Invasions of the pharynx: microbiome of infected respiratory tissues

Supervisory Team: Dr Jan Lindström (Institute of Biodiversity, Animal Health and Veterinary Medicine), Dr Chris Quince (School of Engineering) and Professor Thomas Evans (Institute of Infection, Immunity and Inflammation)

Background and objectives: The main focus of this project is to broaden the scope of infectious disease research which tends to focus on just one organism, the pathogen. However, when pathogens encounter a host, they do not meet a sterile environment but a pre-existing and complex multi-species microbial community that either allows, facilitates or outcompetes the newcomer and consequently determines clinical outcome. For decades ecologists have studied why some ecological communities are more easily invaded by exotic species than others, and developed models of how the outcome of invasion depends on a complex interaction between the invader and the resident community. We will combine the ecological insights of evolutionary community ecology with an up-to-date study of the the composition and stability of the pharyngeal microbial flora and changes that viral infection, antibiotics and immunocompromise produce. The project aims to characterise the microbiota communities of healthy persons, identify key factors of the community structure associated with pathogen colonization and infection and the recovery of those, either with or without treatment of antibiotics.

The student will design the details of the research programme together with the supervisors, and there is therefore scope for developing a portfolio of skills and approaches best suited to the student. The starting point will be, however, addressing the core objectives of the project. We will sample the pharynx of a group of healthy subjects weekly for a full year. This will allow us to (1) *characterise the dynamics of the microbial community structure*, MCS, in terms of both diversity and relative species abundance, *of a healthy person, and quantify its natural variation*. As it is inevitable that at least some of these persons will develop respiratory infections over the year of sampling, we will also (2) *analyse whether there were changes in the MCS prior to the infection, after it, or both*; in other words, whether a change in the present MCS allowed infection or whether the possible change in MCS was caused by it. In addition, (3) *MCS from healthy patients will be compared to MCS in two patient groups: patients treated with antibiotics, and those with HIV*. This second group will include those with ‘normal’ peripheral CD4 counts and those who have low CD4 counts, representing significant immunosuppression. These patients receive long-term prophylactic antibiotics. Microbial DNA will be extracted from all microbial samples and the 16S rRNA gene amplified by PCR. Denaturing Gradient Gel Electrophoresis (DGGE) will be used to provide qualitative information on the microbial community structure. A subset of the stored samples will then be selected for 454 pyrosequencing of the 16S V4-V5 region. Samples will be chosen on the basis of providing maximum statistical power. This will generate a complete MCS snapshot, including both the relative abundance and sequences of taxa. These sequences will be used for taxonomic identification but also to construct qPCR primers for a range of taxa allowing quantification of their absolute abundance in all the samples.

Training Opportunities: The project is by nature interdisciplinary and the student will receive a unique combination of training in a wide range of approaches, including community ecology, bioinformatics, statistical analyses, basic molecular and genomic techniques and metagenomics.

Funding Details: Lord Kelvin – Adam Smith Scholarship, University of Glasgow (£13,590 pa + full fees)

Duration - 4 years, expected start date October 2012 (but can be negotiated)

Eligibility: This position is open to all nationalities but the candidate has to meet all the eligibility criteria (http://www.gla.ac.uk/media/media_168556_en.pdf), including general English language

requirements of postgraduate students in Glasgow University (http://www.gla.ac.uk/postgraduate/howtoapplyforataughtdegree/englishlanguagerequirements/).

How to apply:
We will welcome applications from students with and Honours or Masters degree in microbiology, ecology, evolution, bioinformatics, or other relevant discipline. This 4-year studentship is open to all nationalities but the candidate has to meet all the eligibility criteria (http://www.gla.ac.uk/media/media_168556_en.pdf), including general English language requirements (http://www.gla.ac.uk/postgraduate/howtoapplyforataughtdegree/englishlanguagerequirements/). Informal enquiries can be sent to any of the three supervisors (jan.lindstrom@glasgow.ac.uk, christopher.quince@glasgow.ac.uk, thomas.evans@glasgow.ac.uk).

The formal application should have: full CV + contact details of at least 2 referee and a cover letter indicating motives and qualifications for undertaking the proposed program

Who to send applications to: Ms Lorna Kennedy (lorna.kennedy@glasgow.ac.uk)

Closing date: 2 April 2012

Recent publications by the supervisory team:

Bize, P., Diaz, C.. & **Lindström**, J. 2012: Experimental evidence that adult antipredator behaviour is heritable and not influenced by behavioural copying in a wild bird. — *Proceedings of the Royal Society, ser. B,* in press.

Evans, T. 2009: Bacterial triggering of inflammation by intracellular sensors. *Future Microbiology* 4:65-75.

Lindestam Arlehamn, C.S. & **Evans**, T.J. 2010: *Pseudomonas aeruginosa* pilin activates the inflammasome*. Cellular Microbiology* 13:388-401.

Lindestam Arlehamn, C.S., Petrilli, V., Gross, O., Tschopp, J. & **Evans**, T.J. 2010: The role of potassium in inflammasome activation by bacteria. *Journal of Biological Chemistry* 285:10508-10518.

Lindström, J., Pike, T. W., Blount, J. D. & Metcalfe, N. B. 2009: Optimization of resource allocation can explain the temporal dynamics and honesty of sexual signals. — *American Naturalist* 174:515–525.

Lindström, J., Reeve, R. & Salvidio, S. 2010: Bayesian salamanders: analysing the demography of an underground population of the European plethodontid *Speleomantes strinatii* with state-space modelling. — *BMC Ecology* 10:4.

Parsons, T. L., **Quince**, C. , and Plotkin, J. B. 2010: Some Consequences of Demographic Stochasticity in Population Genetics. — *Genetics* 185:1345-1354.

Quince, C., Lanzen, A., Curtis, T.P. , Davenport, R.J., Hall, N., Head, I.M., Read, F., and Sloan, W.T. 2009: Accurate determination of microbial diversity from 454 pyrosequencing data. *Nature Methods* 6:639-U27.

Quince, C., Lanzen, A., Davenport, R.J. & Turnbaugh, P.J. 2011: Removing noise from pyrosequenced amplicons. — *BMC Bioinformatics* 12:1.