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, even though effective vaccines are available. Rabies victims die 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 inoculum before it reaches the neurons and the central nervous system (CNS). However, since 2005, the “Milwaukee protocol” that helped a girl to survive symptomatic rabies has increased the interest of scientists to develop innovative 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 explored to find active anti-rabies molecules: (1) classical screening of 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.