
OCTOBER 4, 2010
Environment Special:
The oceans—why 70%
of our planet is in danger
The Facebook Movie:
The secret history of
social networking
TIME
How the
first nine
months
shape
the rest
of your life
The new science
of fetal origins
BY ANNIE MURPHY PAUL
www.time.com

"Personalized Medicine"

Matching the right patient and disease with the right drug or drugs

Personalized Medicine

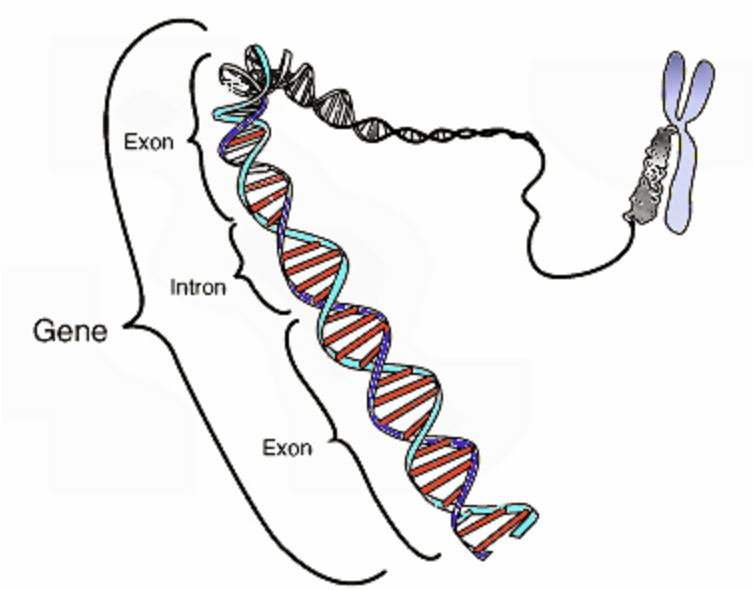
- **“Personalized medicine** is a medical model emphasizing the customization of healthcare, with all decisions and practices being tailored to individual patients. This involves the systematic use of genetic or other information about an individual patient to select or optimize that patient's preventative and therapeutic care.”

Personalized Medicine

- IT Infrastructure
- EMR
- Bioinformatics Core
- Genomic research lab
- Biobank
- Computer Analysis and interpretation
- Money

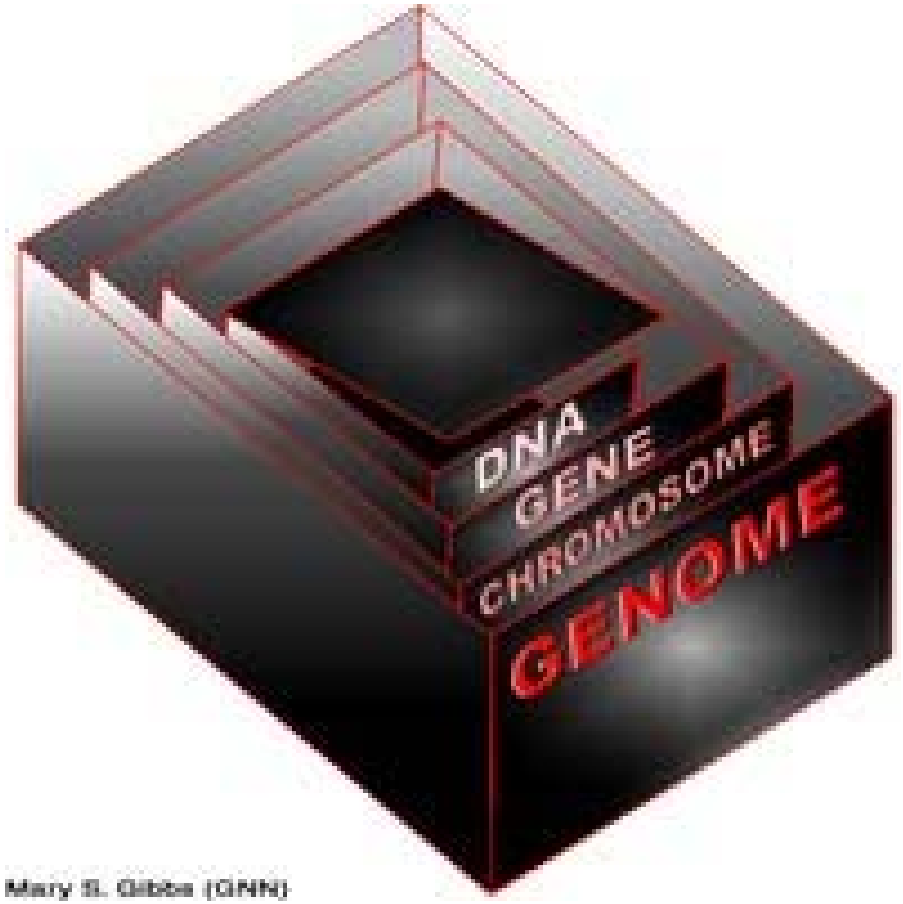
What is a gene?

- A **gene** is a unit of heredity in a living organism. It is a name given to some stretches of DNA and RNA that code for a type of protein or for an RNA chain that has a function in the organism. Living things depend on genes, as they specify all proteins and functional RNA chains.


Exon
Intron
Gene
Exon

What is a Genome?

- A genome is all of a living thing's genetic material. It is the entire set of hereditary instructions for building, running, and maintaining an organism, and passing life on to the next generation.



Mary S. Gibbs (GNN)

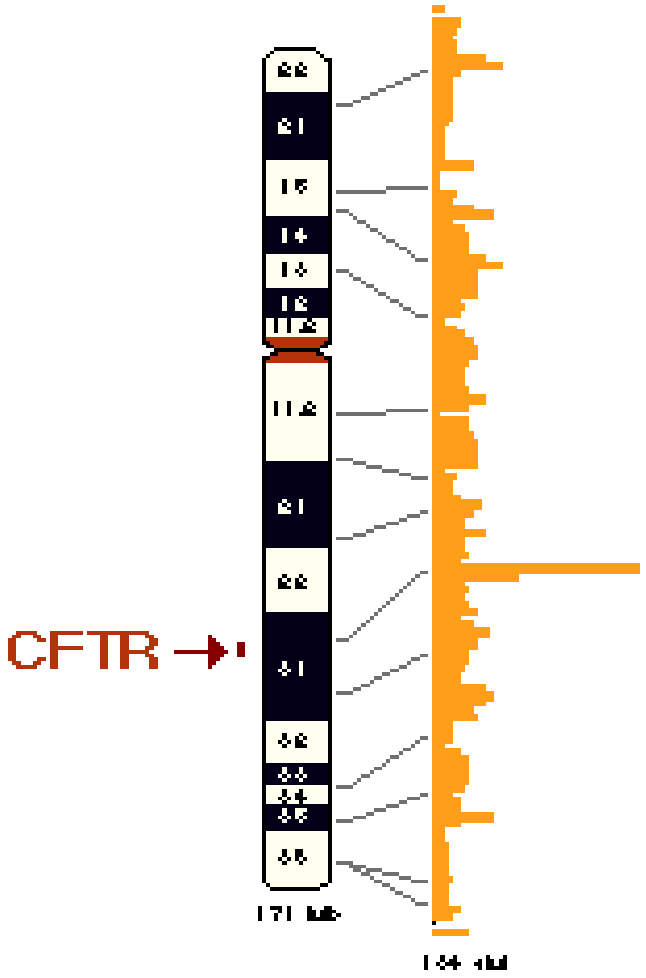
Genome

- Scientists study families affected by a disease, tracing the inheritance of the disease and of specific genome landmarks through several generations. Landmarks that tend to be inherited along with the disease are likely to be located close to the disease gene and become "markers" for the gene in question.

Genome

- Next, they look for genes in that part of the genome and study the genes one by one to learn which one is involved in the disease. For example, they might look for a gene that has a different sequence in people with the disease. Or they might look for a gene with a function that could be related to the disease.

The CFTR gene maps to chromosome 7



Genome

- In the future, researchers hope that more detailed genome maps will help them find genes faster, leading them straight to each gene the way you can look at a road map and determine the sequence of streets that will take you exactly where you want to go.

- Genetics:
- Genomic:
- Proteomics: The proteome is the entire complement of proteins, including the modifications made to a particular set of proteins, produced by an organism or system. This will vary with time and distinct requirements, or stresses, that a cell or organism undergoes.

Genomes behave differently in various environments and circumstances

The Bad

- July 2011—NYT.
- Lung cancer->analyzed the tumor cells looking at gene patterns to determine which drug to use.
- Its gene-based tests proved worthless, and the research behind them was discredited. The woman died-suing Duke University
- Doctors say the heart of the problem is the intricacy of the analyses in this emerging field and the difficulty in finding errors. Even well-respected scientists often “oversee a machine they do not understand and cannot supervise directly”.

Genome study solves twins' mystery condition

- Twins developed a coughing and breathing problem
- She had been diagnosed with a genetic disorder called dopa-responsive dystonia-the dystonia causes abnormal movements
- Symptoms appeared to be getting worse despite treatment

Genome study solves twins' mystery condition

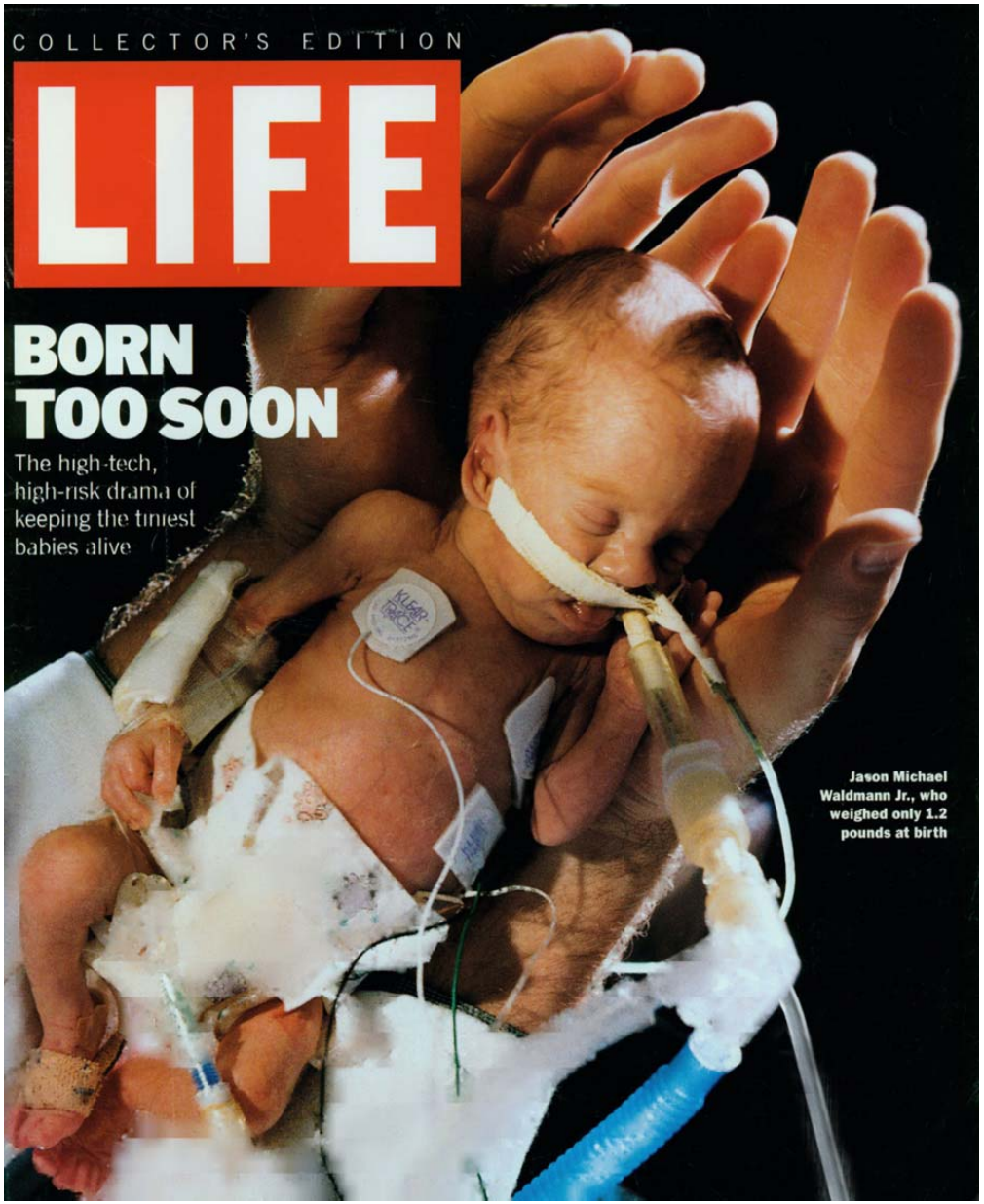
- Father insisted on genomic sequencing
- Discovered that they also carried mutations in the gene called SPR—which was linked to some cases of dopa-resistive dystonia.
- So the study suggested that they might benefit from taking a chemical precursor to the drug they were on—had trouble using the precursors to generate the missing drug
- Added another drug—doing well ever since.

Prematurity has increased 36% in the last 25 years.

1 in 8 of every infant born is premature.

10,440 infants are born prematurely every week in the US.

248 infants are born prematurely in Virginia every week.



Life, May 2000

Prematurity

- Premature- delivery before 37 weeks (40 weeks ---term).

- About 500,000 infants are born preterm each year in the United States.

Prematurity

- Premature delivery accounts for 60-70% of all neonatal morbidity and mortality. Morbidity includes CP, developmental delay, BPD, blindness, and other long term injuries that may have a lifelong impact and consume medical dollars.

- Costs exceed 26 billion per year. The cost for the first year of life for a term infant is approximately $4500.00 and the cost for a premature infant is around $49,000.00. Days in hospital are 2.3 vs 14.2 after delivery.

Prematurity

- Overall the incidence of prematurity is 12-13% of deliveries. In approximately 50% of the cases, the etiology is unknown.

- Prematurity is higher in African Americans (18.4%) vs European Americans (11.7%)-total is around 12-13%. There are multiple potential risk factors-including education, income, physical environment and marital status. Disparities (between ethic groups) possibly related to inadequate utilization of prenatal health care however studies where both groups have equal access, African Americans are still higher.

Prematurity

- Both maternal and paternal ethnicities are contributors: if mother is European American and father is African American--there is still an increase in premature delivery.
- The risk of a second preterm delivery increases by 15% after the first and up to 30% after the second.
- Spontaneous premature birth is a complex interaction of genetics, environment, social and behavioral factors. The pathogenesis is variable (for preterm birth) therefore interventions for prevention of this condition have met with limited success except for possibly cerclage and progesterone.

Prematurity

- Common conditions like preterm birth are generally influenced by multiple genes and the genetics of complex traits do not obey classical Mendelian laws as the impact of these genes is GREATLY influenced by environmental factors.
- There must be consideration of both the maternal, and fetal genetic background, which may independently confer risk of prematurity, or may have synergistic interactions.

Inova Translational Medicine Institute

About the Institute

- **Started in July 2010 with the hiring of Dr. John Niederhuber, former director of the National Cancer Institute**

- **Develop the relationships required to leverage existing Inova resources to accomplish goals, thus minimizing duplication of efforts and costs and decreasing time to operational readiness**

ITMI's Discovery Projects

- **Hypothesis driven research**
  - **Develop researcher driven disease models**
  - **Clinical validation of targets**

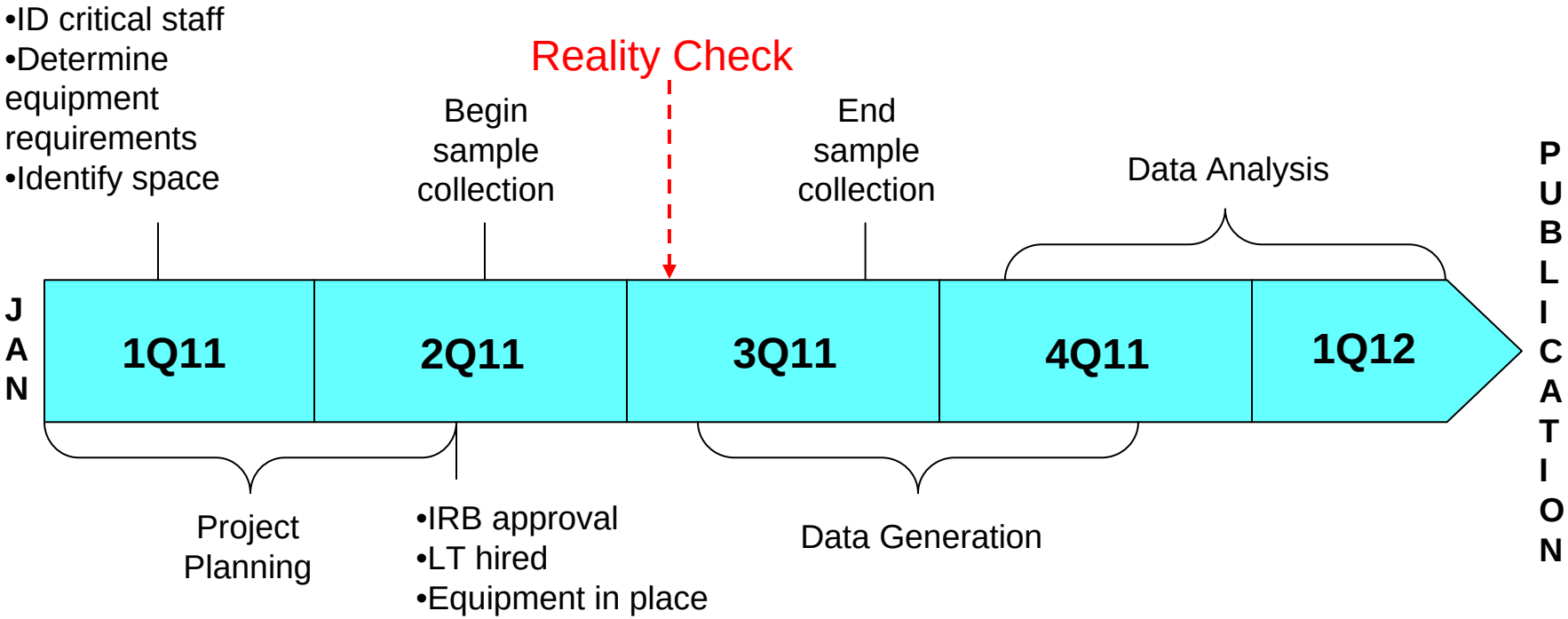
- **Genomic discovery models**
  - **Woman's Health**
  - **Cardiovascular Disease**
  - **Neurologic Disorders**
  - **Oncology**

ITMI: Three Goals

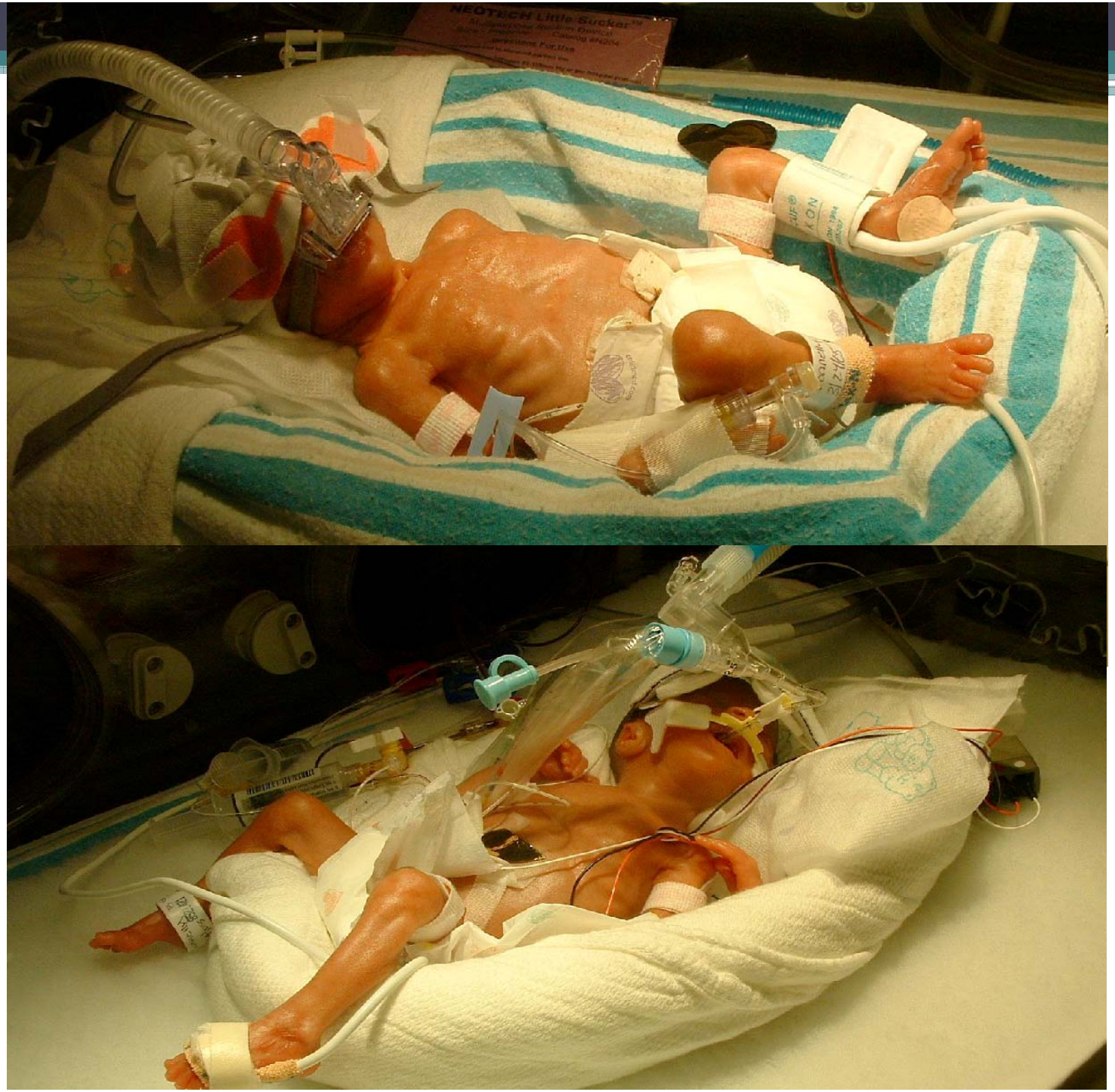
- **Facilitate the modernization DNA-based diagnostics at Inova**
- **Lead a cutting edge team of researchers to identify new genomic-based prognostic, diagnostic and therapeutic targets, utilizing samples from Inova's patient population**
- **Create an intelligence-based knowledge system that will enable the incorporation of new information into clinical practice.**

Woman's Health Phase I: Pre-term Labor

- 250 NICU family cohort, 250 NTD family cohort
- Genomic, proteomic, clinical data
- Molecular associations with pre-term labor



Long Term follow-up: what do they develop in the future—can this be predicted?


NEOTECH Little Sucker


MERRY CHRISTMAS

Future?

- Predictability-psychology
- Ethics
- Cost
- Privacy
- Insurance
- Change the way we practice medicine today?
- If you knew—what would you do different?
- Not a perfect science---yet

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Effect of Direct-to-Consumer Genomewide Profiling to Assess Disease Risk

Cinnamon S. Bloss, Ph.D., Nicholas J. Schork, Ph.D., and Eric J. Topol, M.D.

ABSTRACT

BACKGROUND

The use of direct-to-consumer genomewide profiling to assess disease risk is controversial, and little is known about the effect of this technology on consumers. We examined the psychological, behavioral, and clinical effects of risk scanning with the Navigenics Health Compass, a commercially available test of uncertain clinical validity and utility.

METHODS

We recruited subjects from health and technology companies who elected to purchase the Health Compass at a discounted rate. Subjects reported any changes in symptoms of anxiety, intake of dietary fat, and exercise behavior at a mean (±SD) of 5.6±2.4 months after testing, as compared with baseline, along with any test-related distress and the use of health-screening tests.

RESULTS

From a cohort of 3639 enrolled subjects, 2037 completed follow-up. Primary analyses showed no significant differences between baseline and follow-up in anxiety symptoms ($P=0.80$), dietary fat intake ($P=0.89$), or exercise behavior ($P=0.61$). Secondary analyses revealed that test-related distress was positively correlated with the average estimated lifetime risk among all the assessed conditions ($\beta=0.117$, $P<0.001$). However, 90.3% of subjects who completed follow-up had scores indicating no test-related distress. There was no significant increase in the rate of use of screening tests associated with genomewide profiling, most of which are not considered appropriate for screening asymptomatic persons in any case.

CONCLUSIONS

In a selected sample of subjects who completed follow-up after undergoing consumer genomewide testing, such testing did not result in any measurable short-term changes in psychological health, diet or exercise behavior, or use of screening tests. Potential effects of this type of genetic testing on the population at large are not known. (Funded by the National Institutes of Health and Scripps Health.)

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