**GHI Floor Seminars**

**Special seminar by invited speaker**

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***New insights into pneumococcal biology from dual RNA-seq, Tn-seq and CRISPRi approaches***

*Streptococcus pneumoniae*, the pneumococcus, is the main etiological agent of pneumonia. Pneumococcal infection is initiated by bacterial adherence to lung epithelial cells. To uncover the exact transcriptional changes that occur in both host and microbe during infection, we developed a time-resolved dual RNA-seq model. By comparing transcriptional changes between wild-type encapsulated and mutant unencapsulated pneumococci, we demonstrate that adherent pneumococci, but not free-floating bacteria, repress innate immune responses in epithelial cells. Interestingly, many genes of unknown function were differentially expressed during adherence to human cells. To systematically perform functional analysis on these ‘unknown’ genes, we created a knockdown library targeting 348 potentially essential genes by CRISPR interference (CRISPRi) and show a growth phenotype for 254 of them (73%). Using high‐content microscopy screening and functional analysis, we identified and characterized several new genes involved in cell wall biosynthesis and competence development. Finally, we systematically tagged every essential protein of unknown function to a monomeric superfolder-GFP. By combining Tn-Seq, CRISPRi and GFP-localization data,we identified CcrZ (Cell Cycle Regulator protein Z), which co-localizes with FtsZ and is highly conserved in Streptococci. Marker frequency analysis, suppressor analysis and chromosome labeling experiments showed that, in absence of CcrZ, daughter chromosomes are not properly segregated prior to cell division. Together, these findings indicate that CcrZ acts as a link between DNA replication, chromosome segregation and cell division.

Host: Prof. Melanie Blokesch

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