Identification of immunogenic targets for the production of recombinant therapeutic antibodies against Klebsiella pneumoniae

Résumé

Context

Klebsiella pneumoniae (Kp) is a bacterial species responsible for infections associated with high mortality rates (10-40%). The sharp increase in the prevalence of multidrug-resistant (MDR) Kp strains over the last decades constitutes a significant public health problem that justifies the urgent need to develop new therapies. Monoclonal antibodies (mAbs) are an interesting option to fight bacterial infections. The hypothesis is that by targeting virulence factors or surface proteins, mAbs will inhibit the virulence of bacteria and/or facilitate their elimination by opsonophagocytosis.

Aim

The project will be carried out in several stages. My thesis is the initial step, which aims to identify antigens of interest that can be used to isolate and produce neutralizing human mAbs against Kp.

Materials and methods

The reverse vaccinology approach is used. First, the presence of antibodies against Kp is confirmed by immunoblotting of total bacterial extracts with sera from patients with Kp infection. Then, the genomic and phenotypic characteristics of Kp (MLST typing, plasma resistance, antibiotic resistance ...) are studied by sequencing of complete genomes, human plasma exposure tests, and culture on specific media. Finally, transposon insertion sequencing (Tn-Seq) is used on selected Kp strains to identify target antigens that contribute to the characteristics studied above.

Results and perspectives

This work aims to find immunogenic proteins that are responsible for the virulence and/or resistance of MDR Kp. If successful, specific B cells that produce mAbs against the targets of interest will be isolated from patients and sorted by flow cytometry. The immunoglobulin genes from the selected cells will be amplified by PCR and cloned to produce therapeutic recombinant antibodies capable of treating severe MDR Kp infections.

Mots-Clés: Klebsiella pneumoniae, virulence, antibiotic resistance, antigens, monoclonal antibodies, transposon insertion sequencing