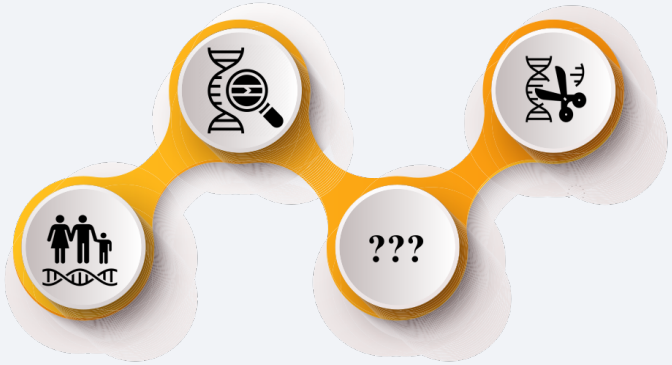
Presentation on

Nucleic acid therapeutics based on biotechnology

Course Code: BMB553



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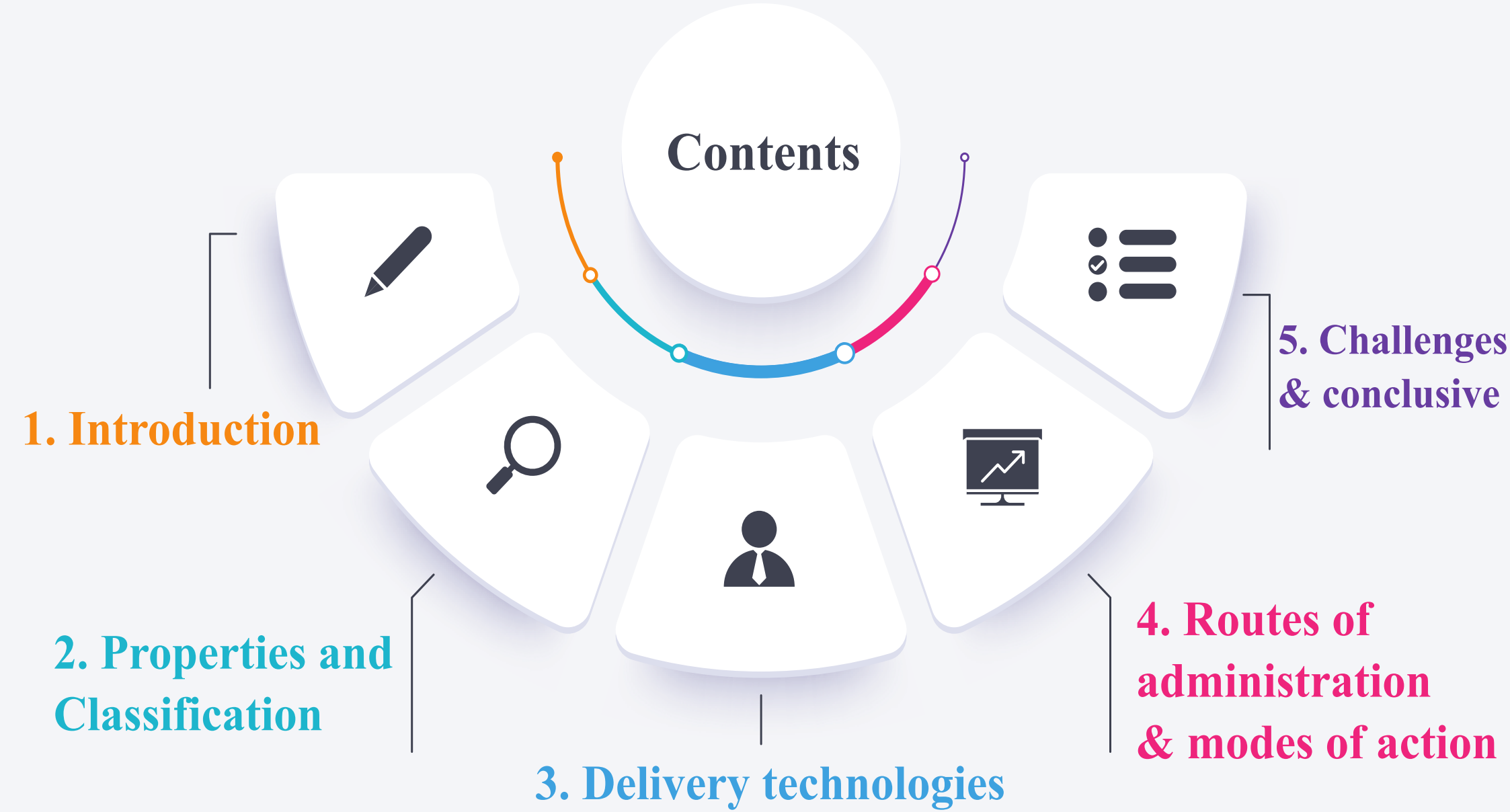
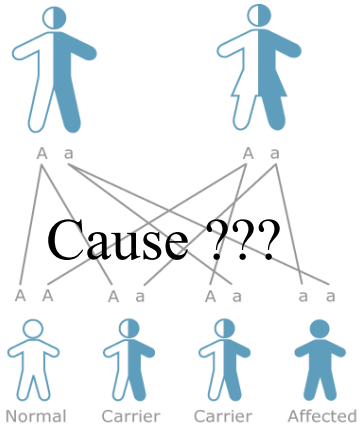
Nucleic acid therapeutics based on biotechnology



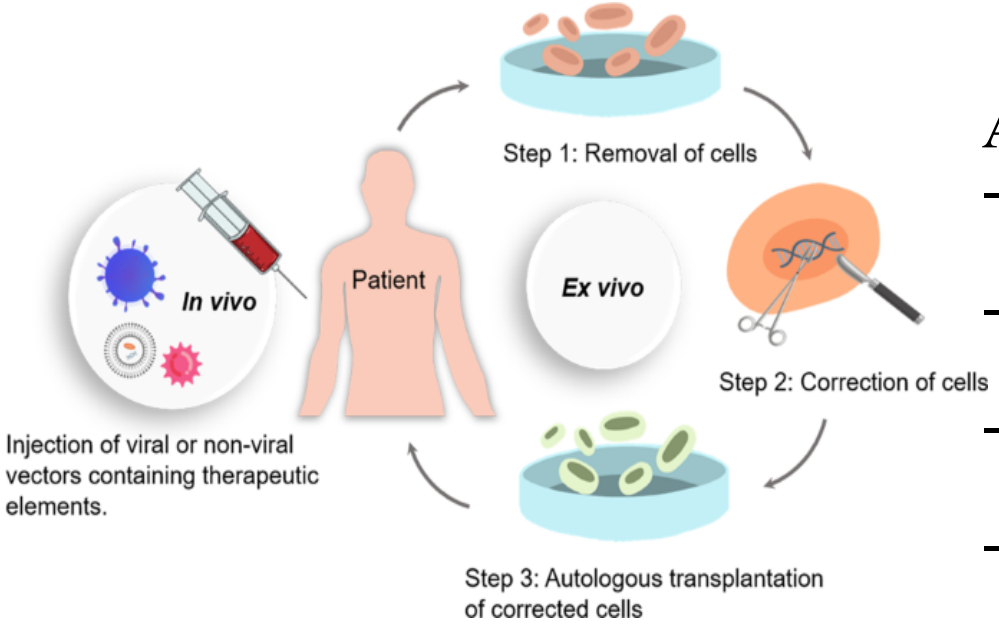
Introduction

Half a century ago;

- **Friedmann** and **Roblin** conceptualilzed that, (**dysfunctional gene products**) are cause of inherited disorders
- It could be treated by introducing a **functional gene copy.**



Inherited disorder



And today;

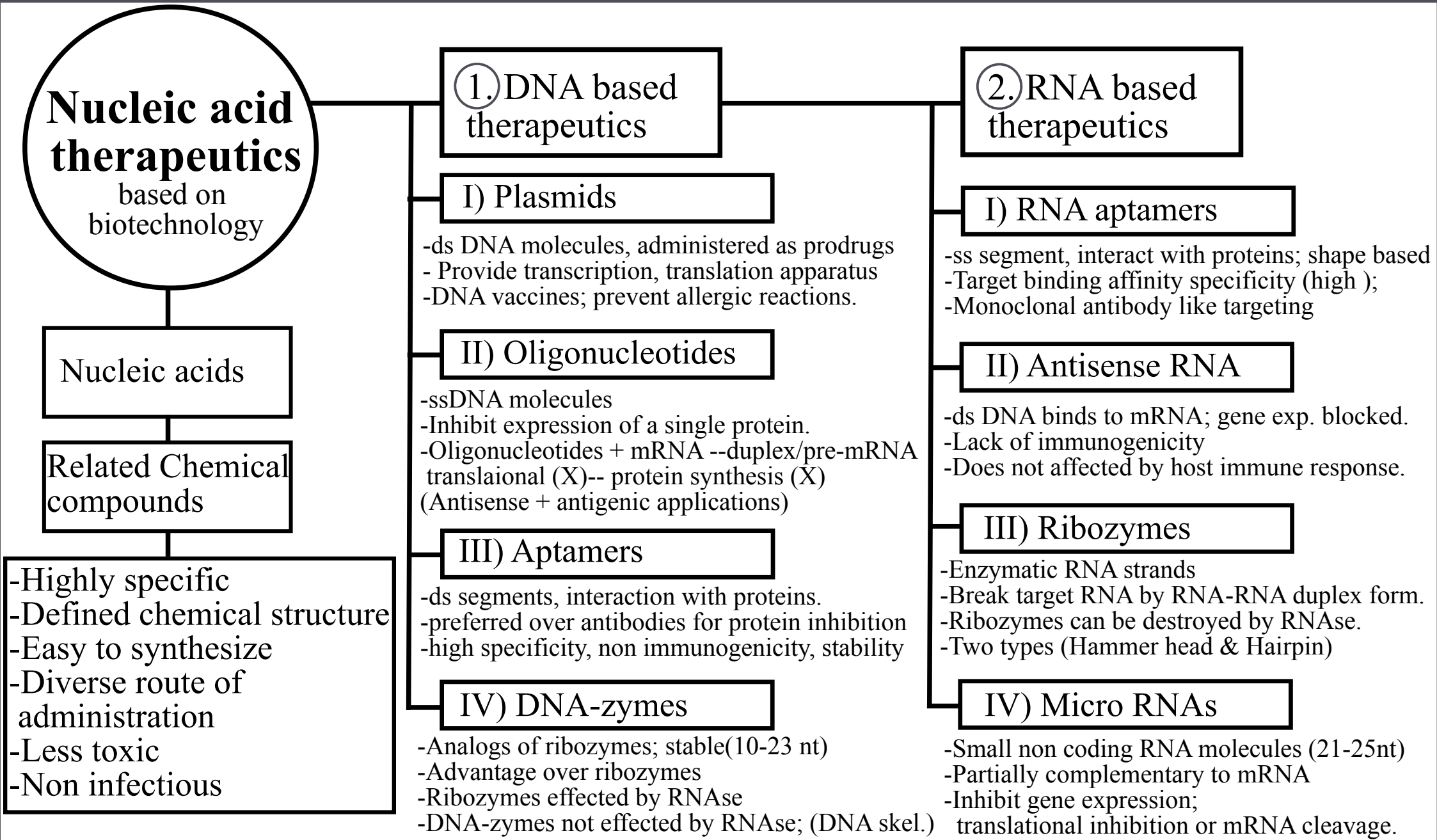
- **COVID-19** is being treated by **nucleic acid therapeutics.**
- Conventional drugs targeting **proteins.**
- Whereas, genetic drugs modulate **gene expression.**
- And giving long term therapeutic effects/cure.

Four platforms based on biotechnologies:

1. **ASOs**; chemically modified antisense oligonucleotides (ASOs)
2. **GalNAc-siRNA**; acetylgalactosamine (GalNAc) ligand-modified short interfering RNA (siRNA) conjugates,
3. **LNPs**; lipid nanoparticles (LNPs),
4. **AAV**; adeno-associated virus (AAV) vectors

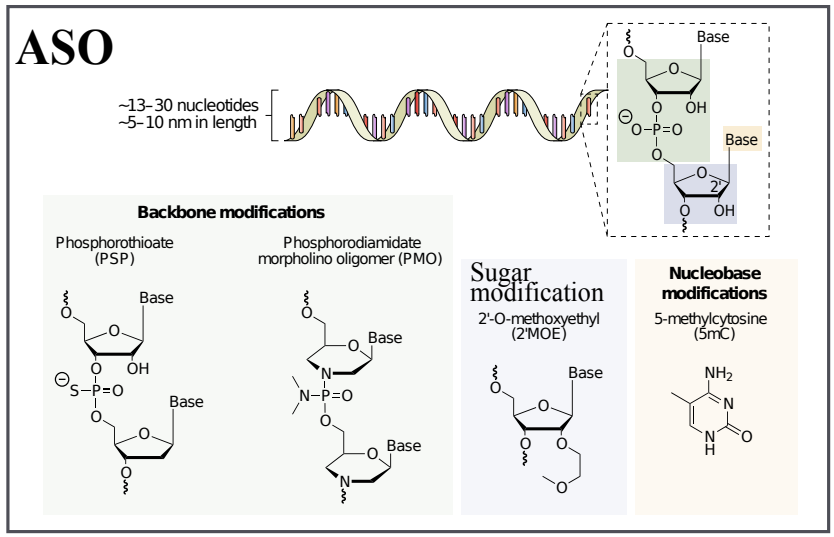
Li, H., Yang, Y., Hong, W. et al. Applications of genome editing technology in the targeted therapy of human diseases: mechanisms, advances and prospects. Sig Transduct Target Ther 5, 1 (**2020**). https://doi.org/10.1038/s41392-019-0089-y

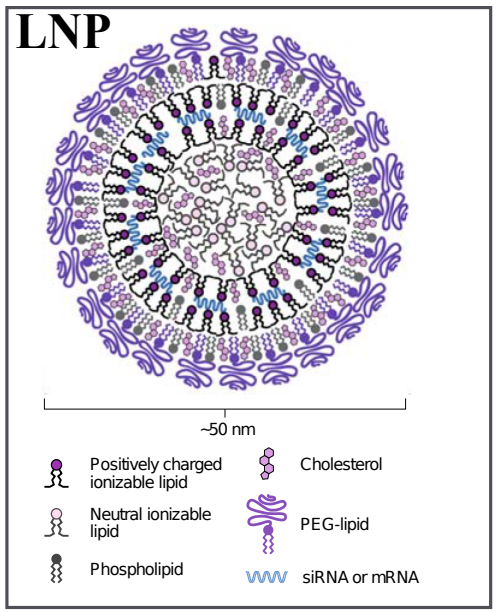
Properties and Classification

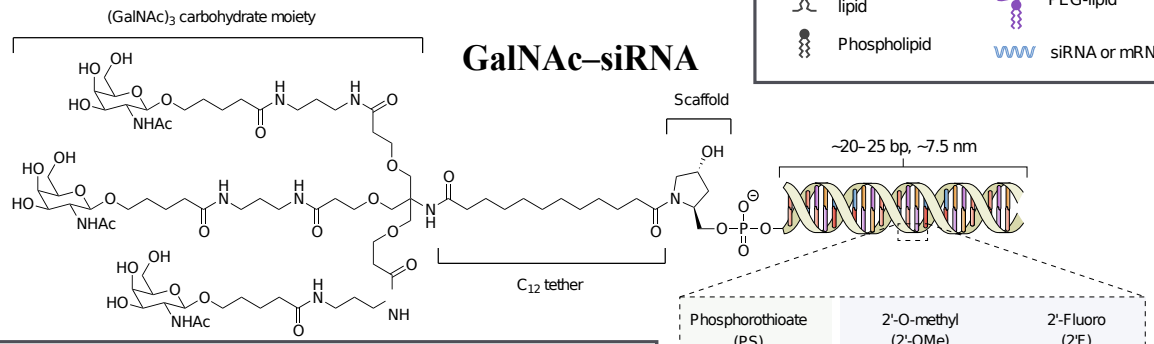


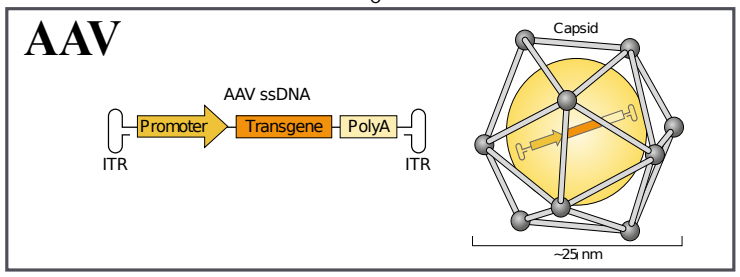
Source: Sridharan K, Gogtay NJ. Therapeutic nucleic acids: current clinical status. Br J Clin Pharmacol. **2016**;82(3):659-672. doi:10.1111/bcp.12987

Delivery technologies









ASOs

- Improve nuclease resistance
- alter circulation characteristics
- modulate immunological properties

LNP containing **GalNAc–siRNA**

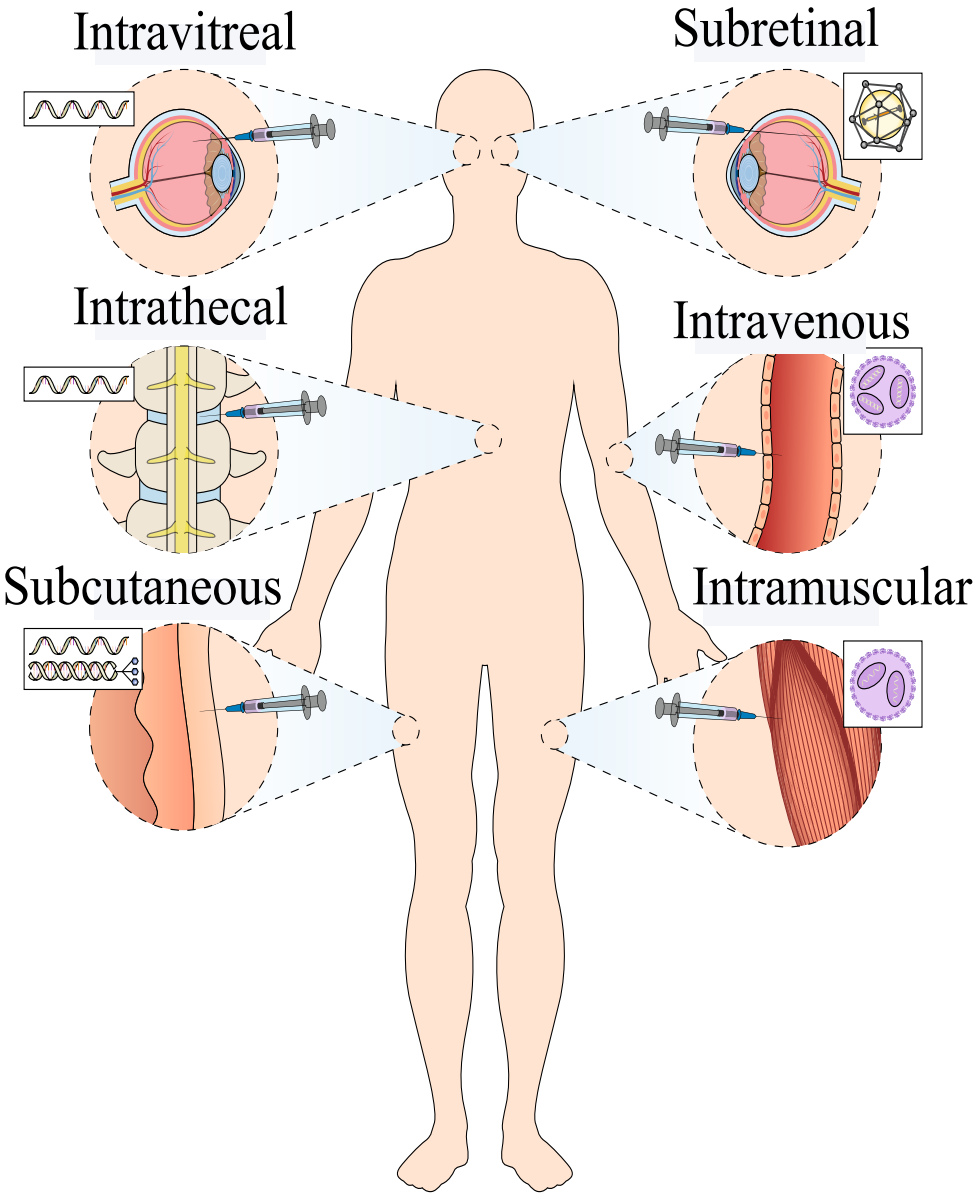
- Terminal **GalNAc** covalently linked to **siRNA**
- The **(GalNAc)3** ligand enable **hepatocyte-specific targeting** of **siRNA** via the **asialoglycoprotein** receptor.

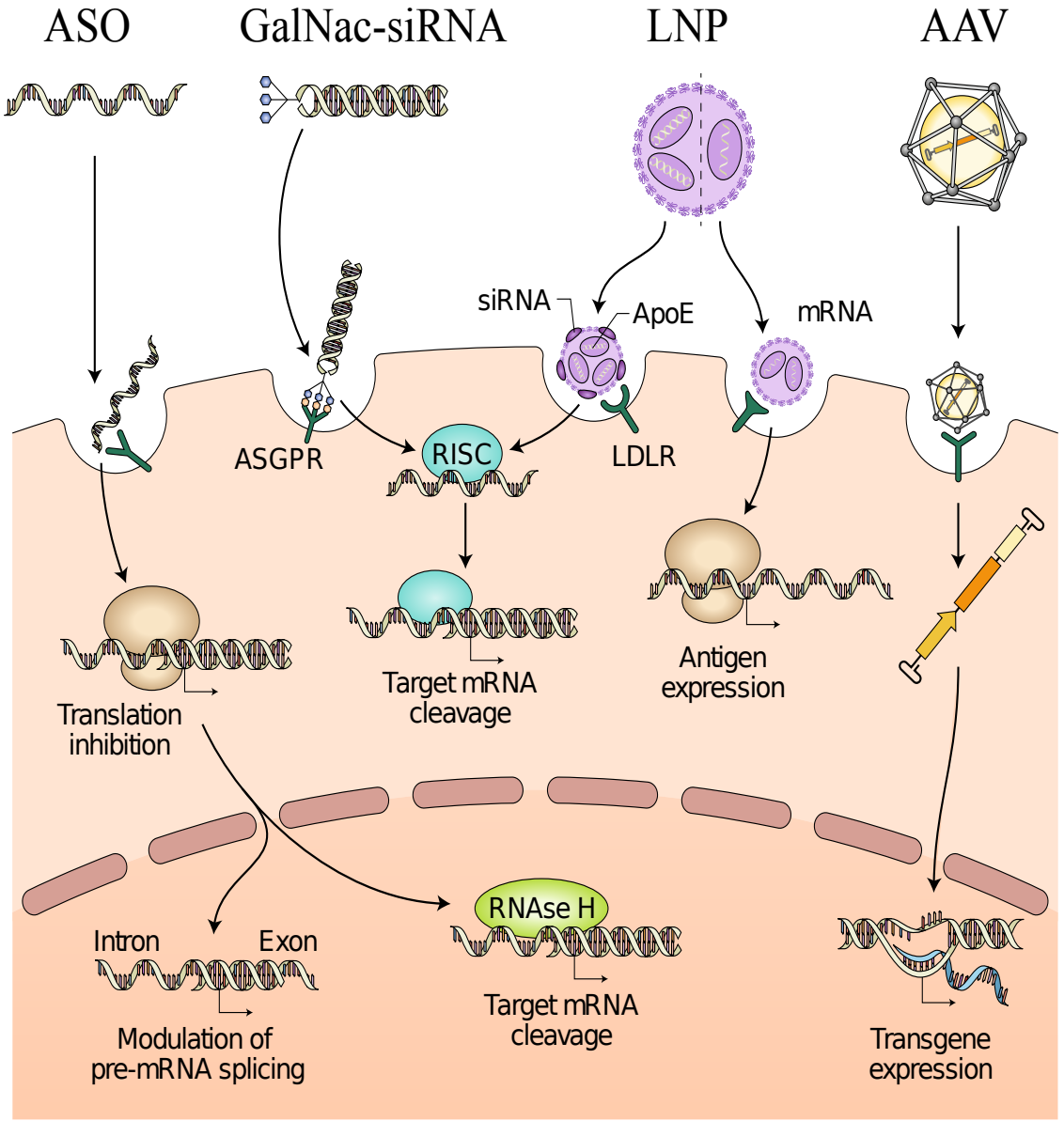
AAV vector

- containing a 4.7-kb ssDNA
- with inverted terminal repeats (ITR)

Kulkarni, J.A., Witzigmann, D., Thomson, S.B. et al. The current landscape of nucleic acid therapeutics. Nat. Nanotechnol. 16, 630–643 (2021). https://doi.org/10.1038/s41565-021-00898-0

Routes of administration and modes of action





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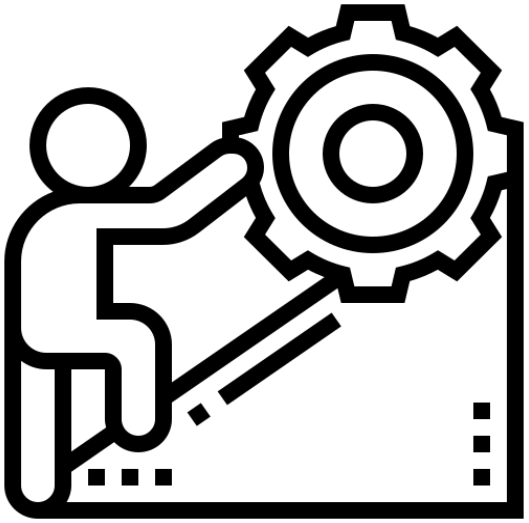
Challenges and Conclusive



Challenges:

- Susceptible to **degradation** by **nucleases**
- Contribute to immune activation
- having unfavourable **physicochemical characteristic** **prevent** facile **transmission** into **cells**
- For safe and effectiveness required **sophisticated delivery platform** technologies

To conclude:

- Transform therapeutics approches from intriguing **theory** into clinical **reality**.
- These therapeutics aim to treat **orphan diseases**,
- Their delivery technologies have **enabled rapid vaccine development** in times of a **pandemic (COVID19).**
- In addition, these emerging therapeutics are **facilitating** the **clinical translation** of novel approaches, such as **gene-editing therapeutics**.
- It is clear that **nucleic acid therapeutics** are poised to have a **revolutionary impact** on many diseases that **previously** had **limited** or no **treatment options.**

Li, H., Yang, Y., Hong, W. et al. Applications of genome editing technology in the targeted therapy of human diseases: mechanisms, advances and prospects. Sig Transduct Target Ther 5, 1 (**2020**). https://doi.org/10.1038/s41392-019-0089-y

Thank you
for your attention