Webinar series: Cell and gene therapy for HIV cure: Platforms, progress and practical considerations

Towards an HIV Cure: Industry Collaboration Group

Webinar 2: Delivery platforms and enabling technologies for gene and cell therapies

The second webinar shifted from conceptual therapeutic strategies (discussed in Webinar 1) toward the technologies required to deliver them effectively, particularly mRNA and lipid nanoparticle (LNP) systems, and translational pathways.

The session highlighted how advances from vaccine development, gene therapy, and regenerative medicine can be leveraged for HIV cure strategies.

1. mRNA–Lipid Nanoparticle Platforms for Gene Delivery

Ying Tam presented advances in lipid nanoparticle (LNP) technology, a delivery system that has rapidly matured due to its use in mRNA vaccines. The talk focused on how these platforms could enable gene-editing and therapeutic delivery strategies for HIV cure research.

LNPs as a versatile delivery technology

- Enable delivery of mRNA, CRISPR components, and other nucleic acids.
- Rapidly programmable and adaptable across disease areas.
- Manufacturing pipelines now well established due to vaccine development.
- Possibility to manufacture thermostable LNP ready to mix wit cargo.

Advantages for gene therapy

- Avoids permanent viral vector integration.
- Allows transient gene expression when appropriate.
- Potential for repeat dosing.

Challenges

- Targeting specific tissues or cell types (e.g., CD4+ T cells).
- Efficient delivery to reservoir sites such as lymph nodes or gut tissue.
- Persistent editing
- Balancing delivery efficiency with safety.

Key takeaway:

LNP platforms could become a foundational delivery engine for HIV gene therapies, but improvements in cell-specific targeting remain essential.

2. Translating mRNA Platforms into Gene Therapy Applications

Edward Kreider discussed how mRNA–LNP technology is transitioning from vaccines to therapeutic gene delivery, including applications relevant to HIV cure research.

Platform versatility

- The same technology used in vaccines can support:
    - Gene replacement
    - Gene editing
    - Immune modulation.

Accelerated development

- Vaccine success demonstrated:
    - Rapid design cycles
    - Scalable manufacturing
    - Clinical feasibility.

Potential HIV applications

- Delivery of CRISPR gene-editing systems.
- Engineering immune cells in vivo.
- Therapeutic protein expression.

Remaining challenges

- Tissue-specific delivery.
- Duration of expression.
- Route of administration that impacts biodistribution
- Regulatory pathways for complex therapies.

Key takeaway:

The mRNA–LNP ecosystem now provides a scalable infrastructure that could accelerate HIV gene therapy development.

3. mRNA Platforms for Shock-and-Kill Strategies

Paula Cevaal presented work using mRNA and LNP technologies to activate latent HIV reservoirs, a key step in the shock-and-kill cure strategy.

The challenge of latency

- HIV reservoirs remain invisible to the immune system under ART.
- Latency reversal is required to expose infected cells.

mRNA technology as a latency reversal tool

- mRNA can encode proteins designed to activate latent virus.
- LNP delivery allows targeted expression.

Advantages

- Highly programmable platform.
- Potentially safer than systemic small-molecule LRAs.
- Can be combined with immune therapies or CAR T cells.

Challenges

- Ensuring sufficient activation of latent cells.
- Avoiding systemic inflammation.
- Integration with downstream “kill” strategies.

Key takeaway:

mRNA technology could enable more precise latency reversal, creating opportunities to combine with immune-based therapies.

4. Regenerative Medicine and Extracellular Vesicle Platforms

Aijun Wang discussed approaches emerging from regenerative medicine, including the use of stem cells and extracellular vesicles, as potential therapeutic tools.

Stem-cell based therapeutic platforms

- Stem cells can serve as both:
    - Therapeutic agents
    - Production systems for therapeutic molecules.

Extracellular vesicles (EVs)

- Natural biological delivery vehicles.
- Can transport proteins, RNA, and signaling molecules between cells.
- Potential to deliver therapeutic cargo with lower immunogenicity.

Applications relevant to HIV

- Targeted delivery of gene-editing tools.
- Immune modulation.

- Regenerative approaches to repair immune damage.

Key takeaway:
Biological delivery systems such as extracellular vesicles may complement synthetic delivery platforms and provide more targeted or biologically compatible delivery mechanisms.

Conclusion

Various delivery strategies are available and could support the development of an effective HIV cure. Delivery mode will be key and more research is needed to ensure that methods are manufacturable at scale and suitable for use in low- and middle-income countries.