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CIC biomaGUNE
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Centro de Investigación Cooperativa en Biomateriales

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SEMINAR

Wednesday, 17th January, 12.00 pm, Seminar Room

Host: Dr. Niels C. Reichardt

Harnessing the *Mycobacterium tuberculosis* cell surface's physiology to generate better anti-infective tools

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One of the historic ironies of tuberculosis (TB) research is the assumption that the current interventions would eliminate this disease. BCG was discovered in 1908 and it has not successfully eliminated the disease due to its limited efficacy. Yet even with better antibiotics, TB is the first cause of death by a bacterial infection. New vaccines are central to future TB elimination program. However, the incomplete understanding of the physiology of its causative agent, *Mycobacterium tuberculosis* (Mtb), precludes the efficacy of the current vaccine approaches.
Mtb and host cells initiate their encounter at the outermost part of the cell surface. Our group is interested in understanding how Mtb shapes its cell surface during the infection process. We are focused in two different physiological processes: (i) alternative secretion systems based on extracellular vesicles (EVs) and (ii) the Mtbl outermost capsule.

(i) Mtb, like many intracellular microbes, depends on specialized export systems. In a variety of both prokaryotic and eukaryotic microorganisms, many of these released factors have been associated with extracellular vesicles (EVs). Our studies showed that EV production could be extended to Mtb and BCG. EV production may provide an alternative mechanism for transport of immunomodulatory compounds and may allow mycobacteria confined within phagosomes to deliver virulence factors to other cellular compartments. Our recent report on the first Mtb gene controlling vesiculogenesis with an attenuated phenotype suggests that EV production might be a regulated process with relevant implication in pathogenesis. *Our current efforts are directed to unravel the molecular machinery of vesiculogenesis in Mtb and the development of novel TB vaccines based on EVs*.

(ii) Most approved vaccines against bacterial pathogens mediate protection by eliciting antibody responses. However, it has been difficult to apply this formula to TB. We recently develop capsular polysaccharide conjugates by linking on the mycobacterial capsular polysaccharide (PS) arabinomannan (AM) to several immunogenic proteins. Conjugate vaccine immunized mice infected with Mtb had lower bacterial numbers in lungs and spleen, and lived longer than control mice. We also showed that AM is antigenically variable and could potentially form the basis for a serological characterization of mycobacteria based on serotypes. *We are currently interested in both tailoring AM-based conjugates and deciphering the global antigenic variability of Mtb capsule. To this end we have combined bioinformatics, genetics and structural biology to unravel how Mtb has shaped it cell surface during its evolutionary history of interaction with the human being*.