FUTURE CHALLENGES IN RABIES VACCINOLOGY

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According to a recent WHO estimation, rabies remains responsible for >55.000 human deaths per year, mainly in Asia and Africa. This situation is no more acceptable assuming that the main tool to control the disease, i.e. the rabies vaccine, has been constantly improved, both for human and animal use, since Louis Pasteur. In humans, safe and potent vaccines produced in cell culture, recommended by WHO, are progressively replacing old vaccines prepared from animal nervous tissue that are less immunogenic and occasionally suspected of adverse effects. In animals, classical vaccines given parenterally under domestic conditions are complemented by a panel of recombinant and attenuated vaccines administrable by oral route to vaccinate non accessible dogs or wildlife. The potency of these vaccines to control rabies has been extensively demonstrated. Systematic vaccination campaigns in Latin America have controlled dog rabies within the last 15 years. The rational use of oral vaccination in Western Europe has almost eliminated rabies from the vulpine reservoir. As a result, a growing number of West-European countries are declared “rabies-free” (OIE rules) when no terrestrial case is found during two consecutive years despite intensive surveillance. Despite these obvious progresses, several challenges are still pending in rabies vaccinology: (1) the development of new oral vaccines for reservoir species that are not easily accessible and/or difficult to immunize orally (feral dogs, wild carnivores, bats); (2) the broadening of the vaccine spectrum from anti-rabies to anti-lyssavirus (the viral genus grouping rabies etiologic agents). The presentation will describe recent developments addressing these challenges: (1) the development of a canine adenovirus vector (deleted or replication-competent) and its potential through oral administration; (2) the use of DNA-based immunization with plasmids expressing chimeric surface G proteins of lyssaviruses. Indeed, seven lyssavirus genotypes (GT) are distinguished today, which segregate into two phylogroups (PG). As cross-neutralisation exists within, but not between PGs, vaccine strains (PG1) do not protect against PG2 lyssaviruses. DNA vaccination with plasmids expressing chimeric G proteins (fusion of the NH2 and COOH halves of different GTs) is efficient to induce humoral and cellular immune responses as well as protection against the two parental GTs, but also against other GTs. This broaden the spectrum of rabies vaccines towards lyssavirus vaccines. Further, the lyssavirus G protein can carry foreign epitopes/antigens in the perspective of multivalent vaccines against various zoonoses for carnivores.