

The authors are grateful for your careful reading and comments on our manuscript. Here are the answers to the reviewer's questions and comments. Thank you very much for taking the time to review this manuscript. Please find the detailed responses below and the corresponding revisions/corrections highlighted/in track changes in the re-submitted files.

Answer to Reviewer 3

Comment 1

The authors merely refer to literature results, without critical evaluation and selection, and therefore do not provide the reader with balanced view of the field and where it is going, in terms of the impact and significance of the numerous contrast agents reported.

Answer

Thank you for the precise comment. We added a few sentences in the introduction to give you overall images of where this review is going and added our personal comments about these researches as possible.

Comment 2

A thorough language editing by a native English-speaking person should be done.

Answer

Thank you for the suggestion. We actually used the English collection service. We made some corrections. We are sorry for the inconvenience in reading our manuscript.

Comment 3

The title of the manuscript is inappropriate because nucleic acid is quite a broad concept and encompass lots of species but in the review only talked about triplex-forming oligonucleotides and peptide nucleic acid. To provide a succinct title would make the manuscript spread among potential readers.

Answer

Thank you for your rightful suggestions. We changed the titles. The new title is "Recent Advancements in Development and Therapeutic Applications of Genome-Targeting Triplex Forming Oligonucleotides and Peptide Nucleic Acids".

Comment 4

In the 2.2.1.1, the author discussed several exsamples with artificial nucleobases but majority

of the word are to describe others' work without further analysis and discussion. Some generality between the examples were welcome to be presented in each type of motifs.

Answer

Thank you for your comment. All the nucleobases were basically designed to form multiple hydrogen bonds at Hoogsteen face, however, several unknown factors are involved in their selectivity and affinity, so generalization of these motifs was not easy. We are sorry for the inconvenience.

Comment 5

Is there any research using the PNA as skeleton to form the triplex?

Answer

To the best of my knowledge, the triplex formation of PNA ended up with partial or complete invasion of the target DNA duplex. There is one crystallographic structure of PNA triplex (ID: 1PNN) however, it is PNA·DNA:PNA triplex.

Comment 6

Therapeutic application part is too short.

Answer

We wanted to add more information in this field. However, the number of recent reports about TFO in the therapeutic context is still limited. Instead, we added more detailed information about Roger's work in section 2.3. We hope the number of research will expand in the future as the advancement in the development of artificial TFO and PNA.

Comment 7

Comments on the Quality of English Language

Minor editing of English language required

Answer

Thank you for the suggestion. We actually used the English collection service. We made some corrections. We are sorry for the inconvenience in reading our manuscript.