PROJECT REVIEW

"Unequivocal detection of AAV-mediated gene doping by pan-AAV immunological profiling"

Drs. G. Ronzitti (INSERM U951, France), **F. Bosch** (Universitat Autònoma Barcelona, Spain)

The same characteristics that make adeno-associated virus (AAV)-based vectors ideal for clinical gene transfer may encourage their misuse for gene doping. Here we propose the development of a method for unequivocal detection of AAV-mediated gene doping based on the hypothesis that gene transfer with AAV vectors will leave a characteristic immunological footprint clearly distinguishable from natural occurring AAV infections with wild-type virus. The project consists in the profiling of anti-AAV antibody responses in serum samples to determine positivity. A sensitive, panAAV antibody ELISA will be developed, validated, and streamlined to distinguish humoral responses triggered by natural exposure to AAV from AAV-mediated gene doping. Baseline levels of panAAV antibodies will be evaluated in humans, non-human primates and dogs and compared to levels measured in AAV-injected individuals and in individuals naturally exposed to the wild-type virus. The use of different species will allow for the comparison of a higher number of serum samples thus increasing the robustness of the method. In conclusion, the ELISA assay developed in the frame of this project will permit to define the baseline levels used as reference values for each athlete and the levels that considered as positive.