IMMUNETHEP

PACE Award Profile: Immunethep, S.A.

Advancing monoclonal antibodies to restore the ability to control bacterial infection

Project title: Monoclonal antibodies targeting bacterial GAPDH as a single immunotherapy to treat infections caused by *E. coli* and *Klebsiella pneumoniae*

Antimicrobial resistance is a major threat to public health globally, but susceptibility to bacterial infection is determined by the immune response. Scientists at Immunethep have found that failure to fight off an infection can arise because bacteria are able to dampen down the body's immune response, using a hitherto unknown mechanism conserved among bacteria including *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumoniae* and members of *Streptococcus*. Studies at Immunethep have shown that the bacteria achieve this by releasing a variant of a protein called glyceraldehyde-3-phosphate dehydrogenase (known as bGAPDH), which shifts the host's immune system towards an anti-inflammatory (and hence more bacteria-susceptible) state.

The Immunethep team has shown that antibody-mediated neutralisation of bGAPDH is highly effective in preventing infections by the above-mentioned bacteria in physiological models of infection and in human cord blood cells. They have already identified 16 monoclonal antibodies targeting bGAPDH from *E. coli* and *K. pneumoniae*, with binding affinities (K_D values) ranging from 30 nM to at least 5 pM.

With funding and close collaborative support from PACE, the four best antibodies will be selected for efficacy and safety studies. At least one of these antibodies will then be chosen for humanisation and subsequent development through to clinical studies in humans.

Success in this project will result in an antibody-based treatment that can be administered to patients at greater risk of infection or those receiving medical interventions. A single dose of the treatment should be effective against both *E. coli* and *K. pneumoniae*, with no associated toxicity, and will not result in antimicrobial resistance.