ERA-NET PathoGenoMics
Consortium: ECIBUG
Interview with Prof. Matthias Maaß

1) If you look back at the first year of funding, what have you managed to achieve?

Firstly, we have nine academic groups that have harmonised their methodologies and techniques to build up an integrative international team that communicates on an almost daily base. Consequently, we are seeing constant adaptation in the research questions across the different laboratories. This has aided in the establishment of a *Chlamydia* research network, which has never existed before in this form.

2) What results have you already obtained on the scientific side?

Although we are still in our first year, we have already produced a range of interesting results. Firstly, we have identified a list of 60 effector proteins that are released into the infected host cell by the bacterium. Among them, we anticipate finding the proteins that initiate the pathological reprogramming of the host cell, which will then be possible candidate targets for new antimicrobial therapies. Secondly, we were able to detect two proteins that potentially mediate the access of the bacteria into the host cell. Thirdly, we managed to identify eight newly defined compounds that show an effect on *Chlamydia* and that will be further analysed for their clinical relevance. Fourthly, we have a better understanding of complex intracellular signalling pathways through which *Chlamydia* species regulate host cell growth and proliferation. We think that these studies provide a basis for explaining the bacteria's role in atherosclerosis and asthma. On top of this, we better understand that *Chlamydia* infections trigger autoimmune reactions that take place via a chlamydial heat shock protein, which is similar to a human heat shock protein. As a new element of this process, we discovered that, through a *Chlamydia* infection, host cells express their own human heat shock protein on the surface of the cell, although it is an intracellular protein. We assume that this surface expression is one of the factors that cause autoimmune reactions.
Finally, we are also developing random mutants of *Chlamydia* species using chemical mutagenesis. With this innovative and risky approach, we are optimistic that we will be the first researchers to generate *Chlamydia* mutants.

3) What is the therapeutic relevance of the work of your consortium?

Regarding the development of therapies, we follow two approaches: One is to generate new compounds with antibiotic effects on *Chlamydia* from databases and, based on animal models or ex vivo models, to evaluate these compounds for possible clinical effectiveness against chronic infections. The other strategy is to analyse how the *Chlamydia* bacterium is able to reprogram the host cell via their secreted effector proteins, and then to target a possible therapy towards these processes. This would not directly interfere with the bacterial metabolism but disturb the interaction of bacterial and human gene products in order to prevent a chronic implantation of *Chlamydia* in the body. From our point of view, this would be of therapeutic relevance. At this point, we are still at a basic research level. We have to identify compounds or strategies that have to be evaluated in complex lab-scale models and *ex vivo* models. Only those strategies that show positive results in both of these models will be further studied in animal models, all of which is some years off. It would be a great success if

we had one compound at the end of this ERA-NET funding that shows potential for an evaluation in animal models.

4) What do you think is the advantage of such an ERA-NET consortium?

From our point of view, this sort of cooperation is desperately needed. The main reason for this is that research into *Chlamydia* infections is extremely difficult because this bacterium cannot be manipulated using classical molecular genetic tools. That's why there is a strong need for cooperation, for the sharing of information and competencies regarding proteomics, genomics, animal models and clinical experiences. We are convinced that only a large integrative network, which we have begun under the roof of the ERA-NET framework, can effectively handle the research on *Chlamydia*.