

Commissioning Editor Future Medicine

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Dear

Please find attached a manuscript entitled "Genital herpes meets its match: A live HSV-2 ICPO" virus vaccine that succeeds where subunit vaccines have failed," which I wish to have considered for publication in Future Virology as a Perspectives article.

I have submitted the necessary forms to have the manuscript published as (1) an Open-Access article, (2) on an Accelerated Publication timeline, and (3) with eight colour figures. At your earliest convenience, please provide me with a sense of the approximate publication costs for this article per these services, as this was not clear to me based on materials provided on the Future Medicine online submission website.

It is my understanding based on the Future Medicine Guidelines that "Perspectives" articles have the same basic structure and length as review articles, but the author is afforded the opportunity to present criticism, address controversy, and a personal angle on a significant issue. I believe the attached manuscript conforms perfectly with these guidelines. A very important issue is addressed; namely, the change-in-course that will be required to deliver an effective live HSV-2 vaccine that is capable of stopping the pandemic spread of genital herpes. In contrast, at least four different herpes vaccine concepts are currently under study that are reiterations of the same HSV-2 subunit vaccine concepts that have been failing since the 1980s.

It is time to break with failing traditions, and try a different approach that should be more effective at preventing the spread of herpetic disease. The contents of this Perspectives article will not be popular with  $\sim\!200$  scientists who are currently recycling the same herpes vaccines concepts that have been failing for decades. I believe that it is time to put the health interests of the  $\sim\!100$  million people who suffer with recurrent genital herpes first. The science here is very simple; genital herpes should be a vaccine-preventable disease, but the only way to achieve that goal will be through the use of a safe and effective live HSV-2 vaccine. This should hardly be surprising, as the live VZV Oka vaccine is similar in principle to a live HSV-2 vaccine, and the VZV Oka vaccine has drastically reduced the global burden of chickenpox and shingles.

The decade of science reviewed and presented in this Perspectives article is solid. That said, it is one of the most unusual articles that I have ever written because it utilizes, for good reasons, an unusual combination of (1) an autobiographical account of the past decade of my research; (2) a retrospective review of the pre-clinical studies of the live HSV-2 *ICPO*<sup>-</sup> virus vaccine; and (3) a forward-looking view of the implications of new, human subjects testing results

of the live HSV-2 *ICPO*<sup>-</sup> virus vaccine. The latter aspect of the article is critical, because scientists dismiss the results of HSV-2 vaccine-challenge studies in mice and guinea pigs despite the evidence that these are excellent models when used, and controlled, properly.

It is my hope that by addressing all counterarguments in this Perspectives article that I may begin to break this stalemate, and send a simple message to the research community: over 1 million people per week are newly infected with HSV-1 or HSV-2 and it would be, given the evidence presented herein, unethical to spend another decade pondering whether or not we should explore the potential of a live HSV-2 vaccine to eradicate herpes.

I have attempted to comply with Future Medicine's instructions to provide a blinded copy of the manuscript for review. However, please be advised that you will be unlikely to find a reviewer who would not deduce within a matter of minutes that William Halford is the author of this Perspectives article. I am the only researcher in the world who has published on HSV-2 *ICPO* mutant viruses or their use as a herpes vaccine. So, I have provided a "blinded copy for review," but I find it unlikely that you will receive any reviews that are truly blind.

I have provided the names of three potential reviewers who are knowledgeable about herpes immunology and/or herpes virology, but who are not vested in the development of HSV-2 vaccines. If you would prefer a longer list of reviewers with other expertise, I would be happy to recommend other potential reviewers. If there is any matter you wish to discuss by telephone, I will be happy to call. If there is any further information that will assist you or the reviewers in evaluating this manuscript, please do not hesitate to ask.

Sincerely yours,

William P. Halford, Ph.D