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PROJECTE DE DOCTORAT INDUSTRIAL EXPEDIENT 2014 DI 044

DADES DE L'EMPRESA I DE L'ENTORN ACADÈMIC

Títol del projecte

Evaluación de exosomas y su aplicabilidad en enfermedades de interés veterinario

Empresa

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BREU DESCRIPCIÓ DEL PROJECTE DE RECERCA

Exosomes are specialized membranous nano-sized vesicles derived from endocytic compartments that are released by many cell types. Exosome biogenesis involves the tightly controlled process of inward budding from the limiting membrane of multivesicular bodies (MVBs). This results in numerous intraluminal vesicles in the lumen of MVBs that contain distinct protein repertoires and which after fusion with the plasma membrane are released to the extracellular space.

First discovered in the maturing mammalian reticulocyte (immature red blood cell), exosomes were shown to participate in selective removal of many plasma membrane proteins as the reticulocyte becomes a mature red blood cell (erythrocyte). Nowadays they are known to be released by all types of cells, albeit variably. Exosomes can transfer molecules from one cell to another via membrane vesicle trafficking, thereby influencing the immune system, such as dendritic cells and B cells, and may play a functional role in mediating adaptive immune responses to pathogens and tumors. Therefore, research and development and innovation on exosomes holds great promising in human and animal health.

Remarkably, reticulocytes are the cells preferentially, if not exclusively, invaded by *Plasmodium vivax*. We thus hypothesized that reticulocyte-derived exosomes (rex) in *vivax* infections, in addition to their role as cargo-disposable machinery, should contain parasite proteins and that these nanovesicles could be used as novel platform and vaccine against *P. vivax*. Proof-of-concept was obtained with a rodent malaria model that infects reticulocytes and in which immunization of animals with rex in combination with adjuvants conferred full and long-lasting protection to animals upon a lethal challenge (PCT/EP2010/070800). INNOVEX



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THERAPEUTICS S.L. is owner of the patent.

The aim of this PhD project is to expand the applicability of rex to diseases of veterinary interest. In the first step of his/her PhD the student will isolate rex in order to characterize them. Due to the large confounding of exosomes from biological fluids, the student will first assay different isolation techniques to develop a unique, scalable and reproducible standard operational procedure (SOP) to obtain and characterize rex. With this SOP the student will then be able to obtain pure fractions of rex to further characterizing them by techniques including, among others, Nanoparticle Tracking Analysis, Electron Microscopy, flow cytometry, proteomics and transcriptomics analyses in order to decipher their molecular composition. After their characterization, rex will be used in experimental infections of animal diseases of veterinary importance to try inducing protective immunity.