BIOGRAPHICAL SKETCH

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NAME: Mattias Johansson

eRA COMMONS USER NAME (credential, e.g., agency login): M.JOHANSSON

POSITION TITLE: Scientist

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Umeå University, Umeå, Sweden		06/ 2003	Master of Science in Engineering Physics, Mathematical Statistics
Umeå University, Umeå, Sweden	PhD	06/ 2008	Epidemiology and genetics of prostate cancer
International Agency for Research on Cancer (IARC)	Postdoctoral training	11/ 2010	Epidemiology and genetics of smoking-related cancers

A. Personal Statement

I am molecular epidemiologist working in the Genomic Epidemiology Branch at the International Agency for Research on Cancer (IARC/WHO). Together with Dr Robbins, I lead the Risk Assessment and Early Detection (RED) team which includes 16 scientists, postdocs and support staff. We have a broad research agenda focusing on multiple cancer sites with two overarching aims; *i)* to elucidate etiological and mechanistic factors contributing to cancer risk and outcome, and *ii)* to develop accurate prediction models for early detection and prognostics. A major theme throughout these studies is integrating information from questionnaire, demographic, biomarker, genetic and genomic data. These studies are typically conducted through international collaborative efforts, and I have extensive experience in coordinating large consortium projects, including the HPV Cancer Cohort Consortium (HPVC3) and the Lung Cancer Cohort Consortium (LC3) which involves 26 cohorts from around the world. Recently, my team has focused on developing and validating tools for cancer risk prediction and early diagnosis (Muller et al. *BMJ.* 2019). I am an MPI of the INTEGRAL-AT program (U19) where I co-lead Project 2 together with Dr Robbins. We have published several papers on cancer risk prediction, screening, and biomarkers that are relevant to the current proposal (e.g. Guida et al. *JAMA Onc.* 2018, Robbins et al. *Br J Cancer.* 2021). Most recently, I led a large-scale discovery study of pre-diagnostic protein biomarkers for lung cancer (LC3, *Nat. Comm.* 2023, Feng et al. *JNCI. 2023*).

Ongoing projects that I would like to highlight include:

NIH 2U19CA203654-07 (Amos, Hung Johansson) 08/01/23-03/31/28
National Institute of Health (NIH)
Integrative analysis of lung cancer etiology and risk – Application and Translation (INTEGRAL-AT) - Project 2 component: Integrating Biomarkers into Lung Cancer Risk Profiling
The main goals of Project 2 are to develop a biomarker-based risk model, evaluate its acceptability in a real-world screening setting, and identify risk markers for never smoking lung cancer.
Role: m-PI, Project leader

NIH 7U19CA203654-02 (Amos, Hung Johansson) 08/01/17-03/31/24
National Institute of Health (NIH)
Integrative analysis of lung cancer etiology and risk - Project 2 component: Biomarkers of lung cancer risk
The main goal is to pursue a comprehensive and complementary set of research agendas to understand predictors of smoking and lung cancer.

Role: m-PI, Project leader

CRUK C18281/A29019 (PI: Martin) 10/01/20-09/30/25
Cancer Research UK
Reducing the Burden of Cancer: causal risk factors, mechanistic targets and predictive biomarkers
The major goals are to provide a robust epidemiological evidence-base for the future development of lifestyle and nutritional interventions in people at risk of, or diagnosed with, cancer; and to identify novel biomarkers of cancer risk and progression.
Role: co-PI

B. Positions and Honors

2001 - 2002 Program management, Department of Physics, Umeå University, Sweden
2004 Research engineer, Akzo Nobel Surface Chemistry, Örnsköldsvik, Sweden
2004 - 2005 Research engineer, Department of Urology, Umeå University, Sweden
2010 - 2012 Temporary staff scientist, Genetic Epidemiology Group, International Agency for Research on Cancer (IARC), Lyon, France
2012 - Fixed-term staff scientist, Genetic Epidemiology Group, International Agency for Research on Cancer (IARC), Lyon, France

C. Contributions to Science

Link to all publications: https://www.ncbi.nlm.nih.gov/myncbi/mattias.johansson.1/bibliography/public/

Projects related to risk prediction and development of biomarkers for lung cancer

In anticipation of widespread low-dose CT screening for early detection of lung cancer, we initiated a major research program focusing on lung cancer risk modelling and identifying biomarkers that are useful in identifying individuals who are likely to benefit from screening. The initial INTEGRAL U19 grant where I lead the biomarker component as m-PI (Project 2) supports most of this work. Our findings initially demonstrated that that circulating tumor-related protein biomarkers have a strong potential to identify those individual destined to develop lung cancer, over and above risk information that can be gained from traditional smoking-based risk prediction models (*Guida et al. JAMA Oncology. 2018*). In parallel, we have also evaluated the benefits and harms of lung cancer screening using the NSLT data (*Robbins et al. Lancet Respir. Med. 2019*). We subsequently carried out a major discovery analyses for early protein markers within the LC3 consortium and identified 36 individual protein biomarkers that predispose lung cancer diagnosis, most of which were novel and improve lung cancer risk discrimination (*LC3. Nat. Comm. 2023, Feng et al. JNCI. 2023*).

- Guida F, Sun N, Bantis LE, … **Johansson M,*** Hanash S*. Assessment of Lung Cancer Risk on the Basis of a Biomarker Panel of Circulating Proteins. *JAMA Oncol.* 2018. PMID: 30003238 ***Senior author**
- Robbins HA, Callister M, Sasieni P ,…, **Johansson M**.* Benefits and harms in the National Lung Screening Trial: expected outcomes with a modern management protocol. *Lancet Respir Med.* 2019. PMID: 31076382 *** Senior author**
- The Lung Cancer Cohort Consortium (LC3). The Blood Proteome of Imminent Lung Cancer Diagnosis. Nat. Com. 2023 Aug 1. **Senior author**
- Feng X, Wu WY, Onwuka JU, …, **Johansson M**. Lung cancer risk discrimination of prediagnostic proteomics measurements compared with existing prediction tools. J Natl Cancer Inst. 2023. PMID: 37260165; PMCID: PMC10483263. **Senior author**

Biomarker studies on cancer etiology

A particular focus spanning my entire research career involves circulating biomarkers of the one-carbon metabolism, such as folate and vitamin B12, initially in relation to prostate cancer development, and more recently in relation to lung, head and neck, and kidney cancer. Whilst the initial studies on prostate cancer did not provide any clear support for an important role of the one-carbon metabolism pathway in prostate cancer etiology (Johansson et al. CEBP. 2008), our initial study on lung cancer suggested strong inverse associations of several one-carbon metabolism biomarkers with lung cancer risk independently of smoking status, in particular vitamin B6, folate, and methionine (*Johansson et al. JAMA 2010*). This analysis triggered the formation of the Lung Cancer Cohort Consortium (LC3) where we concluded that folate, vitamin B6 and methionine were unlikely to substantially modify lung cancer risk (*Fanidi et al. JNCI 2018*). The LC3

collaboration has generated multiple additional biomarker studies, such as our evaluation of C-reactive protein in lung cancer (*Muller et al. BMJ 2019*).

- **Johansson M**, Appleby PN, Allen NE et al. Circulating concentrations of folate and vitamin B12 in relation to prostate cancer risk: results from the European Prospective Investigation into Cancer and Nutrition study. *Cancer Epidemiol Biomarkers Prev.* 2008. PMID: 18268110.
- **Johansson M**, Relton C, Ueland PM, et al. Serum B vitamin levels and risk of lung cancer. *JAMA.* 2010. *PMID: 20551408.*
- Fanidi A, Muller, DC, Yuan, JM, …, **Johansson M.*** Circulating Folate, Vitamin B6, and Methionine in Relation to Lung Cancer Risk in the Lung Cancer Cohort Consortium (LC3). *J Natl Cancer Inst*. 2018. PMID: 28922778 ***Senior author**
- Muller DC, Larose TL, Hodge A, …, **Johansson M.*** Circulating high sensitivity C reactive protein concentrations and risk of lung cancer: nested case-control study within Lung Cancer Cohort Consortium. *BMJ.* PMID: 30606716 ***Senior author**

Projects related to risk prediction and development of biomarkers for head and neck cancer

Our initial analysis on antibodies against human papillomavirus (HPV) in head and neck cancer demonstrated that antibodies against HPV16 E6 can be detected for 35% of future oropharynx cancers, a similar proportion of the underlying fraction of HPV driven oropharynx cancer in Europe, in turn suggesting that this represents the most HPV driven oropharynx cancers (*Kreimer & Johansson et al. JCO. 2013*). That the HPV16 E6 antibodies were only present in a handful of controls (0.6%), and that the sensitivity to predict future oropharynx cancers were constant during the whole follow-up period, suggest HPV16 E6 to be an extremely promising early cancer marker with unparalleled of sensitivity of above 80% and specificity of over 99%. We subsequently evaluated the biomarker in relation anogenital cancers and demonstrated that it is much less sensitive to predict other HPV related cancers, but that they would need to be considered in follow-up of HPV16 E6 healthy subjects (Kreimer et al. *J Clin Oncol. 2015*). These studies led to developing the HPV Cancer Cohort Consortium (HPVC3) which I coordinated to evaluate the potential of HPV16 E6 as screening tool (*Kreimer et al. Ann. Oncol. 2019*). We recently published the final risk model for HPV16 E6-based prediction of oropharyngeal cancer (*Robbins et al. JCO 2022*) which highlighted that HPV16E6 positive men have substantial absolute risk of oropharyngeal cancer.

- Kreimer AR*, **Johansson M***, Waterboer T, et al. Evaluation of human papillomavirus antibodies and risk of subsequent head and neck cancer. *J Clin Oncol*. 2013. PMID: 23775966 ***Joint first-authors**
- Kreimer AR, Brennan P, Lang Kuhs K, … **Johansson M***. Human papillomavirus antibodies and future risk of anogenital cancer: a nested case-control study in the European Prospective Investigation into Cancer and Nutrition (EPIC) study. *J Clin Oncol*. 2015. PMID: 25667279 ***Senior author**
- Kreimer AR, Ferreiro-Iglesias A, Nygard M, …, **Johansson M.*** Timing of HPV16-E6 antibody seroconversion before OPSCC: findings from the HPVC3 consortium. *Ann Oncol.* 2019. PMID: 31185496 ***Senior author**
- Robbins HA, Ferreiro-Iglesias A, Waterboer T, …**Johansson M,*** … Absolute Risk of Oropharyngeal Cancer After an HPV16-E6 Serology Test and Potential Implications for Screening: Results From the Human Papillomavirus Cancer Cohort Consortium. *J Clin Oncol.* 2022. PMID: 35700419 ***Senior author**

Studies on renal cancer

Since moving to IARC in 2008, together Dr Brennan, I co-lead a collaboration with colleagues at the US NCI (Dr Chanock and Dr Purdue) on genome-wide association studies (GWAS) on renal cancer. This led to the first GWAS publication on renal cancer that identified three susceptibility loci on 2p21 (the *EPAS1* gene), 11q13.3, and 12q24.31 (the *SCARB1* gene) (Purdue & Johansson et al. *Nat Genet 2011*). Through subsequent collaborations we have expanded the study population, and now await the third iteration of the renal cancer GWAS with over 20,000 cases. In parallel, I have led various biomarker studies on renal cancer, the most relevant being an evaluation of pathways related to one-carbon metabolism that demonstrated that individuals with higher levels of pre-diagnostic circulating pyridoxal 5'-phosphate (PLP) have substantially increased renal cancer risk, as well as poorer survival following diagnosis (*Johansson et al. JNCI 2014*). We have also carried out a series of studies employing Mendelian randomization techniques to evaluate the causal relevance of putative risk factors. Amongst these, perhaps the most informative was that on renal cancer and obesity

related risk factors that firstly confirmed elevated body-mass index as an important cause of renal, and secondly, identified elevated diastolic blood pressure and circulating insulin as having a novel and important role in mediating the established relation between obesity and renal cancer risk (Johansson et al. *PLoS Med. 2019*). Most recently we published results from the MetKid consortium that highlighted a major role of the blood metabolome in renal cancer development (*Guida et al. PLoS Med. 2021*).

- Purdue MP*, **Johansson M***, Zelenika D, et al. Genome-wide association study of renal cell carcinoma identifies two susceptibility loci on 2p21 and 11q13.3. *Nat Genet*. 2011. PubMed PMID: 21131975; ***Joint first-authors**
- **Johansson M**, Fanidi A, Muller DC, et al. Circulating biomarkers of one-carbon metabolism in relation to renal cell carcinoma incidence and survival. *J Natl Cancer Inst*. 2014. PMID: 25376861
- **Johansson M**, Carreras-Torres R, Scelo G, et al. The influence of obesity-related factors in the etiology of renal cell carcinoma-A mendelian randomization study. *PLoS Med.* 2019. PMID:30605491
- Guida F, Tan TY, Corbin LJ, … **Johansson M***. The blood metabolome of incident kidney cancer: A case-control study nested within the MetKid consortium. *PLoS Med.* 2021. PMID: 34543281 ***Senior author**

Studies employing Mendelian randomization

I have long experience in conducting studies where Mendelian randomization has been central in elucidating modifiable risk factors in cancer etiology, spanning back to my Phd project. At IARC, our research in this area was accelerated by the availability of large GWA data sets and I have led, or co-led with Dr Brennan, several MR studies that have improved our understanding of cancer etiology. For instance, MR studies on obesity-related factors identified elevated body-mass index as an important cause of renal and pancreatic cancer, as well as highlighted fasting insulin as novel causal risk factor (*Carreras-Torres et al. JNCI. 2017, Johansson et al. PLOS Med. 2019*). We further published a study wherein circulating vitamin B12 was evaluated both directly within the Lung Cancer Cohort Consortium (LC3) and by MR, and observed a notable concordance in the association between vitamin B12 and histological subtypes of lung cancer (*Fanidi et al. Int J Cancer. 2018*). In addition, we conducted a study based on UK Biobank that highlighted that obesity causes a higher uptake and intensity of tobacco smoking, an observation that may have important implications in tobacco cessation programs (*Carreras-Torres et al. BMJ 2018*). Most recently, we carried out a comprehensive analysis using both MR and direct exposure measurements in large cohort studies to evaluate whether early and mid-life BMI influences risk of obesity-related cancer (*Mariosa et al. JNCI. 2022).*

- Carreras-Torres R, **Johansson M**, Gaborieau V, et al. The Role of Obesity, Type 2 Diabetes, and Metabolic Factors in Pancreatic Cancer: A Mendelian Randomization Study. *J Natl Cancer Inst.* 2017. PMID: 28954281
- Carreras-Torres R*, **Johansson M***, Haycock PC, et al. Role of obesity in smoking behaviour: Mendelian randomisation study in UK Biobank. *BMJ.* 2018. *PMID: 29769355* ***Joint first authors**
- Fanidi A, Carreras-Torres R, Larose TL, …, **Johansson M.**, Brennan P. Is high vitamin B12 status a cause of lung cancer? *Int J Cancer. 2018.* PMID: 30499135
- Mariosa D, Smith-Byrne K, Richardson TG, … **Johansson M*.** Body Size at Different Ages and Risk of 6 Cancers: A Mendelian Randomization and Prospective Cohort Study. *J Natl Cancer Inst.* 2022. PMID: 35438160. ***Senior author**