DIPARTIMENTO DI FARMACIA E BIOTECNOLOGIE

AVVISO DI SEMINARIO

Il giorno **martedì 1 Ottobre 2019**
alle ore **14:30**,
presso l'Aula A, via Irnerio 48 (ex Farmacologia)

il **Prof. Marco R. Oggioni, PhD**
Department of Genetics and Genome Biology, University of Leicester, UK
(ospite Prof. Davide Zannoni)

terrà un seminario dal titolo:

PHASE VARIABLE EPIGENETIC REGULATION OF MICROBIAL GENE EXPRESSION

Colleghi e studenti sono cordialmente invitati

Commissione Ricerca e Attività Correlate - FaBiT

ABSTRACT

Invasive bacterial infections and transmission impose severe bottlenecks onto bacterial populations, which have developed multiple systems to readily reproduce diversity. High-frequency phase variable type I restriction-modification systems (RMS) are present in many bacterial species and in particular are present in some of the most virulent sub-lineages of *Listeria monocytogenes, Streptococcus suis, Enterococcus faecalis* and in the core genome of *Streptococcus pneumoniae* which could be viewed as a virulent lineage of the *Streptococcus mitis* group. In *S. pneumoniae* the SpnIII RMS has been shown to provide phase variable control to horizontal gene transfer by transformation and phage infection, but importantly has been associated to epigenetic regulation, including regulation of the colony opacity phenotype, related to the infectivity or carriage potential of isolates.

In the pneumococcus the SpnIII RMS generates six different *hsdS* (host specificity determinant) alleles via site specific recombination. Therefore, the methylation target sites differ between single strains expressing stably a single HsdS variant, which results in a different pattern of chromosome methylation. Multiple independent *S. pneumoniae* strains expressing only one of three single *spnIII* alleles (*spnIII*A, *spnIII*B or *spnIII*E) were analysed by RNAseq to determine any difference in gene expression profiles. These data identified a panel of genes which show differential expression and have a methylation site mapping to their predicted promoter region. In this seminar I will present our current data which show that differential methylation of DNA upstream a *luc* reporter construct influences light production in *S. pneumoniae*, with methylated DNA increasing downstream gene expression. These data represent an important step forward in the understanding how phase variable chromosomal methylation might modulate gene expression on a genomic scale.

BIOGRAPHICAL SKETCH

Since 2013 I joined the Department of Genetics and Genome Biology of the University of Leicester as a Chair in Microbial Genetics and, since 2015, I have in addition an Honorary Microbiology Consultant Contract with the University of Leicester Hospitals NHS Trust. I am co-chair of the Leicester Microbial Sciences and Infectious Disease LeMID Network. I went to Medical School at the University of Siena (Italy) and later at the University of Verona (Italy) where I obtained my medical degree (1990). During these years I spent a period as guest investigator at the Rockefeller University, New York (USA). Back at the University of Siena, I obtained a Specialisation degree in Medical Microbiology and Virology (1994). My research work started in Siena with Professor Gianni Pozzi on biotechnological projects aimed at using non-pathogenic streptococci as life vaccine vectors. I was then employed at the University Hospital of Siena 1993 to 2013 where I also had a teaching contract with the University of Siena (Italy).

My research interests span for the physiology of bacterial pathogens during infection, work on bacterial genetics/genomics and antimicrobial drug resistance. My main area of research interest is the discovery of specific details in the interaction of pathogenic bacteria with the host that could lead to new treatment options and the analysis of antimicrobial resistance determinants. I address the study of bacterial virulence mechanisms, by use of genomic tools, the exploration of microbial physiology, and the detailed analysis of events occurring in experimental infection models. Main scope of this work is the recognition of specific phases characterising microbial physiology during infection with the aim of identification of novel drug targets. In this context I have focused in the bacterium *Streptococcus pneumoniae* on carbon metabolism, discovered a novel phase variable methylation mechanism with an epigenetic impact on bacterial phenotypes and that invasive bacterial infection starts form a single bacterial cell. Most recently I have described that pneumococci are capable of replicating in a subset of splenic macrophages prior starting invasive disease in mice and that invasive disease can be prevented by blocking this intracellular replication (Ercoli et al., Nature Microbiology 2018). In order to explore the validity of these findings an ex vivo perfusion model for porcine spleens was developed and intracellular replication of pneumococci in the same subset of splenic macrophages could be confirmed (Chung et al., ALTEX 2019). Most recently MRO was awarded as Chief Investigator by the Health Research Authority a clinical trial to use human spleens in *ex vivo* perfusion models. This work is now providing the first functional analysis of the roles of specific macrophage subsets in the human spleen during the first phases of infection. This innovative work holds promise to rewrite some of the concepts of the pathogenesis of infection and the rational for antimicrobial drug treatment.