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Nano-rare Patient Colloquium 2025

The “Miracles of Science”

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We are Achieving Two Important Goals

- Create a community for nano-rare patients
- Draw attention to the needs of nano-rare patients and families

n-Lorem Annual Meeting is Fully Integrated

- Patients and families are full partners
- Patients and families must make difficult decisions, and we believe that better decisions are made with knowledge
  - Strengths and limits of ASO technology
  - Unfiltered knowledge about the results observed in the clinic
  - Advances in ASO technology
- The science we do isn’t that complex
  - If you speak English and get rid of a lot of the jargon
- But we are all ears: if you have suggestions to improve our meetings, don’t hesitate to let us know

The Focus of This Meeting: Share the Many Important Lessons We are Learning

- These lessons teach us about nano-rare patients
- More broadly, they teach us about health and disease writ large
- Drive a next revolution in medicine

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My Goal for This Presentation: To Put What We Are Doing in a Much Broader Context

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Humans Are Curious By Nature

- There have always been humans who were more curious than the average
- The organized practice of curiosity is called Science and the humans who practice curiosity as an avocation are called scientists
  - But they are just curious humans

Miracles of Science

- Not like fairy tale miracles
- Created by human beings for human beings
- Often centuries in the making
  - Generations of advances over decades to centuries
  - Breakthroughs reflect the power of knowledge that accumulates over time

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The Miracles of Genomics

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The Miracles of Genomics

- How is information transferred from parents to progeny?
- Gregor Mendel and his peas, 1866
  - The rules of genetic information transfer

How is information transferred from parents to progeny?

Gregor Mendel and his peas, 1866

The rules of genetic information transfer

What is the gene made of?

Many possible candidates for genes considered

DNA was thought to be a boring carbohydrate like starch

The invention of x-ray crystallography

The Breakthrough:
Watson and Crick, 1954: The Structure of DNA

- How genetic information is stored and used

The Whole Genome Sequencing Effort

- How genetic information is stored and used
- Decades of work
- The human genome project 1990-2003

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The Miracles of iPSCs

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Humans Have Always Wondered About

- What are we made of and how do we work?
- Why do we get sick and fail?

1590: The Janssens Re-invent the Microscope

- We are made of trillions of tiny little units
  - Let's call them cells
- We are made up of many different types of cells

How Do Cells Work?

Centuries of progress in molecular and cellular biology

How Can We Start as a Single Cell and Become So Many Different Kinds of Cells?

The Miracle of Differentiation

The Breakthrough:
Yamanaka and Takahashi, 2006: iPSCs

Induced Pluripotent Stem Cells (iPSCs)

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The Miracles of the RNA World

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The Miracles of the RNA World

- Cells have another molecule that looks and behaves like DNA, let's call it RNA
- But unlike DNA, RNA seems to be spread throughout the cell
- And RNA seems to come in many sizes and shapes
- What is this stuff? And why does the cell have it? And how does it work?

Decades of Work

- Detailed understanding of the RNA world
- Clear understanding of how RNA is made, processed and used
- Clear understanding of various types of RNA and why they exist and what they do
- Deep understanding of RNA structure and how RNA stores and uses genetic information

The Breakthrough:
Zamecnik and Stephenson, 1978

The Breakthrough: Zamecnik and Stephenson, 1978

- Why don’t we make drugs that use genetic information to bind to RNA?
  - Let’s call it Antisense (ASO) technology
- 1989, Ionis Pharmaceuticals founded to pursue antisense technology
- 2020, n-Lorem founded to use ASO technology to discover, develop, manufacture and provide experimental ASO treatments to nano-rare patients for Free, for Life

The Future is a Product of the Scaffold of Knowledge

Knowledge is power

And

As knowledge accumulates, power multiplies

But

The scaffold of knowledge is fragile

A Next Miracle of Science: A Revolution in Medicine

- No longer focus on the symptoms of diseases
  - Discard archaic, centuries old definitions of disease
- Focus on understanding what are healthy phenotypes and how do we maintain them
- Focus on THE CAUSES of diseases
- Create genetic medicines to address the causes of diseases
- Sequence all newborns at birth
- Initiate treatment much earlier in the course of diseases