

Point-by-point Response to the Reviewers' comments

Reviewers' comments are in small black italics

Our responses are in blue normal text.

Reviewer 1

Comment R1.1: Broader considerations: You may choose to broaden the taxonomic detail of the virus groups by including the most recent ICTV publication relative to the virus family you discuss.

We are not sure to fully understand what the reviewer means but we have added details of the taxonomy of the viruses we cite, when necessary (including genera and families). In general, after mentioning the genus and the family (according to the current taxonomy status), we have maintained the vernacular names and corresponding acronyms of the virus as they were used in the original cited publications, for clarity for readers.

Comment R1.2: In section 3 and 4, perhaps the authors would consider separating the two examples: Potyvirus and Caulimovirus (for example) into two more encompassing sections. This would allow the reader to see the whole process in parallel for two viruses. Providing exemplary figures for this would be even better, but not entirely necessary.

We have willingly entangled the presentation of what is known for the HCs of potyviruses and caulimoviruses for the following reasons. i) It better reflects the history of parallel discoveries in the two viral groups; ii) it illustrates the sequence of mutually inspiring discoveries in the two groups; iii) because the mode of action of HCs is so similar for both, we found more logical to subsection by functional steps rather than by taxonomic groups. In brief, while the proposition by Reviewer 1 is entirely conceivable, our proposition is as well, and we simply made this choice and would like to keep it this way.

Comment R1.3: I think that you start your conclusions section a little early. I would consider putting the sections within your conclusion as sections in the main text. Perhaps under a "Hypotheses in HC" heading.

We have modified the title of section 5, from "5-Conclusion" to "5-New perspectives and prospects" and simply added the section title "6-Conclusion" to the last paragraph of the review.

Comment R1.4: You use "thus" and "very" a lot, most often inappropriately in this scientific context. I would remove this from the manuscript to streamline it.

The text has been amended and most "very" and "thus" have been deleted, except for rare ones that really make sense. It is true that most of them did not.

Comment R1.5: Your reference system seems to include an additional name in each case. Could this be restricted to the last name of the first author (or two in the case of less than 3 authors) followed by et al. and the year?

We have now used the reference format provided by PCJ for Zotero

Comment R1.6: Take care for grammar throughout

We have revised the grammar all through the text, and we hope it is now all fixed.

Reviewer 2

Comment R2.1: The sentence in lines 445/446 suggests that Figure 2 will present the new elements that are incompatible with the theory commonly accepted so far but it does not really do that: the form of the figure, with unnecessarily large and/or numerous cell ultrastructures drawing attention and important proteins being small and represented by squiggles confuses the message which is very well explained in the text of the manuscript. I suggest that either this Figure 2 be thoroughly modified and simplified or deleted.

Figure 2 has been modified to reduce the size of the organelles and their number and to enlarge the viral proteins at the top and legend; colors have also been adjusted. In addition, a following sentence in the next paragraph now specifically indicate were in Figure 2b the classical HC mode of action is questioned. With these modifications, we would like to maintain Figure 2.

Comment R2.2: Ligne 470: An additional (small) sentence to introduce the role of the U4 segment in the text would be appreciated. As it stands, the reader needs to consult the references to get the point.

The sentence “In fact U4 is completely dispensable for infection and aphid-transmission under laboratory condition.” Has been added for clarification.

Comment R2.3: §5.2: I do not understand why the authors limit themselves to proposing persistence of the virus in the lumen. Is there any experimental evidence that the virus is not internalised via a direct interaction with the capsid and that the NSP only intervenes later in the virus circuit through the vector, in the salivary glands for example?

Yes, this evidence exists. In the paper by Di Mattia et al 2020 (J. Virol.) we have shown that the virus is not internalized in midgut cells in the absence of NSP.

Reviewer 2 Typos:

L99: inappropriate format of the bibliographic reference (placement of brackets).

Fixed due to reformatting with the PCJ Zotero style.

Fig1: Change “Aceostyle” to “Acrostyle”

Fixed

Check references throughout the manuscript.

Fixed due to reformatting with the PCJ Zotero style.

L379 – L383: Add the reference Lu et al. 2019 in the text.

Inserted

L 506 : change e.i. into i.e. (?)

Fixed