INNOVATIVE ANTIVIRAL STRATEGIES TARGETING DIFFERENT STEPS OF RABV INFECTION

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Human rabies still accounts for 70.000 deaths per year, mostly in developing countries, eventhough effective vaccines are available. Rabies victimsdie because, due to local unavailability or excessive cost, they cannot :(1) access to preventive vaccines; (2) access to full WHO-recommended “post-exposure“ treatment combining vaccine and rabies immunoglobulin (RIG) instilled locally to “neutralize” the viral inoculumbefore it reaches the neurons and thecentral nervous system (CNS). However, since 2005, the “Milwaukee protocol” thathelped a girl to survive symptomatic rabies has increased the interest of scientists to developinnovative therapeutics against rabies disease. The long incubation period (two months in average) necessary for RABV to infect the CNS provides opportunities to develop strategies blocking the virus at different steps of the infection: entry, fusion, retrograde transport, replication, exit. Different strategies are currently exploredto find active anti-rabies molecules: (1) classical screeningof compounds libraries; (2) design of molecules specifically destabilizing functional interactions between viral proteins; (3) targeting cellular functions indispensable for viral cycle. The presentation will describe examples of this quest for a future anti-rabies therapy. Several non cytotoxic candidates have been found >95% efficient *in vitro*, alone or in combination, and some are currently tested *in vivo* on mouse model. The concerted efforts of several labs gathered in the European program Aklepios (http://asklepiosfp7.eu/) will be in particular presented.