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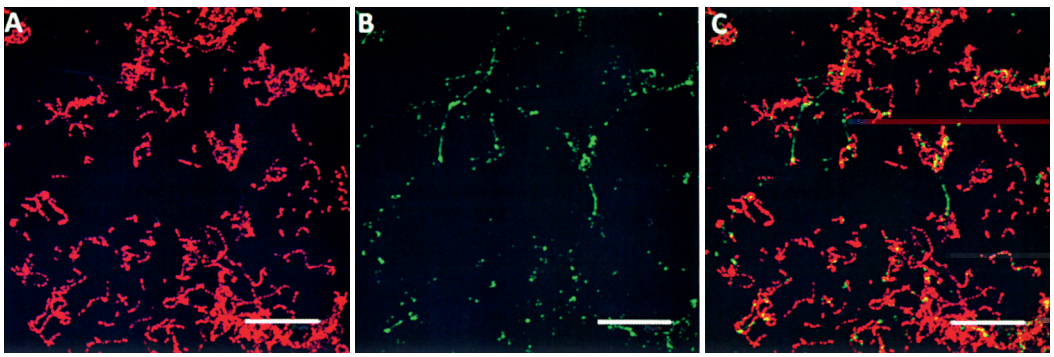
Interacciones Huésped-Parásito en Infecciones Neumocócicas

Streptococcus pneumoniae (neumococo) es uno de los principales patógenos bacterianos y causa principal de morbilidad y mortalidad en niños y adultos de todo el mundo. La enfermedad neumocócica invasiva (ENI) viene precedida por el establecimiento del llamado "estado de portador", es decir, la colonización de la nasofaringe. Este proceso tiene lugar a través de una relación compleja huésped-parásito en la que también se dan interacciones con otros microorganismos que ocupan el mismo hábitat. La mayoría de estas interacciones implican, por un lado, a proteínas de la superficie bacteriana y, por otro, a los mecanismos de defensa del huésped.

En nuestro laboratorio se estudia la implicación de unas proteínas de superficie, denominadas "Choline-binding proteins" o CBPs, en la colonización, el establecimiento de la ENI y la respuesta inmune. Para ello, se han puesto a punto diversas técnicas *in vitro* —como los biofilmes o los cultivos celulares— y modelos animales de infección. Se ha observado que los biofilmes son complejos ya que en su formación están implicados múltiples genes. También se ha demostrado que el DNA y determinadas CBPs son importantes para la formación y mantenimiento del biofilm. Se han identificado uno o más exopolisacáridos que contienen residuos de Glc β(1→4) y GlcNAc β(1→4).

Ante el incremento y difusión de ciertos patógenos multirresistentes, en el laboratorio se estudian diferentes compuestos con actividad antibacteriana, como los ésteres de aminas bicíclicas (que se comportan como análogos de colina) o las lisinas fágicas (endolisinas). Estas enzimas son proteínas modulares e hidrolizan la pared bacteriana por lo que muestran un potente efecto bactericida, tanto en cultivos planctónicos como en biofilmes. Además, suelen ser muy específicas ya que, normalmente, sólo destruyen a las bacterias de las que procede el fago que codifica dicha enzima. La validación de los resultados se lleva a cabo en diferentes modelos de ratón o de embriones de pez cebra.



Host-Parasite Interplay in Pneumococcal Infection

Pneumococcal diseases (acute otitis media, pneumonia, bacteremia, and meningitis) are frequent causes of morbidity and mortality worldwide. The development of invasive pneumococcal disease is preceded by the colonization of the human nasopharynx. Formation/disintegration of pneumococcal biofilms and the antibacterial activity of bicyclic amines and phage-coded lytic enzymes using biofilms and animal models of infection have been studied.

Streptococcus pneumoniae, or pneumococcus, is one of the major bacterial pathogens and a leading cause of morbidity and mortality in children and adults throughout the world. Invasive pneumococcal disease (IPD) is preceded by the establishment of the "carrier state", *i. e,* the colonization of the human nasopharynx. This process takes place through complex interactions between the host immune system and the parasite as well as between the latter and other microorganisms sharing this habitat. Most of these interactions involve one (or more) bacterial surface polymers.

In our laboratory, we have studied the role of several surface-located proteins — the so-called "Choline-binding proteins" or CBPs — in colonization, IPD development and the recognition and triggering of the host immune response. To this aim, *in vitro* biofilm systems and animal models of infection have been employed. Pneumococcal biofilms are structurally and functionally complex structures in which multiple genes are involved, some of them of unknown function. It has also been demonstrated that DNA and certain CBPs are essential components of the extracellular matrix of these biofilms. Moreover, one (or more) polysaccharide containing Glc β(1→4) and GlcNAc β(1→4) residues has been identified in the pneumococcal biofilm matrix.

Given the increase and rapid spread of several multiresistant bacterial pathogens, various compounds showing antibacterial activity have been studied. Among others, these include esters of bicyclic amines (that behave as choline analogues) and phage lytic enzymes (endolysins). Endolysins are modular proteins that hydrolyze the bacterial cell wall peptidoglycan and, consequently, exhibit a strong bactericidal effect against both planktonic cultures and biofilms. Phage endolysins also tend to be very specific because, normally, they only kill the corresponding host bacteria. The validation of the results is made using animal models of infections such as mice and zebrafish embryos.

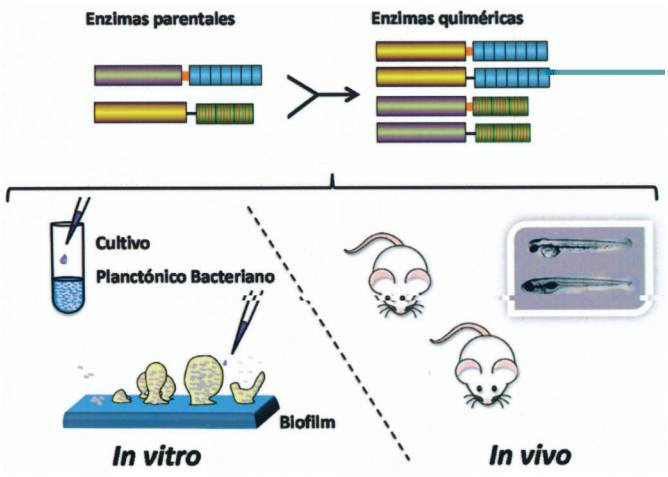


Figura 2 | *Figure 2*

Ejemplo de endolisinas fágicas, parentales y quiméricas. Las proteínas purificadas se emplean en diferentes ensayos *in vitro* (cultivos bacterianos planctónicos y biofilmes) y los resultados se validan en modelos animales (ratones o embriones de pez cebra).

Example of phage endolysins, either parental or chimeric. The purified proteins are used in different *in vitro* assays (bacterial planktonic cultures and biofilms) and results are validated in animal models (mice or zebrafish embryos).

Publicaciones Seleccionadas
Selected Publications

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