anti-citrullinated protein antibody (ACPA) production is observed in several organs even prior to the onset of rheumatoid arthritis (RA), and oral mucosa is considered to be one of the important tissues. Saliva is considered to reflect the oral microbiota including periodontal disease. A gene-environment interaction between cigarette smoking and shared epitope genes in HLA-DRB1*shared epitope (SE) provides a high risk of ACPA-positive RA. However, the interaction of HLA-DRB1*SE, ACPA, cigarette smoking and oral microbiota of RA patients remains to be elucidated. The Nagasaki Island Study, which had started in 2014 collaborating with Goto City, Nagasaki Prefecture, Japan, is intended for research of the preclinical stage of RA, including ACPA, HLA genotype screening, oral microbiota and lifestyle habit. Elucidation of the relationship between the oral MB and ACPA-positive RA might enable prediction of high-risk individuals for RA and preventive intervention in the future.

Reference:

- 1. Tsuji S et al., Clin Exp Rheumatol. 2021 Jan 28. Online ahead of print.
- 2. Fukui S et al., Sci Rep. 2020 Jun 11;10(1):9466.
- 3. Eguchi M et al., Immunol Med. 2018 Mar;41(1):34-38.
- 4. Aramaki T et al, Mod Rheumatol. 2020 Jan;30(1):50-57.
- 5. Michitsuji T et al., 2019 Nov;29(6):1013-1016.
- 6. <u>Tsuji Y et al.</u>, Case Rep Rheumatol. 2015;2015:163952.

Education:

2012 M.D received from Nagasaki University School of Medicine, Japan

2019- Ph.D. present Graduate School of Biomedical Sciences, Division of Advanced Preventive Medical Sciences, Nagasaki University, Japan

Association of FTO genotype with obesity and bone health

Xiao Xu, student pursuing a PhD degree

Department of Public Health, Nagasaki University Graduate School of Biomedical Sciences, Nagasaki, Japan



Abstract:

Aim: The aim of this study was to examine the association of the FTO gene (Fat Mass and Obesity associated gene #610966 on OMIM) with obesity and bone health among community-dwelling adults. Methods: This crosssectional study included 1,828 participants aged 27 to 97 years, residing in a rural city in western Japan (N prefecture). Participants were recruited at medical check-ups in 2014 and 2016 for community dwelling population. Body mass index (BMI) (kg/m2) was calculated. Bone mass of the calcaneus was evaluated using a quantitative ultrasound measurement. Peripheral blood mononuclear cells were obtained from subjects. The SNP rs1421085 was genotyped using hydrolysis probe. The chi-squared test was used to determine whether the variants was in equilibrium in that population. All analyses were carried out using SPSS 23. Results: The mean ages of the participants were 67.6 +/- 11.6 in men and 67.1 +/- 11.3 years in women, respectively (Table 1). There was a significant association between the genotype and overweight, but there was no significant difference in stiffness index. There were significant associations between the minor allele and overweight (Table 2 and 3). Logistic regression analysis showed a significant protective association in men with carriers of minor allele against low bone mass after an adjustment for age and BMI in man aged 50 to 70, not significant in women. Conclusions: Our study indicated a significant association of the genetic polymorphism on FTO gene with bone mass among community dwelling men aged 50 to 70. The polymorphism may play a rule in a part of bone heath with higher BMI and other beneficial functions.

Educational background & professional experience:

2017,MB. received from Fujian Medical University, China 2018,Studying for a PhD in the Graduate School of Biomedical Sciences, Nagasaki University, Japan. HTLV-1 infection and age-associated health problems

Hirotomo YAMANASHI, M.D., Ph.D.

The Department of General Medicine, Nagasaki University Hospital, Nagasaki, Japan



Abstract:

Sarcopenia is defined as the accelerated loss of muscle mass and low muscle strength with aging, and has a medical and economic burden in a super-aged society due to adverse outcomes including falls, disability, long term care placement, and mortality. Human T-cell lymphotropic virus type 1 (HTLV-1) is a human retrovirus that is endemic in Southwest Japan [1]. HTLV-1 is associated with a number of diseases, such as adult T-cell leukemia/lymphoma, and autoimmune/inflammatory diseases [2]. However, little is known about the effect of asymptomatic HTLV-1 infection on age-associated problems. Our previous case-control study using data from the Nagasaki Islands Study, which was a prospective cohort study performed in Goto City in the western islands of Japan (N*4,500) revealed that asymptomatic HTLV-1 infection was positively associated with atherosclerosis as measured by carotid intima-media thickness [3]. As we also found the negative association between atherosclerosis and handgrip strength in our Japanese and Indian cohorts [4], we hypothesize HTLV-1 asymptomatic infection has a negative impact on skeletal muscle and strength. We conducted a cross-sectional study (N=2,811) in our cohort study [5]. HTLV-1 infection was significantly associated with sarcopenia (adjusted OR 1.46, 95% CI 1.03–2.07, P=0.034). Active surveillance and early detection of asymptomatic HTLV-1 infection might be beneficial to reinforce countermeasures to control cardiovascular risks and to inhibit the progress of HTLV infection-associated sarcopenia.

Reference:

- 1. Gessain A, et al. Front Microbiol 2012; 3:388. doi: 10.3389/fmicb.2012.00388.
- 2. Schierhout G, et al. Lancet Infect Dis. 2020;20(1):133-143. doi: 10.1016/S1473-3099(19)30402-5.
- 3. Yamanashi H, et al. Clin Infect Dis. 2018 Jul 2;67(2):291-294. doi: 10.1093/cid/ciy168.
- 4. Yamanashi H, et al. Geriatr Gerontol Int. 2018;18(7):1071-1078. doi: 10.1111/ggi.13312.
- 5. Yamanashi H, et al. Aging (Albany NY). 2020;12(15):15504-15513. doi: 10.18632/aging.103736.
- Educational background & professional experience:
- 2006 M.D. Sapporo Medical University, Japan.
- 2016 Ph.D. received from Graduate School of Biomedical Sciences, Nagasaki University, Japan.
- 2013-2017 Assistant prof. Department of Island and Community Medicine, Nagasaki University, Japan.
- 2018-present Senior lecturer. Department of General Medicine, Nagasaki University Hospital, Japan.

Diabetes and Metabolism Session

Dr. Michael RODEN

Professor of Medicine, Endocrinology and Metabolic Diseases, Director, Division of Endocrinology and Diabetology, Heinrich-Heine University (HHU) and University Clinics Düsseldorf (UKD), Germany Chief Scientific Executive Officer, German Diabetes Center (DDZ), Leibniz Center of Diabetes Research, Düsseldorf Germany E-mail <u>michael.roden@ddz.de</u>

Research focus

My scientific interests comprise clinical-experimental and basic research on the (patho)physiology of energy metabolism with a focus on the understanding of insulin resistance, obesity, nonalcoholic fatty liver diseases (NAFLD) and diabetes mellitus. I have developed and employed methods to non-invasively trace metabolic fluxes using magnetic resonance spectroscopy and stable isotopes in cohorts with and without diabetes mellitus. With this technology, my group contributed paradigm-shifting studies on the regulation of glycogen turnover, ectopic fat stores and mechanism of





lipid- and amino acid-induced insulin resistance in humans. More recently, I focused on the role of mitochondrial function in metabolic diseases.

15 Key publications

Nature 2019 (in press) (Review), Nat Commun 2019 (in press), Nature 562(7725):128-132 (2018), Diabetes Care 4:1235-1243 (2018), Physiol Rev 98:1371-141 (2018) (Review). Lancet Diabetol Endocrinol 7:684-694 (2019), J Clin Invest 27:695-708 (2017), Cell Metab 21:739-746 (2015), Nat Rev Gastro Hepat 14:32-42 (2017) (Review), Proc Natl Acad Sci U S A 111:9597-602 (2014), Lancet Diabetes Endocrinol 3:208-219 (2013), Nat Rev Endocrinol 13:92-103 (2011), Hepatology 50:1079-1086 (2009), PLoS Med 4:e154 (2007), J Clin Invest 97:2859-2865 (1996)

Professional education and training

1986	Graduation as Dr. med. univ., University of Vienna, Austria
1993/97/03	Certification in Internal Medicine, Endocrinology & Metabolism Clinical Pharmacology, Austria
1994-95	Max-Kade-Fellow, Austrian Academy of Science, Yale University, CT, USA
1997-06	Associate Professor, of Medicine, Univ. of Vienna, Austria
2003-08	Head, 1. Med. Dept., Hanusch Hospital, (Teaching Hospital of Medical Univ. Vienna), Vienna,
	Austria
2008-	Chair/Professor/Director, Div. of Metab. Diseases, later Endocrinol.&Diabetol., HHU/UKD,
	Düsseldorf
	Chief Scientific Executive Officer, DDZ, Head, Institute for Clinical Diabetology at DDZ,
	Düsseldorf
2009-	Boards of Speakers, National Health Center - Diabetes (DZD), Germany
2016-	Member, German Council of Science and Humanities (WR), appointed by the President of
	Germany
2017-	Head, Committee Medicine of the WR, Germany

Selected awards

- 2004 International Novartis Award for Innovative Patient Oriented Research, Young Investigator
- 2006 ESCI (Mack-Foster) Award for Excellence in Clinical Sciences, Europ. Soc. for Clin. Invest
- 2006 Oskar-Minkowski Prize, Europ. Assoc. for the Study of Diabetes (EASD)
- 2013 Honorary Doctorate, Dr. h. c., Medical Faculty, University of Belgrade
- 2014 Somogyi Award, Hungarian Diabetes Association
- 2016 Honorary Doctorate, Dr. h. c., Medical School, University of Athens
- 2017 Paul Langerhans Medal, German Diabetes Association
- 2018 19th Aretaeus lecture, Hellenic Diabetes Association
- 2018 G. B. Morgagni Prize Gold Medal Career Achievement Association, Italy

Diabetes and Metabolism Session

Dr. Christian HERDER

Professor (Epidemiology), Medical Faculty, Heinrich Heine University Düsseldorf, Germany

Head of the research group Inflammation, Institute for Clinical Diabetology, German Diabetes Center (DDZ), Leibniz Center for Diabetes Research, Düsseldorf, Germany

Guest scientist, Division of Endocrinology and Diabetology (Director Prof. Dr. Michael Roden), Medical Faculty, Heinrich Heine University Düsseldorf, Germany

E-mail christian.herder@ddz.de

Research focus

We focus on epidemiological and mechanistic studies on the role of inflammation-mediated processes in the development and progression of type 2 diabetes. Our studies sharpened the concept that inflammation - as independent risk factor or induced by lifestyle and environmental factors - contributes to the development of type 2 diabetes and its chronic macro- and microvascular complications and therefore represents a promising therapeutic target in disease prevention and treatment. Recent publications included the first prospective studies on multiple inflammation-related biomarkers and pathways as predictors of incident sensorimotor polyneuropathy.

Key publications

Environ Health Persp 2020;128:127013; Trends Endocrinol Metab 2019;30:286-298; Diabetes Care 2019;42:240-247; Endocr Rev 2019;40:153-192; Diabetes 2018;67:2434-2442; Psychoneuroendocrinology 2018;91:216-225; Arterioscler Thromb Vasc Biol 2017;37:1222-1227; Diabetes Care 2017;40:569-576; Heart 2017;103:63-70; Trends Endocrinol Metab 2015;26:551-563; Diabetologia 2015;58:2269-2277; Diabetes Care 2015;38:91-96; Diabetes 2014;63:4343-4359; Diabetes Care 2014;37:1401-1409; Diabetes Care 2013;36:3663-3670; Diabetes Care 2012;35:2540-2547; Lancet 2012;379:2279-2290; Diabetes Care 2011;34:2320-2322; Environ Health Perspect 2010;118:1273-1279; Diabetes 2010;59:1222-1227; Diabetes Care 2009;32:1921-1923; Diabetes Care 2009;32:421-423; Diabetes Care 2007;30:854-860; J Clin Endocrinol Metab 2007;92:1023-1033; Diabetologia 2006;49:921-929; Diabetes 2005;54:2932-2938.

Professional education and training

1993-1999 Heinrich Heine University Düsseldorf and University of Edinburgh (UK): Studies in Biology

- **1999** Diploma (Biology) Heinrich Heine University Düsseldorf
- 2003 Doctorate (Dr. phil. nat./Biochemistry), Johann Wolfgang Goethe University, Frankfurt am Main, Germany
- 2009 Master of Science (M.Sc.) in Epidemiology, Johannes Gutenberg University Mainz, Germany
- 2012 "Habilitation" in Epidemiology (highest academic qualification in Germany), Medical Faculty Heinrich Heine University Düsseldorf
- 2017 Professor (Apl. Prof.), Epidemiology, Medical Faculty, Heinrich Heine University Düsseldorf,



Selected awards

- 2007 Jühling Prize from the Anna Wunderlich-Ernst Jühling Foundation (Germany)
- 2009 Lecture in the Rising Star Symposium, Annual Meeting of the European Association for the Study of Diabetes (EASD)
- 2013 Ferdinand Bertram Prize (German Diabetes Association/DDG)
- 2016 Hans Christian Hagedorn Grant (German Diabetes Association/DDG)
- 2019 Menarini Grant from the German Diabetes Association (German Diabetes Association/DDG)

Air pollution and Health

Tamara Schikowski, MPH, PHD

Head of Research Group Environmental epidemiology of lung, brain and skin aging



IUF-Leibniz Research Institute for Environmental Medicine E-mail <u>tamara.schikowski@iuf-duesseldorf.de</u> Web site <u>http://www.iuf-duesseldorf.com/schikowski-team.html</u>

Abstract:

The work of the research group focuses on epidemiological aspects of environmentally-induced aging of the lung, the brain and the skin. The main focus is the collection and analyses of data on the effect of long-term exposure to air pollution on chronic diseases (lung, skin and brain) as well as the complex interplay between the organs. We were able to show that chronic exposure to air pollution, in particular PM_{10} and NO_2 as well as living close to major roads, increases the risk of developing chronic obstructive pulmonary disease (COPD) and mild cognitive impairment (MCI) in elderly women. Furthermore, skin aging was enhanced. In addition, the working group could show that high exposure with traffic-related air pollution increases the risk of cardio-pulmonal mortality Worldwide the working group Schikowski was the first one to show that particle exposure from traffic-related sources was associated with diabetes and skin aging (pigment spots and wrinkles).

Research projects:

- Gene-Environment Interaction analyses
- Investigation of air pollution decline on aging and health
- Investigation of the effect of particle pollution on mild cognitive impairment in elderly women
- Investigation of air pollution effects on skin aging and inflammation in China
- Investigation of air pollution effects on skin/lung aging India
- Investigation of the effect of carbon black on health in Manila (
- Investigation of the effect of long-term air pollution on the development and incidence of COPD in particular in non-smoking women and interaction with reproductive factors and obesity

Key publications:

- 1. Benefits of improved air quality on aging lungs Impacts of genetics and obesity. Eur Respir J. 2019 Feb 14.
- 2. Tropospheric ozone and skin aging: Results from two German cohort studies. Environ Int. 2019 Mar;124:139-144
- 3. Nonatopic eczema in elderly women: Effect of air pollution and genes. J Allergy Clin Immunol. 2019 Jan;143(1):378-385.e9. J Allergy Clin Immunol
- 4. The role of air pollution and lung function in cognitive impairment. Eur Respir J. 2018 Feb 21;51(2).
- 5. Atopic dermatitis: Interaction between genetic variants of GSTP1, TNF, TLR2, and TLR4 and air pollution in early life. Pediatr Allergy Immunol. 2018 Apr 6.
- 6. Impact of long-term air pollution exposure on metabolic control in children and adolescents with type 1 diabetes: results from the DPV registry. Diabetologia. 2018 Jun;61(6):1354-1361.
- 7. Long-term air pollution exposure and diabetes in a population-based Swiss cohort. Environ Int. 2014 Sep;70:95-105.
- 8. Association of ambient air pollution with the prevalence and incidence of COPD. Eur Respir J. 2014 Sep;44(3):614-26.
- 9. Effects of long-term exposure to air pollution on natural-cause mortality: an analysis of 22 European cohorts within the multicentre ESCAPE project. Lancet. 2014 Mar 1;383(9919):785-95
- 10. Improved air quality and attenuated lung function decline: modification by obesity in the SAPALDIA cohort. Environ Health Perspect. 2013 Sep;121(9):1034-9.

Educational background & professional experience:

- 1996~ University of Cologne Medical School
- 2001~ Bachelor of Environmental Health, Swinburne University Melbourne
- 2004~ Master of Public Health, Monash University Melbourne
- 2008~ PhD Award Public Health, Heinrich-Heine University Düsseldorf
- 2009- Postdoctoral Researcher, Swiss Tropical and Public Health Institute, Basel Switzerland
- 2013- Working Group Leader, IUF Leibniz Institute for Environmental Medicine, Düsseldorf Germany

Award:

Vichy Exposome Award 2016, The combined effect of air pollution and sun exposome on extrinsic skin aging manifestation in the population-based SALIA study group by Vichy Laboratories, France

TGO Jordan Memorial Prize, Student with the highest academic results in. the final year of the Bachelor of Health Science of 2002 by the Australian Institute of Environmental Health, Victorian Division

HIV-1 cell biology: host factors and pharmacological inhibitors in sensing and restriction

Carsten Münk, PhD

Professor for AIDS Research, Clinic for Gastroenterology, Hepatology and Infectiology University Hospital Düsseldorf, Heinrich-Heine-University Düsseldorf

E-Mail: carsten.muenk@med.uni-duesseldorf.de



Abstract:

We are interested in early events until integration in HIV-1 replication and the Vif-APOBEC3 interaction. We try to develop pathways that interfere with the virus infection and explore new animal models

for HIV-1. At the same time, we working on mechanisms of zoonosis of SIV of chimpanzee (SIVcpz) (see Fig. 1)

Research projects:

1. Vif- APOBEC3 interaction 2. Rolle of USP18 in HIV-1 replication 3. Mechanisms of resistance to integrase inhibitors 4. New animal models for HIV-1 5. Mechanism of restriction of rare HIV-1 N, O, P and SIVcpz **Key publications:** 1. mBio July/August (10) 4 2019 2. Virology (523): 52-63. 2018 3. Journal of Virology 92(20) 2018 4. Retrovirology, 15:38 2018 5. PLoS Pathog. 13(12):e1006746 2017 6. Journal of Virology 90(23):10545-10557. 2016 7. Journal of Virology. 90(22):10193-10208. 2016 8. Science 343 (6176): 1221-8. 2014 9. Nucleic Acid Research: Jan 7; 42 (1): 396-416. 2014 10. Journal of Virology, 86(11):6097-6108. 2012 11. Proc. Natl. Acad. Sci. USA, Jul 21; 106(29):12079-84. 2009 12. Genome Biology, 9 (3): R48, 2008 13. J. of Virology, 81(13): 7048 - 7060. 2007 14. Nucleic Acid Res., 35(11):3784-96. 2007 15. Cell 114 (1):21-31. 2003



Fig 1 A model of SIVcpz's evolutionary path to HIV. SIVcpz to human cross-species transmission likely happened 100 years ago in central Africa. After spillover, SIV adapted to human cells. For high-level replication, SIVcpz had to adapt to human tetherin and evolve a Vif protein able to counteract human APOBEC3H (A3H). Only viruses that were able to adapt to these and possible other host-factors were able to spread globally. Educational background and professional experience:

2008 to present: Professor for AIDS Research, University Hospital, Clinic for Gastroenterology, Hepatology and Infectiology (Director Prof. Dr. D. Häussinger), Heinrich-Heine University Düsseldorf, Germany.

2003-2008: Research Group Leader, Department of Medical Biotechnology (Head Prof. Dr. K. Cichutek), PaulEhrlich-Institute, Langen, Germany.

1999-2003: Postdoctoral Fellow, Infectious Disease Laboratory (Prof. Dr. N. R. Landau), The Salk Institute for Biological Studies, La Jolla, USA. 1999: Graduation, Dr. rer. Nat, University Hamburg, Germany.



Heiner Fangerau (Prof. Dr. med., Dr. h.c. (Bucharest), ML) is Head and director of the Department of the History, Philosophy and Ethics of Medicine, Heinrich-Heine-University Duesseldorf. Before he went to Duesseldorf in 2016 he held chairs in the history, philosophy and ethics of medicine in Ulm (since 2008) and Cologne (2014). He has a strong research record in the history and ethics of modern medicine. He studied medicine at the University of Bochum. In 2000 he finished his doctorate on the history of eugenics at the Institute of the History of Medicine in Bochum (summa cum laude). His habilitation ("post doctoral thesis") on the history of the biomedical model was defended in 2008. He is a member of the German National Academy of Sciences Leopoldina

His main research fields are research ethics, history and ethics of psychiatry and neurology, child and adolescence psychiatry and historical network analyses. A particular focus of Prof. Fangerau has experience in collaborating in several interdisciplinary research

projects, including BMBF and EU projects. Current works include the history and ethics of technology development in medicine including m-health and e-health applications.

Selected publications:

Hansson N, Halling T, Fangerau H (eds): Attributing Excellence in Medicine: The History of the Nobel Prize (Clio Medica 98). Brill & Rodopi, Leiden 2019

Görgen A, Nunez GA, Fangerau H (eds): Handbook of Popular Culture and Biomedicine. Knowledge in the Life Sciences as Cultural Artefact. Springer, Cham 2019

Karenberg A, Fangerau H, Steinmetz H, Berlit P, Grond M (2019): Historical review: a short history of German neurology – from its origins to the 1940s. Neurological Research and Practice 1:14 [6 pages]. Görgen A, Fangerau H (2018): Deconstruction of a taboo: press coverage of sexual violence against children in pedagogical institutions in Germany 1950–2013. Media, Culture and Society 40(7):973-991 Marazia C, Fangerau H (2018): Imagining the brain as a book: Oskar and Cécile Vogt's "library of brains". Progress in Brain Research 243:181-203

Fangerau H (2017): Scope for action at the psychiatric periphery around World War I. A public sanatorium for 'nervous diseases' in the Province of Hanover. In: Müller T (Hrsg.): Zentrum und Peripherie in der Geschichte der Psychiatrie. Regionale, nationale und internationale Perspektiven. Steiner, Stuttgart, S. 99-112.

Fangerau H (2017): Experimental Biology and the Biomedical Ideal around the Year 1900. In: Müller GB (ed): Vivarium. Experimental, Quantitative, and Theoretical Biology at Vienna's Biologische Versuchsanstalt. MIT Press, Cambridge Ma, pp. 77-94.

Fangerau H, Braune F, Lenk C (2017): Predictive Diagnostic Testing for Late-Onset Neurological Diseases in Asymptomatic Minors: 'Do No Harm' and the Value of Knowledge. In: Gadebusch Bondio M, Spöring F, Gordon J-S (eds): Medical Ethics, Prediction, and Prognosis: Interdisciplinary Perspectives. Routledge, New York/ London, S. 55-65

Fangerau H (2013): "Evolution of knowledge from a network perspective: recognition as a selective factor in the history of science". In Fangerau H, Geisler H, Halling T, Martin W (Hrsg.): "Classification and Evolution in Biology, Linguistics and the History of Science. Concepts, Methods, Visualization", Steiner, Stuttgart 2013, S. 11-32

Fangerau H (2009): "From Mephistopheles to Iesajah: Jacques Loeb, Science and Modernism", Social Studies of Science 39: 229-256.

Matthis Krischel, PhD

Lecturer

Institute for the History, Philosophy and Ethics of Medicine Centre for Health and Society, Medical Faculty Heinrich Heine University Düsseldorf <u>matthis.krischel@hhu.de</u> <u>matthiskrischel.de</u>



Research Interests

History and ethics of medicine and the life sciences, especially

- Nazi medicine and its commemoration
- History and ethics of human genetics
- History and ethics of urology, venereology and sexology
- Ethics and History of dentistry

Representative Publications (in English)

- Krischel M (2021) Dentists in National Socialist Germany. A Fragmented Profession. In: Hildebrandt S, Offer M, Grodin M (Hrsg) Regognizing the Past in the Present. New Studies on Medicine before, d uring, and after the Holocaust. Berghahn Books, New York, 190-203
- Hansson N, Krischel M, Södersten P, Moll F, Fangerau H (2020) "He gave us the cornerstone of Sexu al Medicine" – A Nobel plan but no Nobel Prize for Eugen Steinach. Urologia Internationalis 104, 50 1-509
- Krischel M, Hansson N (2017) Ageing: Rejuvenation study stirs old memories. Nature 546 (7656), 33.
- Krischel M, Moll F, Van Kerrebroeck P (2014) A stone never cut for: A new interpretation of 'The cure of folly' by Jheronimus Bosch. Urologia Internationalis 93 (4), 389-393
- Krischel M (2014) German Urologists under National Socialism. World Journal of Urology 32 (4), 10 55-1060

Education and Experience

Since 2017: Member of the Clinical Ethics Committee, Düsseldorf University Hospital

Since 2016: Lecturer at the Department of History, Theory and Ethics of Medicine, Heinrich Heine University Düsseldorf

2013: PhD in History and Philosophy of Medicine, Ulm University, Germany

2013: Research Prize on the Role of Doctors during the Nazi Era, German Medical Association ("Herbert Lewin Research Prize")

2007: M.A. in History of Science, University of Oklahoma, USA

Ute Linnenkamp



		Master					
09/2010 – 08/2012	Erasmus Degree awarde	Mundus d: European M	Master aster in Public	European Health: Europu	Public bhealth	Health	
University of Copenhagen (DK), Institute of Public Health08/2011 - 06/20122nd Module of the dual Master degree in Public Health09/2010 - 06/2011University of Sheffield (UK), School of Health and Related Research 1st Module of the dual Master degree in Public Health							
09/2007 - 08/2010University of Maastricht, Faculty of Health, Medicine and Life Sciences Degree awarded: Bachelor of Science European Public Health09/2008 - 08/2010Honours Degree: Governance of health care innovations						Degree	

Publications

 Brüne, M., Linnenkamp, U., Andrich, S., Jaffan-Kolb, L., Claessen, H., Dintsios, C.-M., Schmitz- Losem, I., Kruse, J., Chernyak, N., Hiligsmann, M., Hermanns, N., Icks, A., 2020. Health Care Use and Costs in Individuals With Diabetes With and Without Comorbid Depression in Germany: Results of the Cross-sectional DiaDec Study. Diabetes Care dc192487. <u>https://doi.org/10.2337/dc192487</u>

Linnenkamp, U., Gontscharuk, V., Brüne, M., Chernyak, N., Kvitkina, T., Arend, W., Fiege, A., Schmitz-Losem, I., Kruse, J., Evers, S. M.

A. A., Hiligsmann, M., Hoffmann, B., Andrich, S., & Icks, A. (2020). Using statutory health insurance data to evaluate non-response in a cross-sectional study on depression among patients with diabetes in Germany. International Journal of Epidemiology, dyz278. https://doi.org/10.1093/ije/dyz278

2018 Grobosch, S., Kuske, S., Linnenkamp, U., Ernstmann, N., Stephan, A., Genz, J., Begun, A., Haastert, B., Szendroedi, J., Müssig, K., Burkart, V., Roden, M., & Icks, A. (2018). What information needs do people with recently diagnosed diabetes mellitus have and what are the associated factors? A cross-sectional study in Germany. BMJ Open, 8(10), e017895. https://doi.org/10.1136/bmjopen-2017-017895

Bächle, C., Claessen, H., Maier, W., Tamayo, T., Schunk, M., Rückert-Eheberg, I.-M., Holle, R., Meisinger, C., Moebus, S., Jöckel, K.-H., Schipf, S., Völzke, H., Hartwig, S., Kluttig, A., Kroll, L., Linnenkamp, U., & Icks, A. (2018). Regional differences in antihyperglycemic medication are not explained by individual socioeconomic status, regional deprivation, and regional health care services. Observational results from the German DIAB-CORE consortium. PLOS ONE, 13(1), e0191559. <u>https://doi.org/10.1371/journal.pone.0191559</u> 2017 Guariguata, L., Linnenkamp, U., Makaroff, L. E., Ogurtsova, K., & Colagiuri, S. (2018). Global Estimates of Hyperglycaemia in Pregnancy: Determinants and Trends. In R. Rajendram, V. R. Preedy, & V. B. Patel (Hrsg.), Nutrition and Diet in Maternal Diabetes (S. 3–15). Springer International Publishing. https://doi.org/10.1007/978-3-319-56440-1_1

Ogurtsova, K., Heise, T. L., Linnenkamp, U., Dintsios, C.-M., Lhachimi, S. K., & Icks, A. (2017). External validation of type 2 diabetes computer simulation models: Definitions, approaches, implications and room for improvement—a protocol for a systematic review. Systematic Reviews, 6(1), 267. <u>https://doi.org/10.1186/s13643-017-0664-7</u>

2016 da Rocha Fernandes, J., Ogurtsova, K., Linnenkamp, U., Guariguata, L., Seuring, T., Zhang, P., ... Makaroff, L. E. (2016). IDF Diabetes Atlas estimates of 2014 global health expenditures on diabetes. Diabetes Research and Clinical Practice, 117, 48–54. http://doi.org/10.1016/j.diabres.2016.04.016

Kvitkina, T., Bruene, M., Chernyak, N., Begun, A., Andirch, S., Linnenkamp, U., ... Icks, A., (2016). Protocol of the DiaDec-study: Quality of life, health care utilisation and costs in patients with diabetes: The role of depression. Journal of Diabetology and Endocrinology, 1(2), 12–17. http://doi.org/10.14312/2398-0281.2016-3

2014 Linnenkamp, U., Guariguata, L., Beagley, J., Whiting, D. R., & Cho, N. H. (2014). The IDF Diabetes Atlas methodology for estimating global prevalence of hyperglycaemia in pregnancy. Diabetes Research and Clinical Practice, 103(2), 186–196. <u>http://doi.org/10.1016/j.diabres.2013.11.004</u>

Guariguata, L., Linnenkamp, U., Beagley, J., Whiting, D. R., & Cho, N. H. (2014). Global estimates of the prevalence of hyperglycaemia in pregnancy. Diabetes Research and Clinical Practice, 103(2), 176–185. <u>http://doi.org/10.1016/j.diabres.2013.11.003</u>

Curriculum Vitae Sara Kress

PhD student/ Research Associate

Research group: Environmental epidemiology of lung, brain and skin aging IUF – Leibniz Research Institute for Environmental Medicine Email: Sara.Kress@IUF-Duesseldorf.de

Research Profile

One main target of our research group is the investigation of risk factors for the development of allergies, skin and lung diseases. In my PhD, I will focus on polygenic risk scores and gene-environment interaction effects on respiratory health to explore the interplay between air pollution exposure and genetic susceptibility on respiratory health. Assuming unequal susceptibilities, we will investigate the difference in gene-environment interaction effects between age stages and ethnic groups, e.g. non-Caucasian individuals.

Research projects/ collaborations

- 1) Polygenic susceptibility in chronic air pollution exposure associated adverse respiratory health in adolescents: a meta-analysis (collaboration between GINIplus/LISAplus (DE), PIAMA (NL), BAMSE (SE), and ALSPAC (UK))
- 2) SpiroMeta Haplotype Reference Consortium Age-Stratified Genome-wide association analysis of lung function
- 3) Gene-Environment analysis in eczema: A collaboration between the UK-TREND and the Early Genetics and Lifecourse Epidemiology (EAGLE) consortium
- 4) EAGLE Genome-wide association analysis in atopic dermatitis

Publications

- S Kress, O Razum, K A Zolitschka, J Breckenkamp, O Sauzet: Does social cohesion mediate neighbourhood effects on mental and physical health? Longitudinal analysis using German SocioEconomic Panel data (2020) *BMC Public Health*, 20: 1043. DOI: 10.1186/s12889-020-09149-8.
- Q Zhao, S Kress, I Markevych, D Berdel, Avon Berg, M Gappa, S Koletzko, C-P Bauer, H Schulz, M Standl, J Heinrich, T Schikowski: Air pollution during infancy and lung function development into adolescence: The GINIplus/LISA birth cohorts study (2021) *Environmental International*, 146: 106195. DOI: 10.1016/j.envint.2020.106195.
- Q Zhao, S Kress, I Markevych, D Berdel, Avon Berg, M Gappa, S Koletzko, C-P Bauer, H Schulz, M Standl, J

Heinrich, T Schikowski: Long-term air pollution exposure under EU limits and adolescents' lung

function: Modifying effect of abnormal weight in GINIplus/LISA birth cohorts (in press) CHEST

A Dalecká, C Wigmann, S Kress, H Altug, V Jiřík, J Heinrich, M J Abramson, T Schikowski: The Mediating Role of Lung Function on Air Pollution-induced Cardiopulmonary Mortality in Elderly Women: The SALIA Cohort Study with 22-year mortality follow-up (in press) *International Journal of Hygiene and Environmental Health*

Work Experience

 10/2019 – PhD student/ Research Associate
 today IUF – Leibniz Research Institute for

 Environmental Medicine, Düsseldorf

09/2017 –	Research Assistant
08/2018	Epidemiology & International Public Health, Bielefeld University
02/2015 –	Trainee & Student Assistant
08/2016	Centre for Urban Epidemiology, University Hospital Essen

Educational ba	ackground
10/2016 -	MSc in Public Health
09/2018	University of Bielefeld, Bielefeld
10/2012 –	BSc in Bio Science and Health
04/2016	Rhine-Waal University of Applied Sciences, Kleve
Awards	
12/2019	Award of the AOK for an outstanding master thesis
09/2019	Master thesis award of the German Society of Social Medicine and Prevention

Ashtyn Tracey Areal

Doctoral Candidate/Research Assistant

Research group: Environmental epidemiology of lung, brain, and skin aging IUF- Leibniz Research Institute for Environmental Medicine

Email: AshtynTracey.Areal@IUF-Duesseldorf.de

Research Profile

One main focus of our research group is the collection and analyses of data on the effect of exposure to air pollution on chronic diseases (lung, skin and brain). In my doctoral project, I am investigating the potential interactive effect of air pollution and temperature on health outcomes with a particular focus on respiratory health. We aim to establish whether there is an interactive effect between temperature and air pollution on respiratory health as well as to develop statistical models to assess the affect of this interaction within cohort studies.

Research Projects

The interactive effect of air pollution and temperature on blood pressure within the SALIA cohort.
 The interactive effect of air pollution and temperature on Lung Function in the GINIplus/LISAplus cohort

3. The interactive effect of air pollution and temperature on respiratory mortality in North-Rhine Westphalia, Germany.

Key Publications

1) Melanie Boeckmann, Thomas Roux, Matthew Robinson, Ashtyn Areal, et.al. Climate change and control of diarrhoeal diseases in South Africa: Priorities for action connections between temperature and diarrhoeal disease. (2019) South African Medical Journal (SAMJ), 109: 6. DOI: 10.7196/samj.2019i6.14075.

2) Matthew Chersich, Minh Duc Pham, Ashtyn Areal, et.al. Associations between high temperatures in pregnancy and risk of preterm birth, low birth weight, and stillbirths: systematic review an metaanalysis. (2020) BMJ, 31:m3811. DOI: 10.1136/bmj.m3811.

Educational background and professional experience

2013-2016 Bachelor of Science in Molecular Biology and Biotechnology; Stellenbosch University, South Africa

2017-2018 Master of Science in Epidemiology; Maastricht University, The Netherlands.

2018-2020 Research intern in the Climate Change and Heat-Health Study group.

2018-2019 Master of Science in Global Health; Maastricht University, The Netherlands.

2020- Doctoral student/ Research Assistant at the IUF-Leibniz Research Institute Environmental Medicine; Düsseldorf, Germany

Curriculum Vitae

Khurshid Pia Jahan Scientific employee

Research group: Environmental epidemiology of lung, brain and skin aging IUF – Leibniz Research Institute for Environmental Medicine



Pia.jahan@IUF-Duesseldorf.de

Research Field

Our research group focuses on epidemiological aspects of environmentally-induced aging of the lung, the brain, and the skin. The research group also investigate the risk factors for the development of allergies and lung diseases. I am working on the project "Air pollution exposure on aging-related outcomes in the Indian population". This project aims to assess skin aging in three Indian cities, namely Delhi, Bangalore, and Mumbai, and to identify genetic susceptibilities to environmental factors associated with skin aging in the regions mentioned above of India.

WORK EXPERIENCE

Aug 2011 — Apr 2016

Student Assistant IUF – Leibniz Research Institute for Environmental Medicine, Düsseldorf

May 2016 — Nov 2016

Student Assistant Institute of Human Genetics, Düsseldorf

March 2018 — July 2018

Trainee

IUF – Leibniz Research Institute for Environmental Medicine, Düsseldorf

July 2018 — Current Scientific Employee IUF – Leibniz Research Institute for Environmental Medicine, Düsseldorf

EDUCATION

2000 — 2006

Secondary and Higher Secondary School Certificates Viqarunnisa Noon School and College, Dhaka, Bangladesh

Nov 2007 — May 2008

German Language course (B-2 Level) EURASIA, Berlin

Sept 2008 — July 2010

Preparatory Course for medical school Goethe University Frankfurt

Oct 2010 — Apr 2015

Pre-Clinic of medical school (First Part of the Medical Examination - 5 Terms out of 12.5 Terms) Heinrich Heine University Düsseldorf

Oct 2015 — Feb 2018

Bachelor of Science in Biology Heinrich Heine University Düsseldorf

Oct 2019 — Present

Master in Public Health Heinrich Heine University Düsseldorf

LANGUAGE SKILLS

Bengali, English, German, Hindi

Dr. Dr. Haifa MAALMI **Clinical Epidemiologist**



Personal Info

Address **German Diabetes Center** Auf'm Hennekamp 65 40225 Düsseldorf, Germany Phone 004917674535502 E-mail haifa.maalmi@ddz.de LinkedIn www.linkedin.com/in/haifamaalmi



German



Technical Skills

(A2)

Project Management of Epidemiological Studies Data Analysis SAS Programming



Soft Skills

Big picture thinking Rigorous planning Achievement orientation Communication



Postdoc representative (DDZ 2020)





Professional Experience

y		
Certificate in Epidemiology and Statistics University of Tunis El Manar, Tunisia		
01		

- 2019 **Travel Grant for Conference**
- 2015 PhD Scholarship (Klaus Tschira Foundation)

2015	Participation in The Lindau Nobel Laureate Meeting
2013	Travel Grant for Research Stay Abroad (Ministry of High Education and Research in Tunisia)

List of top 10 selected publications

2020 Maalmi H*, Wouters K*, Savelberg HHCM, Van der Velde JHPM, Reulen JPH, Mess W, Schalkwijk CG, Stehouwer CDA, Roden M, Ziegler D, Herder C, Schaper NC. Associations of cells from both innate and adaptive immunity with lower nerve conduction velocity: The Maastricht Study. BMJ Open Diabetes Res Care 2020 (Accepted)

2020 Herder C, Schneider A, Zhang S, Wolf K, Maalmi H, Huth C, Pickford R, Laxy M, Bönhof G, Koenig W, Rathmann W, Roden M, Peters A, Thorand B, Ziegler D. Association of Long-Term Air Pollution With Prevalence and Incidence of Distal Sensorimotor Polyneuropathy: KORA F4/FF4 Study. Environ Health Perspect 2020 (Accepted)

2020 Boakye D, Jansen L, Schöttker B, Jansen EHJM, Halama N, Maalmi H, Gào X, Chang-Claude J, Hoffmeister M, Brenner H. The association of vitamin D with survival in colorectal cancer patients depends on antioxidant capacity. Am J Clin Nutr 2020 (Accepted)

2020 Maalmi H, Herder C, Strassburger K, Urner S, Jandeleit-Dahm K, Zaharia OP, Karusheva Y, Bongaerts BWC, Rathmann W, Burkart V, Szendroedi J, Roden M. Biomarkers of Inflammation and Glomerular Filtration Rate in Individuals with Recent-Onset Type 1 and Type 2 Diabetes. J Clin Endocrinol Metab 2020;105(12)

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