The Essential Role Played by a Previously Unknown Mechanism in Viral Pathogenesis Leading to Effective New Vaccines and Post-Exposure Immune Treatments of Viral Infections

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In the article published in English by Bijlenga [1] I mentioned that an "active component" of the standard rabies virus is responsible for the paralytic symptoms and death. The complete virus is not causing these symptoms and death. The development of this process seems to be an interaction during the infectious process of the whole virus with a sensitive cell. An apoptotic mechanism reported by Machetti et al. [2] takes place triggered by probably an enzyme followed by release of a protein as active component which component kills the cells. This hypothesis is of great important for the understanding how the process of infection proceeds towards symptoms and death and why we can explain for instance variable- and fixed incubation periods after exposure and the early and enhanced death phenomena. The latter observation can easily be explained through dilution of the vaccine strain and loss of "the active component".

It was assumed by other virologists that the only possibility that a non-sedimented virus of the original sample (probably a mutant) can only cause such reactions. But based on my experience for years working with natural and vaccine strains of rabies I have never observed large plaques of natural (street) virus without an adaptation of many passages in Baby Hamster Kidney (BHK) 21cell culture. Also that "the active isolated component" produced immediately very high titers in the first BHK-21 cell culture experiment, and antibodies against "the active component" intracerebrally (IC) applied, neutralizes a CVS infection completely, just before paralytic symptoms develop in other control mice IC inoculated with Fetal Bovine Serum (FBS).

The NIH potency test for rabies vaccines for use in humans does not measure really protection after exposure. The test is based on two weekly vaccinations and followed by a challenge one week after the second vaccination provides only post-vaccination values expressed in International Units (IU)/dose. One measures only values to surface (glycoproteins) antigens and nothing is known about other antibodies to be stimulated.

I have developed some years ago, a potency test which simulates natural infection [3] and found that almost all the rabies vaccines did not protect after exposure including the Reference Vaccine for use in the NIH potency test. It is possible in the future, if the finding of the "active component" is found by other investigators, to develop a potency test without making use of laboratory animals, thus in vitro. Also the real protective value of animal rabies vaccines is not known due to the fact that vaccines which produce antibodies to the "active component" are not yet available.

At the end of my published article mentioned above [1] reference to a similar mechanism in Human Immunodeficiency Virus (HIV) is expressed. Of course the mechanism of HIV infection is completely different to rabies virus infections. However, recent experiments carried out in China under the guidance of Prof. Jean Marie Andrieu, from the University Laboratory of Saint Pères, Descartes in Paris and the Research Director Louis Wei Lu, from the Institute of Research Development (IRD) in Montpellier, a review has also been published as a document in a French magazine WE DEMAIN, based on an interview with Prof. Andrieu, by Pierre Kaldy [4] The detailed publication of successful protection of vaccinated macaques against Simian Immunodeficiency Virus (SIV) challenge by Wei Lu et al. [5] is reported.

I selected the following experiment in macaques performed in China, at the Institute of Tropical Medicine in Canton. I shall refer only on their positive results with a heat inactivated SIV vaccine.

The monkeys are orally vaccinated along with a large amount of Lactobacillus plantarum.

This latter product is given due to its inhibitory effect on the activity of the lymphocyte T4+. The control SIV monkeys received only the Lactobacillus or the vaccine without the Lactobacillus. Three months after vaccination the monkeys were challenged with high doses of SIV.

Fifteen out of 16 vaccinated survived the challenge and remained healthy, whereas all the controls showed symptoms of SIV infection and some died as a result of the infection. The vaccinated monkeys remained completely sero-negative in SIV test routinely used and resisted infection after repeated infections with different SI viruses. Also 4 of these vaccinated monkeys were intravenously (IV) infected and showed no infection one month later.

In conclusion one may question if the SIV vaccine was completely inactivated. Based on the in vitro control mentioned in the publication, it was indeed. How can it be explained that protection still takes place?

Instead of the above mentioned investigation it is here proposed, due to the results obtained with rabies virus, to perform a similar investigation with the SIV, but towards a component that does not destroy the mechanism of defence but as inactivated product stimulates antibodies against SIV. This component can be applied as a vaccine. Repeated vaccinations can produce high titers and a therapeutic serum can be obtained, which can be used to recover eventually infected monkeys, The development of a SIV vaccine can also be applied for a HIV vaccine. With this possibility one can try to cure HIV patients therapeutically with hyper immune serum.

This concept may be the solution of the worldwide struggle for 30 years to find an effective vaccine.

References

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