Biotechnology and the Emergence of New Therapeutics

Part 1: What does it take to make a drug? Vini Mani

Part II: Current methods in drug discovery Kat Pak

Part III: Emerging classes of therapeutics Dima Ter-Ovanesyan
What’s next?

Moving beyond small molecules and proteins:

• Gene Therapy: DNA-based therapeutics

• RNA interference (RNAi): RNA-based therapeutics
What’s next?

Moving beyond small molecules and proteins:

• **Gene Therapy**: DNA-based therapeutics

• **RNA interference (RNAi)**: RNA-based therapeutics
Central Dogma of Molecular Biology

DNA → RNA → Protein
Mutation - change in DNA
Adrenoleukodystrophy (ALD)

**ABCD1 Gene**

**ABCD1 RNA**

**ABCD1 Protein**
Accumulation of Toxic Fat Molecules in ALD

Very Long Chain Fatty Acids (VLCFA)

Inactive ABCD1

Accumulation of VLCFAs

Toxic to Brain
Brain cells need myelin

Normal brain cell (neuron) surrounded by myelin
Adrenoleukodystrophy (ALD) patients lose myelin.

Normal brain cell surrounded by myelin.

Demyelination in brain cell of ALD patient.

Cannot send signals.
Taken with permission from Cartier et al., *Science* 2008.
How can we fix this disease?

**Gene Therapy** – Insertion of normal copy of gene (DNA) into patient’s cells so that patient’s cells will produce the normal protein.
Choosing cell type for gene therapy

Blood Stem Cell

Red Blood Cell

Immune Cell

Microglial Cell (Brain)
Put Normal ABCD1 Gene into Blood Stem Cells

Insert normal DNA

Isolate blood stem cell from patient

Inject modified blood stem cells Back into patient
How to get DNA into cell?

Hijack virus to deliver normal ABCD1 gene instead of Viral DNA
Destroy RNA to prevent protein production

TTR Gene

TTR RNA

Guide targeting TTR RNA

RNAi machinery
Interfere with RNA to prevent protein production

TTR Gene

RNAi machinery

guide targeting TTR RNA

TTR RNA

TTR Protein
RNAi delivery

- RNA is quickly degraded in blood
- RNA does not get into cells:
  - Too large

Put siRNA in protective ball
RNAi delivery

• RNA is quickly degraded in blood
• RNA does not get into cells:
  – Too large

Put siRNA in protective ball
Types of Therapeutics

DNA

RNA

Gene Therapy

RNAi

Protein

proteins, small molecules
QUESTIONS?
Thank you!

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