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Dr Anne Marie Krachler MSc, PhD

Birmingham Fellow and EMBO Fellow

School of Biosciences (/schools/biosciences/index.aspx)

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About

(/university/colleges/les/research-gallery/anne-marie-krachler.aspx) Anne-Marie Krachler joined the University of Birmingham as a Birmingham Fellow and EMBO Fellow in 2012 and is based at the Institute of Microbiology and Infection within the School of Biosciences. Her lab studies interactions between bacterial pathogens and their host and how this knowledge can be used to fight bacterial infections and gain novel insight into eukaryotic signaling mechanisms.
Krachler Lab website: https://sites.google.com/site/krachlerlab/ (https://sites.google.com/site/krachlerlab/)

Qualifications

- PhD in Biochemistry, University of York
- MSc in Chemical Engineering, Vienna University of Technology

Biography

Following completion of an MSc degree in Chemical Engineering at the University of Technology in Vienna, Anne-Marie undertook her PhD research at the University of York as a Marie Curie Early Stage Fellow. Her graduate work under the supervision of Prof. Colin Kleanthous focused on the biochemical and structural characterization of protein-protein complexes involved in maintaining integrity of the cell envelope of Gram-negative bacteria. As a postdoctoral research fellow at UT Southwestern Medical Center in Dallas, Anne-Marie studied the activity of virulence factors from pathogenic bacteria and discovered and entirely new family of proteins involved in host-pathogen interactions.

Teaching

BIO303 - Applied and Environmental Microbiology (I teach about Public Health and Emerging Infections and supervise the Diagnostic Medical Microbiology practical).

BIOM22 - Medical Microbiology (I teach about clinically important Vibrio sp.).

BIOM23 - Host-Pathogen Interactions (I teach about virulence factors and evolution of virulence).

BIOM24 - Antibiotics, Microbial Surfaces and Surface Interactions (I teach about secretion systems).

I also act as a tutor for Biological Sciences BSc students and supervise final year and masters lab and literature projects.

Postgraduate supervision

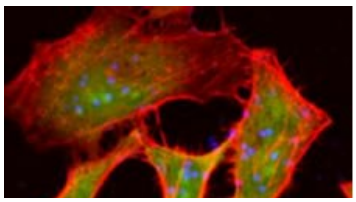
Students looking for Summer Work Experience Placements and masters and PhD students interested in our research should contact Anne-Marie via email: **a.krachler@bham.ac.uk (mailto:a.krachler@bham.ac.uk)**

PhD studentships are awarded each year competitively within the School of Biosciences. Funding options are also available for international students including Darwin Trust and Elite scholarships.

Research

The Krachler lab focuses on how host-pathogen interaction and in particular bacterial adhesion triggers changes in host signaling pathways to favor infection. In addition, she is investigating the application of bacterial adhesins as tools in anti-adhesion therapy and as probes for host membrane structures.
Krachler Lab website: https://sites.google.com/site/krachlerlab/ (https://sites.google.com/site/krachlerlab/)

Development of a bacterial adhesin into a next generation antimicrobial agent



Pathogen attachment to host tissues is one of the initial and most crucial events during the establishment of bacterial infections and thus interference with this step could be an efficient strategy to fight bacterial colonization. Our recent work has identified one of the factors involved in initial binding of host cells by a wide range of Gram-negative pathogens, Multivalent Adhesion Molecule (MAM) 7. Interference with MAM7-mediated attachment, for example by pre-incubation of host cells with recombinant MAM7, significantly delays the onset of hallmarks of infection, such as pathogen-mediated cytotoxicity or the development of other adhesive structures such as actin pedestals. Thus, we are trying to develop tools based on MAM7 that can be used to prevent or diminish certain bacterial infections.

Biochemical and structural characterization of MAM7 adhesin - host cell receptor interactions

The bacterial adhesion MAM7 contains seven mce (mammalian cell entry)-repeat domains mediating a complex interaction with the host receptors fibronectin and phosphatidic acid. While the interaction of MAM with the lipid phosphatidic acid is of high affinity and a single mce domain is sufficient to mediate binding, fibronectin-binding is of low affinity and requires multiple mce domains. We are performing a detailed characterization of the interaction between MAM7 and its receptors using both biochemical assays and structural biology approaches. The focus is on identifying key determinants of binding-affinity and -specificity to construct MAM7 derivatives with improved affinity and altered host-specificity for use as therapeutics and as probes for host membrane structures.

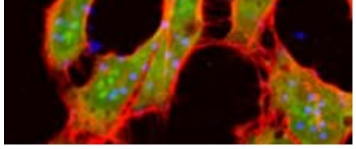


Figure 1. Bacterial adhesin molecules coupled to fluorescent beads (blue) bind to mammalian cells and inhibit subsequent bacterial infection.

Publications

For a full list of publications please visit **PubMed.gov (http://www.ncbi.nlm.nih.gov/pubmed?term=%22Krachler%20AM%22%5BAuthor%5DAnd/)** or **Dr Krachler's Google Scholar profile (http://scholar.google.co.uk/citations?user=zsRLlqkAAAAJ&hl=en)**

Selected publications

Hawley CA, Watson CA, Orth K, **Krachler AM** (2013). A MAM7 peptide-based inhibitor of Staphylococcus aureus adhesion does not interfere with in vitro host cell function. *PLoS One*. 8(11):e81216.

Altura MA, Heath-Heckman EAC, Gillette A, Kremer N, **Krachler AM**, Brennan C, Ruby EG, Orth K, McFall-Ngai MJ (2013). The first engagement of partners in the Euprymna scolopes-Vibrio ischeri sumbiosis is a two-step process initiated by a few environmental symbiont cells. *Env Microbiol.* doi: 10.1111/1462-2920.12179.

Krachler AM and Orth K (2013). Made to Stick: Anti-Adhesion Therapy for Bacterial Infections. *ASM Microbe.* July 2013.

Krachler AM and Orth K (2013). Targeting the bacteria-host interface: Strategies in anti-adhesion therapy. *Virulence.* 4(4):284-94.

Krachler AM, Mende K, Murray C and Orth K (2012). In vitro characterization of Multivalent Adhesion Molecule 7-based inhibition of multidrug-resistant bacteria isolated from wounded military personnel. *Virulence.* 3(4):389-99.

Zhang L,**Krachler AM**, Broberg CA, Li Y, Mirzaei H, Gilpin CJ, Orth K (2012). Type III effector VopC mediates invasion for Vibrio species. *Cell Rep.* 1(5):453-60.

Krachler AM and Orth K (2012). Use of the bacterial Multivalent Adhesion Molecule 7 as an antimicrobial agent. *Virulence.* 3(1):68-71. (Article featured on the cover).

Krachler AM, Woolery AR, Orth K (2011). Manipulation of host kinase signalling pathways by bacterial pathogens. *J Cell Biol.* 195(7):1083-92.

Krachler AM, Orth K (2011). Functional characterization of the interaction between the bacterial adhesin Multivalent Adhesion Molecule (MAM) 7 and its host cell ligands. *J Biol Chem.* 286(45):38939-47.

Krachler AM, Ham H, Orth K (2011). Outer membrane adhesion factor multivalent adhesion molecule 7 initiates host cell binding by Gram-negative pathogens. *Proc Natl Acad Sci U S A.* 108(28):11614-9. (Article highlighted in Nature 2011, 475:9 and in Nature Rev Microbiol 2011, 9(9):627).

Orth K, Ham H, **Krachler AM** (2011). Modulating bacterial MAM polypeptides in pathogenic disease. WO Patent 2,012,138,570.

Krachler AM and Orth K (2010). Black Spot, Black Death, Black Pearl: Tales of Bacterial Effectors. Book Chapter in *Avancées et nouvelles technologies en Toxinologie – Advances and new technologies in Toxinology* (SFET, ed.). ISSN 1760 – 6004

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