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Perspective

Final title: Current issues with antibody-conjugated lipid nanoparticles

Title at submission: Current issues with antibody-conjugated lipid nanoparticles: A perspective

Submission date: 28 Oct 2024 Revised submission: 2 Feb 2025

Accepted: 5 Feb 2025

Reviewer B: Sarwar Alam, ORCID: 0000-0001-9627-3617

1. Comment Accept submission

Response Thank you very much recommending acceptance.

Reviewer F: Md. Fakhrul Islam Khaled, ORCID: 0000-0002-1003-6598

1. Comment Areas for improvement or clarifications:

1. Immunogenicity concerns:

The discussion on self-epitopes created by antibody fragments could benefit from elaboration on specific mechanisms. For example, how does the absence of an Fc domain exacerbate these risks? Providing a clearer mechanistic link would enhance scientific rigor.

Response Thank you for the concern. The mechanistic link has been summarised at line 44 (highlighted).

2. **Comment** 2. Comparison of tumor localization:

The write-up mentions that acLNPs may not significantly improve tumor localization compared to non-targeted LNPs. This is an important insight, but further clarification on why this is the case (e.g., systemic distribution challenges, off-target effects) would strengthen the argument.

Response

Thank you for pointing this out. The argument has further been clarified at line 56 (highlighted).

3. **Comment** 3. Optimization challenges:

Although the need for optimization of physicochemical properties like size and charge is mentioned, specific examples of what parameters have been successfully optimized in similar studies could make this discussion more actionable.

Response

Thank you for mentioning this. The parameters have been discussed at line 63 (highlighted).

4. Comment

4. Potential solutions:

While the challenges are well-articulated, the conclusion could briefly propose potential strategies to overcome these limitations (e.g., use of alternative targeting ligands, dual delivery systems, or novel conjugation techniques).

Response

Thank you for the correction. Potential strategies have now been mentioned at line 82 (highlighted).

Editor: M Mostafa Zaman, ORCID: 0000-0002-1736-1342

1. **Comment** Replace the highlights with "Key Message". This should be a descriptive statement of the message of the article not exceeding 50 words. This is due to a recent change in the Journal's style.

Response Noted. The highlights title has been replaced at line 15.