Targeting cells of the HIV latent reservoir with antibody-conjugated nanocapsules

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Background:
A major barrier to an HIV cure is the latent viral reservoir, which persists for the lifetime of the host and can reactivate to cause infection. This reservoir involves multiple cell types, including CD4+ T cells and macrophages, that are located in multiple organs/tissues throughout the body. Thus, any treatment or cure strategy aimed at the latent reservoir will require specific strategies to direct them to the target cells. To address this, we aim to target nanocapsules (capable of carrying RNA therapeutics) to CD4+ cells and macrophages by antibody coupling.

Methods:
Four CD4+ T cell and two macrophage surface receptors were assess as targets. Antibodies to these receptors were tagged with azide groups and reacted with dibenzocyclooctyne-tagged fluorescent polymer nanocapsules via copper-free click chemistry. The antibody-tagged nanocapsules were added to peripheral blood mononuclear cells (PBMCs) or monocyte-derived macrophages (MDMs) from healthy donors and analysed by flow cytometry.

Results:
Increased uptake of all antibody-conjugated nanocapsules was observed compared to unconjugated nanocapsules: up to 12 times in MDMs and between 6 and 20 times in CD4+ cells. One of the four CD4+ T cell targeting antibodies showed the greatest potential, as it increased uptake in CD4+ cells two times more than CD4- cells.

Conclusion:
These preliminary results show that targeting with antibodies increases binding of nanocapsules to CD4+ cells and macrophages, as well as reduces unspecific delivery. This will be highly effective in delivering RNA therapeutics via antibody-targeted nanocapsules as an HIV cure block and lock strategy for maintaining HIV latency.

Disclosure of Interest Statement:
All authors report no conflict of interest.