# Host-directed therapy for intracellular bacterial Infections

Korbee, C.J.

# Curriculum Vitae

Born in Leiden on November 29th, 1982, Cornelis Jacob (Kees) Korbee grew up in Noordwijk aan Zee. There, his interest for medical biology was sparked during his VWO education while attending a practical course in biology class, dissecting heart tissue. However, this did not directly lead him to higher education in biology. After a brief departure to study multimedia design in Rotterdam in 2001, he saw the light and was drawn back to his city of birth in 2002 to study Biomedical Sciences. Upon graduation in 2008, he started his research to attain his Ph.D. at the Department of Infectious Diseases of the Leiden University Medical Center, resulting in this thesis.

His frequent work with (genetically modified) human pathogens at a high containment level, combined with his more than frequent student supervision activities in the laboratory, subsequently led him to a career in biological safety. Kees placed his first steps in this field as a Biological Safety Officer at Erasmus MC in 2017, where he learned the trade for half a year. The lessons learned during his Ph.D. regarding genetic modification, infectious diseases and safely working in a BSL-3 facility will be more than valuable in his current occupation as Biological Safety Officer at the Netherlands Cancer Institute - Antoni van Leeuwenhoek in Amsterdam.

# List of Publications

1. **Novel Host-Directed Chemical Compounds Inhibit Intracellular Bacteria by Targeting PCTAIRE Kinases.**
   **Korbee, C.J.***, Heemskerk, M.T.*, Walburg, K.V., Van den Nieuwendijk, R., Van Strijen, E., Kuijl, C., Schreuders, C., Eken, J., Savage, N.D.L., Neefjes, J.J., Overkleeft, H.S., Ottenhoff, T.H.M.**, Haks, M.C.**.
   *Manuscript in preparation.*

2. **Combined chemical genetics and data-driven bioinformatics approach identifies receptor tyrosine kinase inhibitors as host-directed antimicrobials.**
   **Korbee, C.J.***, Heemskerk, M.T.*, Kocev, D., Van Strijen, E., Rabiee, O., Franken, K.L.M.C., Wilson, L., Savage, N.D.L., Džeroski, S., Haks, M.C.**, Ottenhoff, T.H.M.**.
   *Nature Communnications* **9**, 358. doi:10.1038/s41467-017-02777-6 (2018)**.**

3. **The DNA damage-regulated autophagy modulator DRAM1 links mycobacterial recognition via TLR-MYD88 to authophagic defense.**
   Van der Vaart, M., **Korbee, C.J.**, Lamers, G.E.M., Tengeler, A.C., Hosseini, R., Haks, M.C., Ottenhoff, T.H.M., Spaink, H.P., Meijer, A.H..
   *Cell Host and Microbe* **15**, 753–767. doi:10.1016/j.chom.2014.05.005 (2014).

4. **Systems Microbiology: Current Topics and Applications; Chapter 5 - Manipulating the Fight Between Human Host Cells and Intracellular Pathogens.**
   Barsacchi, R.*, Sundaramurthy, C.*, **Korbee, C.J.**, Neefjes, J.J., Ottenhoff, T.H.M., Scanu, T., Zerial, M..
   *Caister Academic Press*. ISBN: 978-1-908230-02-7 (2012).

5. **Mycobacterial secretion systems ESX-1 and ESX-5 play distinct roles in host cell death and inflammasome activation.**
   Abdallah, A.M.*, Bestebroer, J.*, Savage, N.D.L., De Punder, K., Van Zon, M., Wilson, L., **Korbee, C.J.**, Van der Sar, A.M., Ottenhoff, T.H.M., Van der Wel, N.N., Bitter, W., Peters, P.J..
   *The Journal of Immunology* **187**, 4744–4753. doi:10.4049/jimmunol.1101457 (2011).

6. **Nuclear Localization of CXCR4 Determines Prognosis for Colorectal Cancer Patients.**
   Speetjens, F.M., Liefers, G.J., **Korbee, C.J.**, Mesker, W.E., Van de Velde, C.J.H., Van Vlierberghe, R.L., Morreau, H., Tollenaar, R.A., Kuppen, P.J.K..
   *Cancer Microenvironment* **2**, 1-7. doi:10.1007/s12307-008-0016-1 (2009).

* Contributed equally
** Contributed equally

# Portfolio

| Courses | Year |
|---|---|
| Basiscursus Regelgeving en Organisatie voor Klinisch Onderzoekers (BROK) | 2016 |
| PhD Introductory Meeting | 2016 |
| Basic Methods and Reasoning in Biostatistics | 2015 |
| LIFI Course in Immunology | 2011 |
| **Conferences** | **Year** |
| Antibiotics Alternatives for the New Millennium (London).<br>*Invited speaker.* | 2014 |
| Keystone Symposium - (Keystone, CO, USA).<br>*Presented work;*<br>*2 Posters at poster session.* | 2014 |
| CiPKeBIP Annual Conference on: Immune response and host microbiota in disease development (Ljubljana, Slovenia).<br>*Presented work (invited speaker).* | 2012 |
| NVVI Conference (Noordwijkerhout, The Netherlands).<br>*Presented work.* | 2011 |
| Keystone Keystone Symposium - Tuberculosis: Immunology, Cell Biology and Novel Vaccination Strategies (Vancouver, BC, Canada).<br>*Attended conference.* | 2011 |
| NVVI Conference (Noordwijkerhout, The Netherlands).<br>*Attended conference.* | 2010 |
| **Teaching** | **Period** |
| Supervision of student internships.<br>*8 Students in total (BSc., MSc., HLO).* | 2010-2015 |
| Biomedical Sciences Bachelor's Course Pathogen-Host Interactions.<br>*Gave lectures;*<br>*Supervised work groups;*<br>*Prepared and evaluated exam questions.* | 2011-2014 |
| Biomedical Sciences Master's Course Pathogen-Host Interactions.<br>*Prepared and supervised practical course.* | 2011-2014 |
| Supervised research proposal writing<br>*2 Students* | 2013-2014 |

# List of Abbreviations

| | |
|---|---|
| **3-MA** | 3-Methyladenine |
| **ADC** | Albumin dextrose catalase |
| **AMPK** | Adenosine monophosphate-activated protein kinase |
| **ANOVA** | Analysis of variance |
| **AUC** | Area under the curve |
| **AVG** | Average |
| **CDK** | Cyclin-dependent kinase |
| **CFU** | Colony forming unit |
| **Cq** | Chloroquine |
| **DMSO** | Dimethyl sulphoxide |
| **Dpf** | Days post-fertilization |
| **Dpi** | Days post-infection |
| **DRAM1** | DNA-damage regulated autophay modulator |
| **DS** | Drug-sensitive |
| **ECL** | Enhanced chemiluminescence |
| **EGFR** | Epidermal growth factor receptor |
| **EM** | Electron microscopy |
| **ER** | Endoplasmic reticulum |
| **FACS** | Fluorescence-activated cell sorting |
| **FBS** | Fetal bovine serum |
| **FDR** | False discovery rate |
| **GEO** | Gene Expression Omnibus |
| **GFP** | Green fluorescent protein |
| **GM-CSF** | Granulocyte macrophage-colony stimulating factor |

| | |
|---|---|
| **GO** | Gene ontology |
| **HDT** | Host-directed therapy |
| **Hpi** | Hours post-infection |
| **HTS** | High-throughput sampler |
| **IFNγ** | Interferon gamma |
| **IFNγR** | Interferon gamma receptor |
| **IL1R** | Interleukin-1 receptor |
| **IMDM** | Iscove's Modified Dulbecco's Medium |
| ***K. pneumoniae*** | *Klebsiella pneumoniae* |
| **$K_i$** | Dissociation constant |
| **LAM** | Lipoarabinomannan |
| **LAP** | LC3-associated phagocytosis |
| **LB** | Luria-Bertani |
| **LC3** | Microtubule-associated protein 1 light chain 3 |
| **LOPAC** | Library of pharmacologically active compounds |
| **LPS** | Lipopolysaccharide |
| **M-CSF** | Macrophage-colony stimulating factor |
| **MDR** | Multi-drug resistant |
| ***Mm*** | *Mycobacterium marinum* |
| **MODC** | Mouse ornithine decarboxylase |
| **MOI** | Multiplicity of infection |
| **Mϕ** | Macrophage |
| **Mϕ1** | Type 1 macrophage |
| **Mϕ2** | Type 2 macrophage |
| ***Mtb*** | *Mycobacterium tuberculosis* |
| **mTOR** | Mammalian target of rapamycin |
| **Myd88** | Myeloid differentiation primary response 88 |

| | |
|---|---|
| **NAI** | NF-κB activation inhibitor |
| **ns** | Not significant |
| **NTRK1** | Neurotrophic receptor tyrosine kinase 1 |
| **OD** | Optical density |
| **$OD_{600}$** | Optical density at 600 nm |
| **PCT** | Predictive clustering tree |
| ***Pfal*** | *Plasmodium falciparum* |
| **PFDHOD** | *Plasmodium falciparum* dihydro orotate dehydrogenase |
| **PI(3)P** | Phosphatidylinositol 3-phosphate |
| **PKC** | Protein kinase C |
| **PknG** | Protein kinase G |
| **PMA** | Phorbol 12-mystirate 13-acetate |
| **qPCR** | Quantitative polymerase chain reaction |
| **RD1** | Region of difference 1 |
| **RNA** | Ribonucleic acid |
| **RNAi** | RNA interference |
| **ROS** | Reactive oxygen species |
| **RPMI** | Roswell Park Memorial Institute |
| **RTK** | Receptor tyrosine kinase |
| ***S.* Paratyphi** | *Salmonella enterica* serovar Paratyphi |
| ***S.* Typhi** | *Salmonella enterica* serovar Typhi |
| **Saa** | Serum amyloid A |
| **SCV** | *Salmonella*-containing vesicle |
| **SDF** | Structure-data format |
| **SEM** | Standard error of the mean |
| **SFK** | SRC family kinase |
| **siRNA** | Small interfering RNA |

| | |
|---|---|
| **SPI1** | *Salmonella* pathogenicity island 1 |
| **SPI2** | *Salmonella* pathogenicity island 2 |
| **STDEV** | Standard deviation |
| ***Stm*** | *Salmonella enterica* serovar Typhimurium |
| **T3SS** | Type III secretion system |
| **TANK** | TRAF-associated NF-κB activator |
| **TB** | Tuberculosis |
| **TBK1** | TANK-binding kinase-1 |
| **TDR** | Totally drug resistant |
| **TGFßI** | Tumor growth factor ß type-1 |
| **TGFßII** | Tumor growth factor ß type-2 |
| **TGFßRI** | TGFß type-1 receptor |
| **TGFßRII** | TGFß type-2 receptor |
| **TLR** | Toll-like receptor |
| **TRAF** | Tumor necrosis factor receptor-associated factor |
| **TTSS** | Type III secretion system |
| **VEGFR** | Vascular endothelial growth factor receptor |
| **XDR** | Extensively drug resistant |