GENOMICS: THE POWER OF NEW DISCOVERIES & APPLYING THEM TO TODAY'S HEALTHCARE

Leadership Institute
October 19, 2018

TGen – Translational Genomics Research Institute

- Non-profit biomedical research institute

- Founded 2002

- Precision medicine pioneer

Purpose

TGen seeks to *change the practice of medicine* by applying wisdom* in using the most sophisticated genomic technology to patient benefit **today**.

"What, who and how behind TGen's Precision Medicine."

Technology

Science

- Genome

- Transcriptome

- Epigenome

- Proteome

- Metabolome

- Microbiome

- Early Phase & Investigator Initiated Trials

- Targeted Drug Development

- Experimental Design

- Protocol Development

- Annotation

- Molecular Profiling

- Biomarker Discovery

- Hypothesis

- Modeling

- Feasibility & Scale

Purpose

Unravel genetic components of complex diseases to improve patient outcomes through accurate individualized diagnoses and targeted treatments

Deliver discoveries from bench to bedside
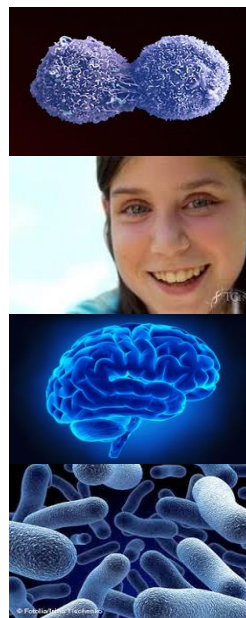
Oncology

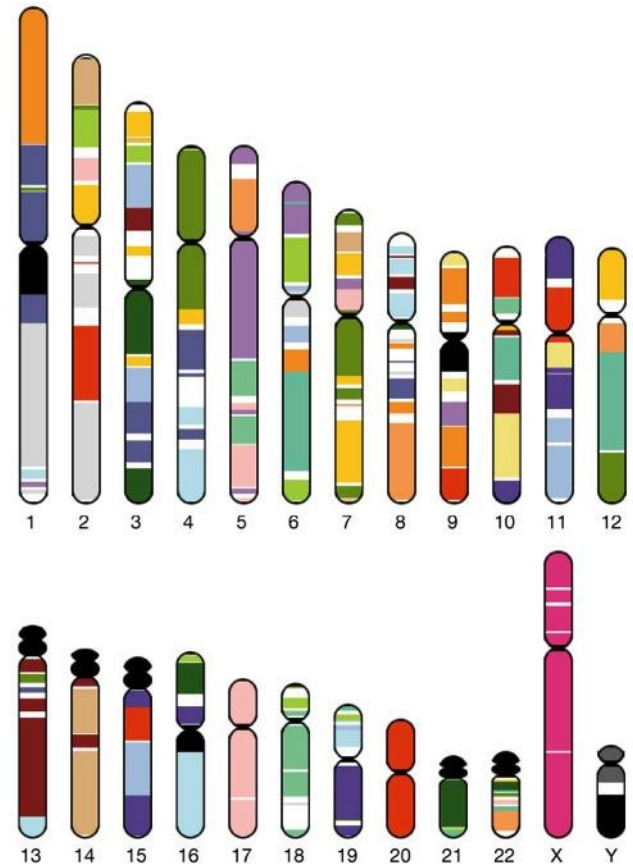**Rare genetic disorders**

Neurological disorders

Infectious disease

DNA Basics

Genome is an organism's complete set of DNA

The Human Genome consists of:

- 23 pairs of chromosomes
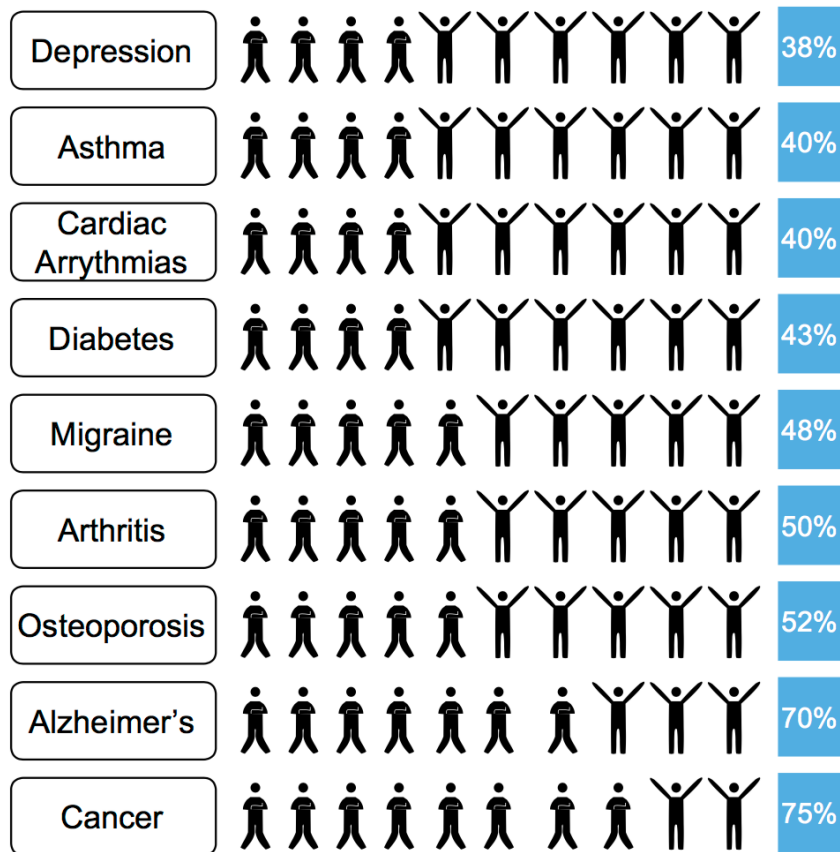- ~25,000 genes
- 3 billion base pairs

Human Genome Project
1993-2003 ~ $2.7 billion

Interventions Work Differently on Different People…

Percentage Lack of Benefit

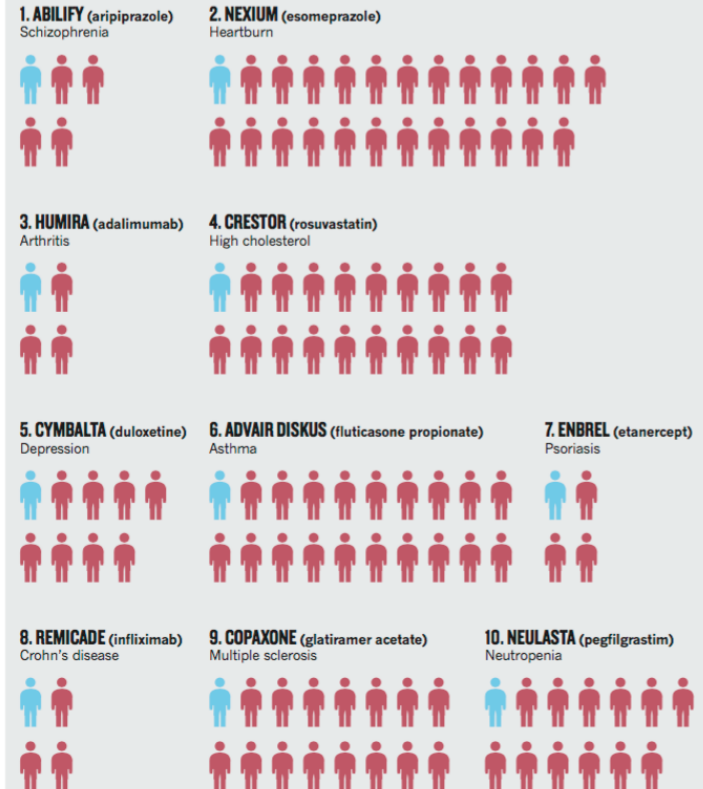| Condition	Percentage
Depression	38%
Asthma	40%
Cardiac Arrythmias	40%
Diabetes	43%
Migraine	48%
Arthritis	50%
Osteoporosis	52%
Alzheimer's	70%
Cancer	75%

Based on Spear et al. Trends Mol Med. (May, 2001; 7(5):201-4)

IMPRECISION MEDICINE
For every person they do help (blue), the ten highest-grossing drugs in the United States fail to improve the conditions of between 3 and 24 people (red).

1. ABILIFY (aripiprazole) Schizophrenia

2. NEXIUM (esomeprazole) Heartburn

3. HUMIRA (adalimumab) Arthritis

4. CRESTOR (rosuvastatin) High cholesterol

5. CYMBALTA (duloxetine) Depression

6. ADVAIR DISKUS (fluticasone propionate) Asthma

7. ENBREL (etanercept) Psoriasis

8. REMICADE (infliximab) Crohn's disease

9. COPAXONE (glatiramer acetate) Multiple sclerosis

10. NEULASTA (pegfilgrastim) Neutropenia

Based on published number needed to treat (NNT) figures. For a full list of references, see Supplementary Information at go.nature.com/4dr78f.

Schork. Nature (30 April 2015; Vol. 520)

City of Hope.

tgen
AN AFFILIATE OF City of Hope.

Genomics Today – Beginnings of Precision Medicine

Personalized healthcare helps us move towards providing

the right patient — the right drug — the right dose — at the right time

Cancer Genomics

5 FDA APPROVALS FOR NEW CANCER TREATMENTS

23,500+ SAMPLES SEQUENCED

500+ PROJECTS WORLDWIDE

FIRST TO PERFORM WHOLE GENOME SEQUENCING TO INFORM CANCER THERAPY

world's first PRECISION MEDICINE CLINICAL TRIAL FOR CHILDREN'S CANCERS

LARGEST **BLOOD CANCER** STUDY: 1,000 GENOMES FOR MULTIPLE MYELOMA

City of Hope.

tgen®
AN AFFILIATE OF City of Hope.

Neuro Genomics

Illumina → C8RAJACXX

460 PATIENTS SEQUENCED AT OUR CENTER FOR RARE CHILDHOOD DISORDERS

40% HAVE RECEIVED A DIAGNOSIS VS. 25% NATIONALLY
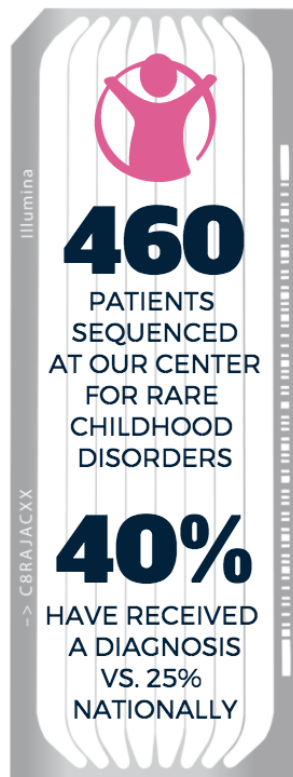
IDENTIFIED *Kibra* GENE RELATED TO MEMORY

DISCOVERED THE BROKEN HEART GENE

mind**crowd**
A research project by TGen

75,000 people
141 countries
6 continents

TAKE THE QUIZ AT WWW.MINDCROWD.ORG

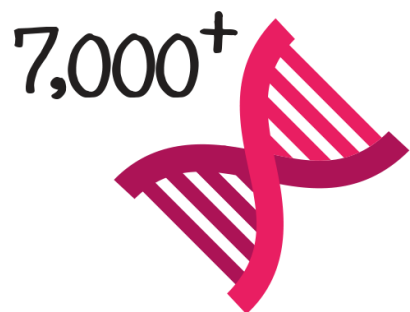WE'VE COMPILED **LARGEST** CIRCULATING RNA DATASET AS POTENTIAL BIOMARKERS FOR CONCUSSIONS AND BRAIN INJURY

Diagnosing the Rare

How Rare is Rare?

7,000⁺

RARE DISEASES
affect 1 in 150 births
in the United States

80%

FAULTY GENES
cause 4 out of 5 rare disorders

ARIZONA FAMILIES
3/4 of our patients live in Arizona
2/3 are on Medicaid

Diagnostic Odyssey

Rare disease patients and families spend immeasurable time and money, often undergoing invasive, painful tests, to find an accurate diagnosis:

an average of
7 years searching

with visits to 8
or more specialists

and as many as 3 misdiagnoses

Precision (Individualized) Medicine

- Individual molecular 'lesions' are nuanced and unique
- Targeting these lesions can lead to medicines tailored to an individual
- The whole enterprise needs an *objective framework*

FEATURE

Is personalized medicine finally arriving?

Malorye Allison

It's no gold rush, but dozens of players are emerging in personalized medicine, with biotechs, big and small, leading the way. Some big pharma companies and even payers remain skeptical, but economics aside, the real winners will be patients.
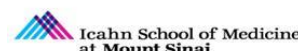
NATURE BIOTECHNOLOGY   VOLUME 26   NUMBER 5   MAY 2008

EDITORIAL

What happened to personalized medicine?

Personalized medicine falls a long way short of the predictive and preventative healthcare paradigm it once promised.

NATURE BIOTECHNOLOGY   VOLUME 30   NUMBER 1   JANUARY 2012

Current Questions: How to **identify** and then **prove** that a 'personalized' treatment actually *works*? Need to collect appropriate data, identify associations with outcomes, refine associations going forward

Precision Medicine of the Future and Big Data

- High Risk Individuals
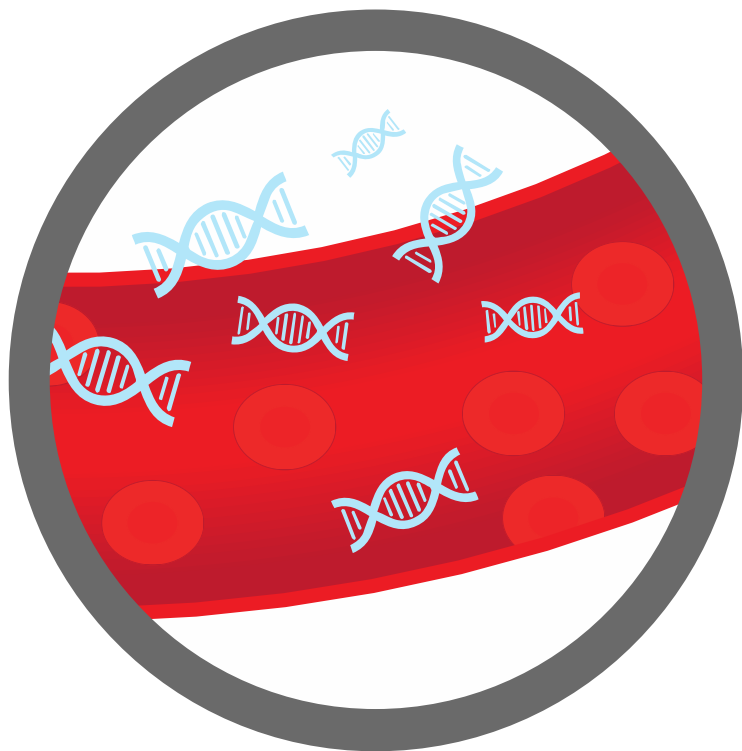- Early Detection
- Prevention

Early Detection of Cancer

- Some cancers takes between 5–10 years to manifest

- Pancreatic tumors can take nearly 20 years

- Some cancers, such as mesothelioma, take even longer

Blood Based Molecular Diagnostics

- Germline (inherited) DNA
  - Risk variants
  - Pharmacogenomics
- Cell free DNA
- Cell free micro RNA
- Extracellular vesicles
- Nanovesicles
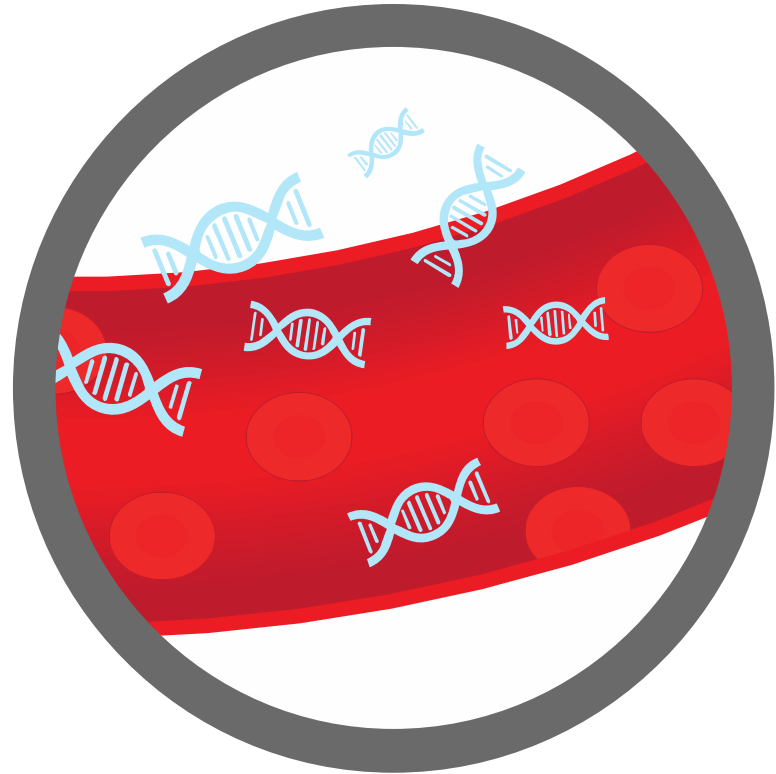
How can it help?

- Early detection of cancer
- Guide treatment decisions
- Targeted drug development and delivery

Monitoring of…
- Treatment response
- Drug resistance
- Disease recurrence

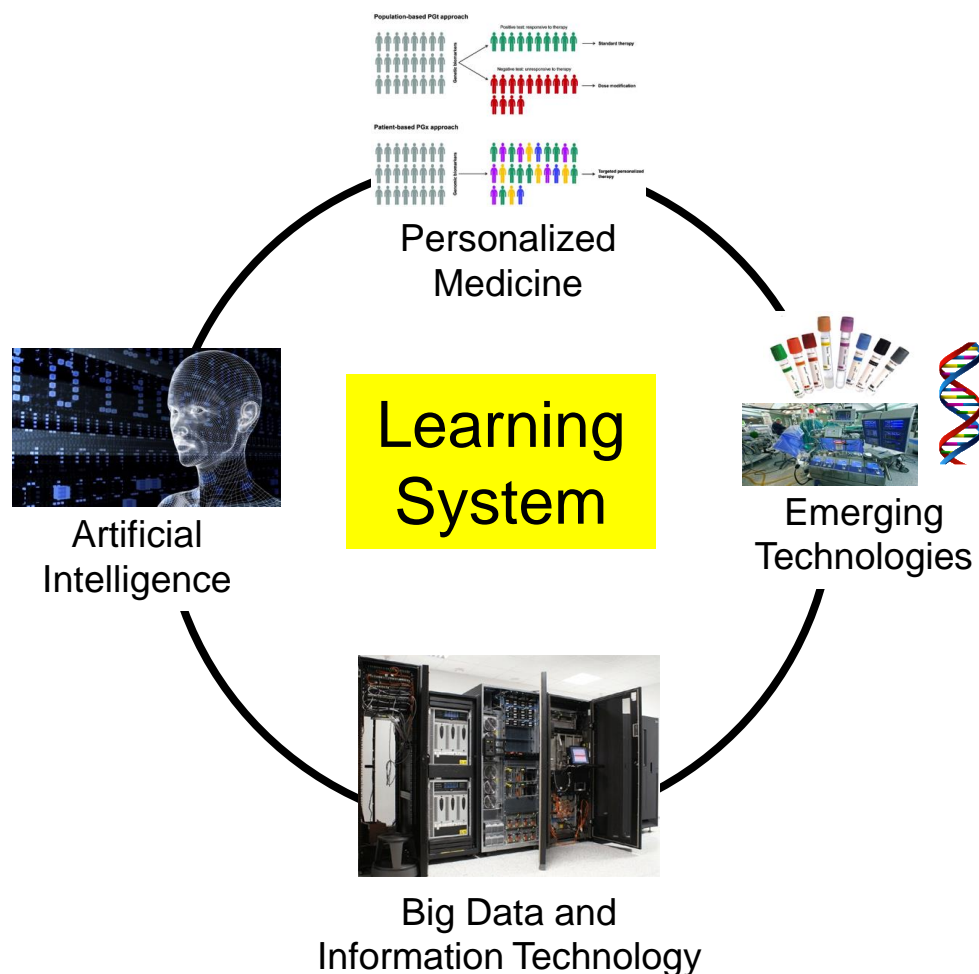# Internet of Things – What to do with all that data?

IOT and advances in communications have spurred innovation and created new opportunities to improve research and healthcare

Why tomorrow will not look like today

- Big Data in the cloud

- Apps (i.e)

- Sharing without borders (or ownership)

- Blurring of roles and agency

Big Data - Rapid Learning System

Personalized Medicine

Learning System

Artificial Intelligence

Emerging Technologies

Big Data and Information Technology

Rapid Learning Systems:

- Provide appropriate means for data integration

- Leverage growing advances in AI

- Quickly incorporate new assays, measures, and technologies

- Can be used to evaluate quality of care (general QC) in real time

- Provide vetted **decision support information** to physicians and health care workers

- Increase efficiency, QC, and competitive stance

Questions?