Gene Therapy – Unpacking where we are and where we are going

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Transforming lives with stem cell medicine

The Novo Nordisk Foundation Center for Stem Cell Medicine (reNEW) is supported by a Novo Nordisk Foundation grant number NNF21CC0073729

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Who am I?

- Originally a biomedical scientist (immunology/microbiology)
- Brief foray into secondary school teaching
- Moved into clinical research in 2016, with the Melbourne Children's Trials Centre at MCRI
- Master of Bioethics 2018-2019
- Gene Therapy Trials Readiness Coordinator at MCTC since 2020
- 2023 – began PhD

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Outline

- How are clinical trials of gene therapies regulated?
- What are the regulatory challenges?
- What are the ethical considerations with clinical trials of gene therapies?

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Types of vector-mediated gene therapy

- *Ex vivo*
  - The change in the genetic material occurs outside the patient
  - Delivery of the vector to cells that are outside the patient, then infusing the cells into the patient
- *In vivo*
  - The change in the genetic material occurs inside the patient
  - Direct delivery of the vector into the patient

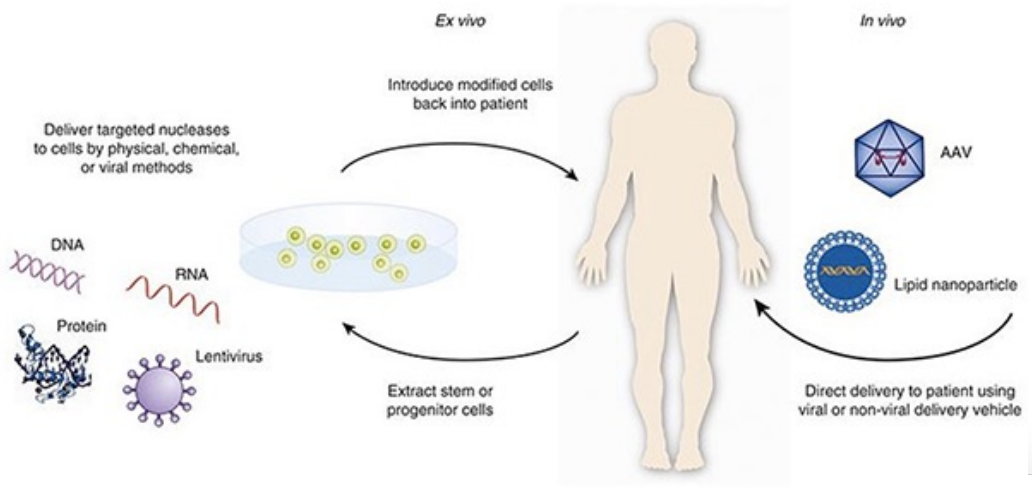

Image credit: FDA, https://www.fda.gov/vaccines-blood-biologics/cellular-gene-therapy-products/what-gene-therapy

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Who is involved in reviewing gene therapy clinical trials?

- Therapeutic Goods Administration (TGA)
- Human Research Ethics Committee (HREC)
- Research Governance Office (RGO)

- Office of the Gene Technology Regulator (OGTR)
- Institutional Biosafety Committee (IBC)

Genetically Modified Organisms (GMOs)

Mythbuster
Not all gene therapy products will need OGTR review.

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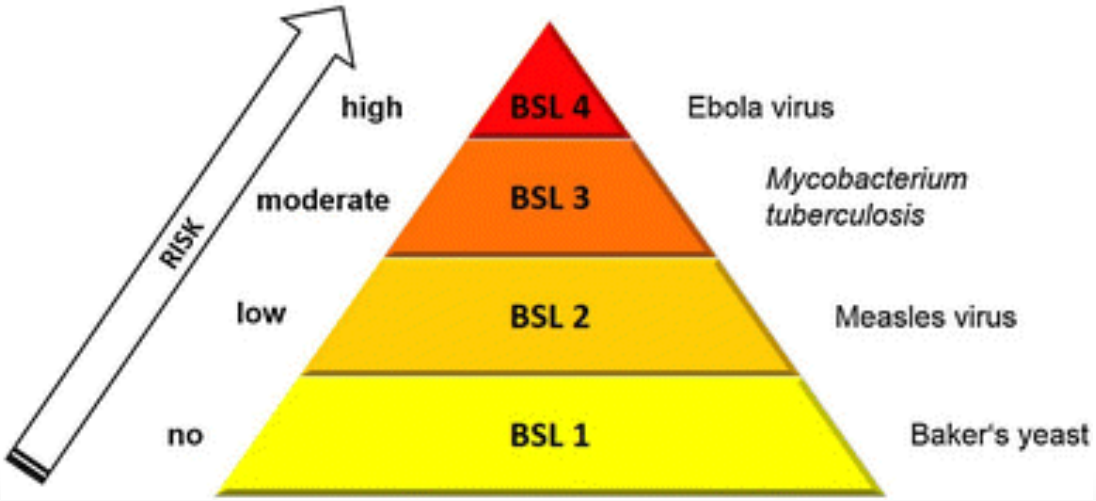
Why regulate GMOs?

- Risk to patients
- Risk to healthcare workers
- Risk to the public



Mythbuster

GMO medicines are not more dangerous than other medicines.

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The challenges of regulation in an emerging field

- Processes may not be fit for purpose
- Need to develop efficiencies
- Oversight
- Regulation cannot keep pace with discovery

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Gene therapy trials – How are they different?

- Gene therapy has the potential to be curative
- Gene therapies can be single doses
- Intense follow-up, especially immediately following dosing
  - In some cases, daily follow-up is required for a week, and participants may have to stay near the hospital for around a month following dosing
  - Need for life-long monitoring

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Ethical considerations – impact of the therapy

- Limited human data to use for prediction
- Being given a gene therapy may exclude you from future therapy
  - Exposure to viral vector may produce an immune response that means future gene therapy would not be possible
  - Effect of gene therapy given in trial may exclude participants from future gene therapy trials
- Permanent change in the body

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Ethical considerations – patient expectations and consent

- Decision making with so many unknowns is difficult
- Explaining gene and cell therapy is hard
- Hype in the media and battling misconceptions
- Pressures around the time available to make a decision about these therapies

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Ethical considerations – design of clinical trials

- Are placebos and randomisation appropriate?
- Burden on participants and their families
- How do we decide who gets to be involved?
- Can we do this in children?
- Are the trial results translatable to the population?

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Additional considerations – Systems, processes and regulation

- Is the system perpetuating or exacerbating existing inequalities?
- Can the system deal with the amount of unknowns? How?
- If these therapies work, how do we make them available? Can our healthcare system do this?
- Sustainability – How do we pay for it? How do we decide what and who to pay for?

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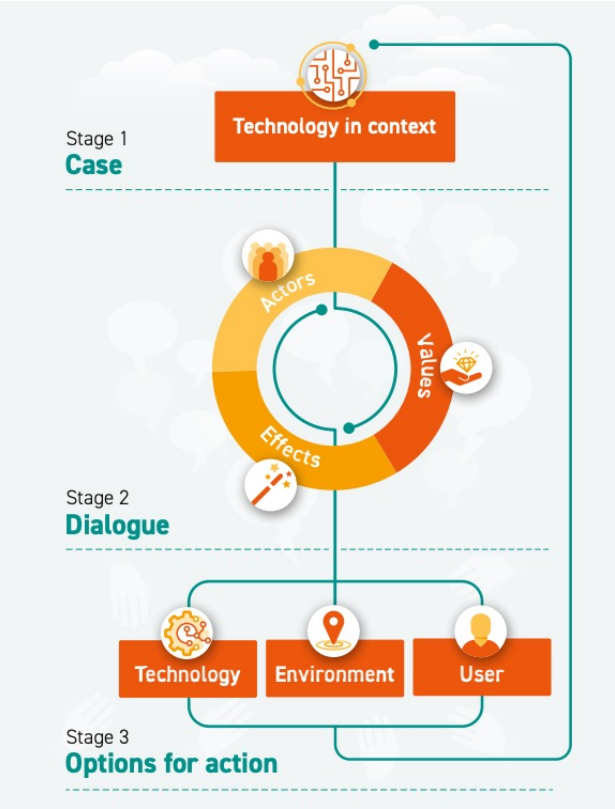
Where to next?

- This is where PREPARE comes in.
  - Multidisciplinary team: ethicists, sociologists, anthropologists, economists, regulatory experts.
  - Exploring questions of how we can make the world ready for these therapies.

- My work looks at how we can support the system that is making decisions about these medicines, the funding of them, and the implementation strategy, in a way that is socially responsible, robust and sustainable.
  - Exploring a “Guidance Ethics Approach” for advanced therapies



Verbeek, P., & Tijink, D. (2020). *Guidance Ethics Approach*. ECP | Platform voor de InformatieSamenleving. https://ecp.nl/publicatie/guidance-ethics-approach/

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Be PREPAREd, not alarmed

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