



## UvA-DARE (Digital Academic Repository)

### Systems biology of the host response to severe infection

Khan, H.N.

**Publication date**  
2022

[Link to publication](#)

#### **Citation for published version (APA):**

Khan, H. N. (2022). *Systems biology of the host response to severe infection*. [Thesis, fully internal, Universiteit van Amsterdam].

#### **General rights**

It is not permitted to download or to forward/distribute the text or part of it without the consent of the author(s) and/or copyright holder(s), other than for strictly personal, individual use, unless the work is under an open content license (like Creative Commons).

#### **Disclaimer/Complaints regulations**

If you believe that digital publication of certain material infringes any of your rights or (privacy) interests, please let the Library know, stating your reasons. In case of a legitimate complaint, the Library will make the material inaccessible and/or remove it from the website. Please Ask the Library: <https://uba.uva.nl/en/contact>, or a letter to: Library of the University of Amsterdam, Secretariat, Singel 425, 1012 WP Amsterdam, The Netherlands. You will be contacted as soon as possible.

## *Appendix*

## PhD PORTFOLIO

**Hina Naz Khan**

**PhD period:** August 2015 – October 2019

**PhD supervisors:** Prof. Dr. T. van der Poll, Prof. Dr. A.H.Zwindermaan  
and Dr. Brendon P. Scicluna

<b>Courses</b>	<b>Year</b>
- Genetic epidemiology	2016
- Scientific writing	2016
- Unix	2016
- System medicine	2016
- Practical biostatistics	2017
- E-Science	2017
- MIAGE course (Multi-omics integrative analysis of gene expression), CIPF, Valencia, Spain	2018
<b>Seminars, workshops, retreats and master classes</b>	
- Annual Amsterdam Infection and immunity institute (AI & II) PhD retreat	2016
- ARTeC seminar AMC/VUMC	2017
- BBMRI-omics workshop, Utrecht	2017
- Masterclass Prof. Douglas Golenbock	2017
- CEMM Journal Club	2015-2019
- CEMMinars	2015-2019
- Infectious diseases retreat (congress center Mennorode in Elspeet)	2017
- Kickoff symposium (Microbiota center Amsterdam)	2018
<b>(Inter)national conferences</b>	
- Summers Frontiers 2016: System Biology of innate immunity. Nijmegen, The Netherlands	2016
- 17 <sup>th</sup> International Congress of European Shock society. Paris, France	2017
- Sepsis 2017: New Successes, New challenges. Paris, France	2017
- New Frontiers in Innate immunity and Inflammation. Cluj-Napoca, Romania	2018

---

## Oral Presentations

---

- "The circulatory small non-coding RNA landscape in health and community-acquired pneumonia." 2017  
17<sup>th</sup> International Congress of European Shock society. Paris, France
- "Identification of blood transcriptional networks dependent on lipopolysaccharide dose in human endotoxemia." 2017  
All&I PhD Retreat 2017.
- "Canonical and non-canonical RNA splicing in specific peripheral blood mononuclear cells of critically ill patients with sepsis". 2018  
New Frontiers in Innate immunity and Inflammation. Cluj-Napoca, Romania

---

## Poster Presentations

---

- "The circulatory small non-coding RNA landscape in health and community-acquired pneumonia." 2016  
Summers Frontiers 2016: System Biology of innate immunity. Poster presentation
- "Identification of blood transcriptional networks dependent on lipopolysaccharide dose in human endotoxemia." 2017  
All&I PhD Retreat 2017.
- "The circulatory small non-coding RNA landscape in health and community-acquired pneumonia." 2017  
Sepsis 2017: New Successes, New challenges. Paris, France
- "Canonical and non-canonical RNA splicing in specific peripheral blood mononuclear cells of critically ill patients with sepsis". 2018  
New Frontiers in Innate immunity and Inflammation. Cluj-Napoca, Romania

---

## Tutoring, Mentoring

---

- Student monitoring in "Identification of blood transcriptional networks dependent on lipopolysaccharide dose in human endotoxemia" project

## List of publications

1. **Khan HN**, Perlee D, Schoenmaker L, van der Meer AJ, Franitza M, Toliat MR, Nürnberg P, Zwinderman AH, van der Poll T, Scicluna BP. Leukocyte transcriptional signatures dependent on LPS dosage in human endotoxemia. *J Leukoc Biol.* 2019 Nov;106(5):1153-1160. doi: 10.1002/JLB.4A0219-050R. Epub 2019 Jul 7. PMID: 31280495; PMCID: PMC6852106.
2. **Khan HN**, Brands X, Aufiero S, Hoogendijk AJ, Klarenbeek AM, van Engelen TSR, Haak BW, van Vught LA, Horn J, Schultz MJ, Zwinderman AH, van der Poll T, Scicluna BP. The circular RNA landscape in specific peripheral blood mononuclear cells of critically ill patients with sepsis. *Crit Care.* 2020 Jul 13;24(1):423. doi: 10.1186/s13054-020-03146-4. PMID: 32660590; PMCID: PMC7359566.
3. **Khan HN**, Jongejan A, van Vught LA, Horn J, Schultz MJ, Zwinderman AH, Cremer OL, Bonten MJ, van der Poll T, Scicluna BP. The circulatory small non-coding RNA landscape in community-acquired pneumonia on intensive care unit admission. *J Cell Mol Med.* 2021 Aug;25(16):7621-7630. doi: 10.1111/jcmm.16406. Epub 2021 Jul 17. PMID: 34272809; PMCID: PMC8358855.
4. Matsumoto H, Scicluna BP, Jim KK, Falahi F, Qin W, Gürkan B, Malmström E, Meijer MT, Butler JM, **Khan HN**, Takagi T, Ishii S, Schultz MJ, van de Beek D, de Vos AF, van 't Veer C, van der Poll T. HIVEP1 Is a Negative Regulator of NF- $\kappa$ B That Inhibits Systemic Inflammation in Sepsis. *Front Immunol.* 2021 Nov 5;12:744358. doi: 10.3389/fimmu.2021.744358. PMID: 34804025; PMCID: PMC8602905.
5. Ykema BLM, Hoefnagel SJM, Rigter LS, Kodach LL, Meijer GA, van Leeuwen FE, **Khan HN**, Snaebjornsson P, Aleman BMP, Broeks A, Meijer SL, Wang KK, Carvalho B, Krishnadath KK, van Leerdam ME; GIOCA-OES. Gene expression profiles of esophageal squamous cell cancers in Hodgkin lymphoma survivors versus sporadic cases. *PLoS One.* 2020 Dec 21;15(12):e0243178. doi: 10.1371/journal.pone.0243178. PMID: 33347497; PMCID: PMC7751872.

6. Kloek AT, **Khan HN**, Valls Seron M, Jongejan A, Zwinderman AH, Baas F, van der Ende A, van de Beek D, Ferwerda B, Brouwer MC. Variation in coagulation and fibrinolysis genes evaluated for their contribution to cerebrovascular complications in adults with bacterial meningitis in the Netherlands. *J Infect.* 2018 Jul;77(1):54-59. doi: 10.1016/j.jinf.2018.03.007. Epub 2018 May 7. PMID: 29746949.

#### **Submitted and in preparation Manuscripts:**

1. **Khan HN**, Brouwer MC, Geldhoff M, Scicluna BP, Zwinderman AH, van de Beek D., Bart Ferwerda. Protein quantitative trait locus of cerebrospinal fluid inflammatory mediators in patients with pneumococcal meningitis.
2. Malmström E, **Khan HN**, van't Veer C, Stunnenberg M, Meijer MT, Matsumoto H, Otto NA, Geijtenbeek TBH, Alex F. de Vos, van der Poll T and Scicluna BP. The long non-coding antisense RNA JHDM1D-AS1 regulates inflammatory responses in human monocytes
3. Hoefnagel SJM, Koemans WJ, **Khan HN**, Koster J, Meijer SL, van Dieren JM, Kodach LL, van Sandick JW, Calpe S, del Sancho-Serra CM, Correia AC, Van Laarhoven HWM, Van Berge Henegouwen MI, Gisbertz SS, Hulshof MCCM, Krishnadath KK. Subgroup analyses and predictive RNA signatures for response to chemoradiotherapy in esophageal adenocarcinoma: an aid towards personalized therapy.
4. Uhel F, Scicluna BP, Peters-Sengers H, Butler J, **Khan HN**, van Vught LA, Cremer OL, Bonten MJ, Schultz MJ, and van der Poll T. Comparative analysis of the host response to septic and non-septic shock.

## List of contributing authors

### **Amsterdam University Medical Centers, location Academic Medical Center *Center for Experimental and Molecular Medicine***

Tom van der Poll	Brendon P. Scicluna
Xanthe Brands	Erik Malmström
Alex F. de Vos	Fabrice Uhel
Bas Haak	Tjitske S.R. van Engelen
Lonneke A. van Vught	Desiree Perlee
Lieke Schoenmaker	Cornelis van't Veer
Mariska T. Meijer	Hisatake Matsumoto
Natasja A. Otto	Teunis B.H. Geijtenbeek
Maryse A. Wiewel	Arie J. Hoogendijk
Anne-Jan van der Meer	

### ***Neuroinfections Amsterdam***

Diederik van de Beek	Matthijs Brouwer
Bart Ferwerda	

### ***Department of Clinical Epidemiology, Biostatistics and Bioinformatics***

Aeilko H. Zwinderman	Simona Aufiero
Aldo Jongejan	

### ***Department of Intensive Care***

Marcus J. Schultz	Janneke Horn
Olaf L. Cremer	

### **University Medical Center, Utrecht**

#### ***Department of Medical Microbiology***

Marc J. Bonten

### **University of Cologne, Cologne Center for Genomics (CCG), Germany**

Mohammad Reza Toliat	Marek Franitza
Peter Nürnberg	

## **Acknowledgements**

The process of earning a doctorate and writing a dissertation is long and arduous and it is certainly not done singlehandedly. Completing this thesis, a product of several years' work, I feel deeply indebted to a great many people who have appreciably inspired, encouraged, supported, and have contributed to my research and development during my PhD study at Amsterdam UMC- locatie AMC.

Foremost, I want to offer my endeavour to GOD Almighty for the wisdom he bestowed upon me, the strength and good health to make this thesis a reality. I would like to express my gratitude to my promotors; Prof. dr. T. van der Poll and Prof. dr. A.H. Zwinderman, thank you for giving me the opportunity to pursue my PhD. Dear Tom, you are a very dedicated person to your team, constantly supporting them with positive energy and high optimism. You have a special ability to motivate people to work hard and your guidance and feedback were always valuable input for this thesis. Dear Koos, thanks for providing valuable comments on all my projects and always available to give statistical advice. I would like to thank for your support and understanding over these past years.

My big appreciation goes to my co-promotor, Dr. B.P. Scicluna, for his marvellous supervision, guidance, and encouragement. Sincere gratitude is extended to his generous participation in guiding, constructive feedback, kind support, and advice during my PhD. When I look at this thesis, I realize the importance of your positive criticisms and valuable suggestions on my work. I enjoyed our scientific discussions that brought insight to my perspective and shaped my ideas. I will always remember your encouragement "write, write and write" and "go ahead," when I hesitated to move forward sometimes during the writing. From the inception to its completion, you have devoted so much. Thank you very much!!!!



I sincerely thank my supervisors from the research group Neuroinfections Amsterdam, Prof. Dr. Diederik van de Beek and Dr. Matthijs Brouwer for their guidance, great feedback, and excellent encouragement. It would certainly be a remiss to not mention and sincerely thank Dr. Bart Ferwerda. I would like to recognize the invaluable assistance given and thank him for his supervision and support. Your detailed explanation on every stage of the projects enabled me to fill the gaps on my background knowledge in genetics smoothly. Without your expertise and advice, the meningitis research project would have not happened.

Many thanks to all the PhD committee members; Prof. dr. W.J. Wiersinga, Prof. dr. Y.M. Pinto, Prof. dr. E.M.A. Aronica, Prof. dr. L. Vermeulen, Prof. dr. ing. A.H.C. van Kampen and Prof. dr. J. Knight, for taking the time to review and evaluate my thesis manuscript. It is a great privilege to have you as a member of my committee.

From the bottom of my heart, I would like to say big thank you to all the Tommies group members for their energy, understanding and help throughout my projects. It was a pleasure working with you all. Xanthe, I really admire your energy and passion in whatever you do and the smile you never lose!! Thank you for being so supportive. Mariska, I appreciate your assistance whenever I needed and ofcourse for the guidance when I was looking for a new house. Stijn, I enjoyed sharing a project with you and truly has been a very good time in the lab. Thanks to my wonderful roommates (Joe, Hessel, Fabrice, Lonneka, Tjitske), our office was always gezellig.

This journey would not be possible without the support of my family. I express my deepest gratitude for my parents and parents-in-law. I am grateful for the constant love and support that kept me motivated and confident. My accomplishments and success are because you all believed in me. My sense of respect goes to my father who offered his regular encouragement in every step to make me in present stage. Sometimes just hearing your voice is all I need. My

mother is my superhero. You raised all your daughters to be an independent woman in this world. Everything I have and everything I am, I owe it all to you. Thank you, my two lifelines. It's my fortune to have such loving father-in-law and mother-in-law, you two mean a lot to me. I salute you two for the selfless love and care you did to shape my life and willing to support any decision I made.

Many others have been instrumental in this process. I would like to acknowledge my sisters (Neelam, Kiran, Sulfia, Mehwish, Ayesha, Sehrish and Maryam), brothers-in-law, Marielle and brother from another mother, Imdad, you all have been extremely supportive during the whole process. Thank you for giving me the perspective when I needed it, for sharing optimism and celebrating every achievement of mine. Ayesha, thank for all your support and generous care throughout the research tenure and of course the help with my kids when I needed it the most. Kiran, thanks for designing the cover and the layout of my thesis, in house designer is a blessing.

Finally, I must express my unfailing gratitude and love to my husband, Adeel, for keeping things going and for always showing how proud he is of me. Thank you for providing me with constant support and continuous encouragement throughout. The last word goes for my children, Inaaya and Huzaifah, who have been the light of my life. You two have made me stronger, better, and more fulfilled than I could have ever imagined. I love you to the moon and back.

Hina Naz Khan

March 2022, Barendrecht

## About the author



Hina Naz Khan was born on 12<sup>th</sup> may 1984 in Rawalpindi, Pakistan. She received her primary and secondary education at different schools in Pakistan. In 2007 she obtained her Bachelor's degree in bioinformatics. Then in 2010 she attained her Master's degree in Bioinformatics and composed her master thesis entitled "Identification of an antiepileptic

compound with a more selective activity using *In-silico* approach". She has worked as a lecturer for O levels biology in Beaconhouse educational complex and also worked as lab instructor and a lecturer in Mohammad Ali Jinnah University, Pakistan.

In 2012 she moved to Netherlands. She pursued her education and received another master's bioinformatics degree in 2015 from Vrij Universiteit Amsterdam. She spent 8 months in Erasmus MC as a graduate trainee under the supervision of Dr. Andrew Stubbs and Dr. Pim French. She studied the application and validation of RNA-Seq for Glioblastoma patients' stratification in a clinical trial setting.

In August 2015, she started her PhD at Amsterdam UMC, location AMC, University of Amsterdam, under the supervision of Prof. dr. Tom van der Poll, Prof. dr. A.H. Zwinderman and Dr. Brendon P. Scicluna. During her PhD, she presented a number of transcriptomic signatures and cellular signaling pathways that may play a role in the pathophysiology of severe infections. The results of these studies are described and discussed in this thesis.

After her PhD, Hina continued her research and working as postdoctoral researcher (Bioinformatics) in the department of molecular genetics, Erasmus MC.