My Genome is an iron overloaded, lipid accumulating, metabolic minefield

Carrier

- Hemochromatosis
- Neiman Pick
- Galactosemia
- Spinal Muscular Atrophy

600 variants of undetermined significance
And I might drop dead!

Long QT Syndrome:

Medications that prolong the QT wave should be avoided.
### Use with great caution

**Infectious disease**
- Atazanavir **L1 U3** 27.40

**Oncology**
- Belinostat **U4** 192
- Irinotecan **L1 U1** 139.95
- Nilotinib **U2** 13
- Pazopanib **L1 U3** 1

### Use with caution

#### Analgesic/Anesthesiology
- Carisoprodol **L1 SL** 1
- Codeine **L1 X** 119.20, 99
- Hydrocodone ? 119.20
- Oxycodone **L1** 119.20
- Tramadol **L1 X** 1.12, 19, 20.

#### Anticoagulant/Antiplatelet
- Clopidogrel **L1 T** 191.92

#### Cardiovascular
- Carvedilol **SH** 1
- Clonidine **SH** 1
- Flecainide **L1 SH** 1.2
- Labetalol **SL** 1
- Metoprolol **L1 SH** 1.2
- Propranolol **SH** 1
- Procaainamide **SH** 1
- Simvastatin **L1!!** 1.35, 102.92
- Timolol **SH** 1.07

#### Gastroenterology
- Dexlansoprazole **SL** 1
- Dolasetron **SH** 1
- Esomeprazole **L1 SL** 1.2
- Lansoprazole **L1 SL** 12.99
- Omeprazole **L1 SL** 12
- Pantoprazole **L1 SL** 1

#### Infectious disease
- Atovaquone/Proguanil **T** 1
- Voriconazole **SL** 1.2

#### Neurology
- Brivaracetam **SL** 1
- Clobazam **L1 SL** 1

#### Oncology
- Tamoxifen **X** 1.2

#### Psychiatry
- Amitriptyline **L1 SH** 12.33, 14
- Aripiprazole **L1 SH** 12.104
- Atomoxetine **L1 SH** 1.2
- Brexpiprazole **L1 SH** 1
- Citalopram **L1 SL** 12.30, 304, 312, 46.58, 79.62
- Clozapine **L1 SH** 12.33
- Desipramine **L1 SH** 12.33
- Dextroin **L1 SH** 12.33
- Escitalopram **L1 SL** 12.32
- Fluoxetine **SH** 1
- Haloperidol **L1 SH** 12.80, 93, 104
- Iloperidone **L1 SH** 1
- Imipramine **L1 SH** 12.33
- Mirtazapine **SH** 12.52, 61.09
- Nefazodone **SH** 144.108
- Noroxiptilin **L1 SH** 1.23, 97.06
- Perphenazine **L1 SH** 11.6
- Pimozide **L1 SH** 1.04
- Protriptyline **SH** 1
- Thoridazine **L1 SH** 1

#### Pulmonary
- Dextromethorphan **SH** 1

#### Rheumatology
- Cevimeline **SH** 1

#### Urology
- Tamsulosin **SH** 1
- Tolterodine **SH** 1
## Use with great caution

**Infectious disease**
- Atazanavir L1 U3 27.40

**Oncology**
- Belinostat U4 1.192
- Irinotecan L1 U1 1.29.95
- Nilotinib U2 1.3
- Pazopanib L1 U3 1

## Use with caution

**Analgesic/Anesthesiology**
- Carisoprodol L1 SL 1
- Codeine L1 X 1.98.99
- Hydrocodone 2 1.98.20
- Oxycodone L1 1.98.30
- Tramadol L1 X 1.2.19.20.63.91

**Anticoagulant/Antiplatelet**
- Clopidogrel L1 T 1.91.92

**Cardiovascular**
- Carvedilol SH 1
- Clonidine SH 1
- Flecainide L1 SH 1.2
- Labetalol SL 1.2
- Metoprolol L1 SH 1.2
- Propafenone L1 SH 1.3
- Propranolol SH 1.2
- Simvastatin L1 !! 1.84.102.01
- Timolol SH 1.09

**Gastroenterology**
- Dexlansoprazole SL 1
- Dolasetron SH 1
- Esomeprazole L1 SL 1.2
- Lansoprazole L1 SL 1.2
- Omeprazole L1 SL 1.2
- Pantoprazole L1 SL 1

**Infectious disease**
- Atovaquone/Proguanil T 1
- Voriconazole SL 1.2

**Neurology**
- Brivaracetam SL 1
- Clobazam L1 SL 1

**Psychiatry**
- Amitriptyline L1 SH 1.23.14
- Aripiprazole L1 SH 1.2.104
- Atomoxetine L1 SH 1.2
- Brexiprazole L1 SH 1
- Citalopram L1 SL U2.3.32.4.0.61.9.9.5.2
- Clonipramine L1 SH 1.23.3
- Desipramine L1 SH 1.23.3
- Doxepin L1 SH 1.23.3
- Escitalopram L1 SL 1.23.2
- Fluoxetine SH 1
- Haloperidol L1 SH 1.2.80.93.104
- Iloperidone L1 SH 1
- Imipramine L1 SH 1.23.11
- Mirtazapine SH 1.2.82.6.6.6.6.6.100
- Nefazodone SH 1.4.4.208
- Nortriptyline L1 SH 1.22.77.105
- Perphenazine L1 SH 1.76
- Pimozide L1 SH 1.04
- Protriptyline SH 1
- Thiolidazine L1 SH 1

**Pulmonary**
- Tramipramine L1 SH 1.33.59
- Venlafaxine L1 SH 1.23.109
- Vortioxetin SH 1

**Rheumatology**
- Dextromethorphan SH 1

**Urology**
- Cevimeline SH 1
- Tamsulosin SH 1
- Tolterodine SH 1

---

!! – Statin Myopathy
Which means I might have muscle pain, weakness, trouble standing up or climbing stairs

!! – Statin Myopathy
But – some good news about Me!

- **Negative** for 1,596 hereditary conditions (including cancer and neurodegenerative)
- **Negative** for known family mutation
- Less need for any future genetic testing
- Lower diagnosis complexity
- Safer and more effective drug choice
- Lower health care costs and better quality?
24% of individuals who have genome sequenced have new medically interesting finding.

25 participants: Factor V Leiden, Arrhythmia, Allopurinol, Hemochromatosis, Malignant hyperthermia, Cystic fibrosis
3.5% of patients who had genome sequenced had unrecognized and medically significant findings.
An Epiphany
Statistics on Genetic Disorders

• 4 million births each year – 3% will be born with a genetic disease or major birth defect.
• 1% of all babies will be born with chromosomal abnormality, which can cause physical problems and mental retardation.
• 20% of infant deaths are caused by birth defects or genetic conditions (e.g. congenital heart defects, abnormalities of the nervous system, or chromosomal abnormalities).
• ~10% of all adults and 30% of children in hospitals are there due to genetically related problems.
SO WHAT IF?

Everyone (and their partner) knew their genetic risk of inherited disease?

Reduction in Disease Scourges - Thalassemia, Sickle Cell, Hemophilia, Cystic Fibrosis

Unknown consequences
SO WHAT IF?

Everyone (and their partner) knew their genetic risk of inherited disease?

Reduction of Disease Scourges - Thalassemia, Sickle Cell, Hemophilia, Cystic Fibrosis

Unknown consequences
5-10% of cancers are inherited

SO WHAT IF?
Everyone at genetic risk of cancer was aware and engaged in preventive tactics?

~35,000 deaths prevented every year
SO WHAT IF FINDING CANCERS AT THEIR EARLIEST STAGE WAS A SIMPLE BLOOD TEST?

GRAIL
A new company tackling the early detection of cancer on a global scale

MISSION: Enable the early detection of cancer in asymptomatic individuals through a blood screen

VISION: Massively decrease global cancer mortality by detection at a curable stage
Adverse Drug Events (ADEs)

1.5 Million ADEs Each Year in the U.S. Healthcare System

Source: atom Alliance
WHAT IF EVERYONE KNEW WHAT DRUGS WERE SAFE AND WHAT DOSE WAS EFFECTIVE?

<table>
<thead>
<tr>
<th>Use with great caution</th>
</tr>
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<tbody>
<tr>
<td><strong>Allergy</strong></td>
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<tr>
<td>-</td>
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<tr>
<td><strong>Analgesic/Anesthesiology</strong></td>
</tr>
<tr>
<td>Codeine LI X 1,8,9,27</td>
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<tr>
<td>Cyclobenzapine SH 1,30</td>
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<td>Hydrocodone X</td>
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<td>Methadone SH 1</td>
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<td>Oxycodone LI X 1,8,9</td>
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<td>Tramadol LI X 1,2,3,9</td>
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<td><strong>Ant-inflammatory</strong></td>
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<tr>
<td>Celecoxib SH 1</td>
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<td>Diclofenac SH 1</td>
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<td>Flurbiprofen SH 1</td>
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<td><strong>Anticoagulant/Antiplatelet</strong></td>
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<td>Clopidogrel LI X 1,24,36</td>
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<td>Warfarin LI SH W 1,6,14</td>
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<td><strong>Cardiovascular</strong></td>
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<tr>
<td>Azilsartan SH 1</td>
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<td>Carvedilol SH 1</td>
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<td>Chloridine SH 1</td>
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<td>Flecaïnide LI SH 2</td>
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<td>Guanabenz SH</td>
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<td>Labelotol SH</td>
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<td>Lidocaine SH 10,20</td>
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<td>Losartan SH 1</td>
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<td>Metoprolol SH 1,2</td>
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<td>Propafenone LI SH 1,2</td>
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<td>Verapamil SH 1,28</td>
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<td><strong>Endocrinology</strong></td>
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<td>Glimpiride SH 1</td>
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<td>Glyburide SH 1</td>
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<td>Tolbutamide SH</td>
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<td><strong>Gastroenterology</strong></td>
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<td>Dexamethasone SH 1</td>
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<td>Rabeprazole SH 1</td>
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<tr>
<td><strong>Immunosuppressives</strong></td>
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<td><strong>Infectious Disease</strong></td>
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<tr>
<td>Nelfinavir SH 1</td>
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<td>Terbinavine SH 1</td>
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<td>Voriconazole LI SH 1,2</td>
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<td><strong>Neurology</strong></td>
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<tr>
<td>Clobazam LI SH 1</td>
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<td>Phenytoin LI SH 03 P 1,7</td>
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<td>Tetrabenazine LI SH 1</td>
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<td><strong>Oncology</strong></td>
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<td>Tamoxifen LI X 1,2</td>
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<td><strong>Pulmonary</strong></td>
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<td>Dextromethorphan LI SH 1,26</td>
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<td>Allopurinol LI 1,4,11,12,15</td>
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<td>Carisoprodol LI SH 1,16</td>
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<td><strong>Sleep Medicine</strong></td>
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<td><strong>Urology</strong></td>
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<tr>
<td>Tamsulosin SH 1</td>
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<tr>
<td>Tolterodine SH 1</td>
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</tbody>
</table>
Utopia or Hype?

- Less cancer
- No unavoidable inherited disease
- Decreased need for testing
- More precise diagnosis
- Fewer side effects of drugs
Wish it was true, but good to see some cover(age)
modernhealthcare.com/article/201702 ...
@modrnhealthcr by @JConnHIT
PIVOT TO CLINIC

Whole-exome sequencing (WES) for patients with...

- advanced cancer
- rare disease

Gene panels: Cancer, Neuropathy, Cardiology, Liquid Biopsy

Non-invasive prenatal testing

Pharmacogenomic rules

Predictive genomics
Clinical Sequencing Indications 2016
10,891 Individuals @ Mayo Clinic

NGS testing ordered

- Oncology, 5531
- Maternal-Fetal, 2605
- Inherited Disease, 1860
- Neurologic, 561
- Cardiovascular, 334
Clinical Sequencing Indications 2016
10,891 Individuals @ Mayo Clinic

+ ~4800 clinical decision support alerts for 9 genes / 18 drugs

NGS testing ordered

Oncology, 5531
Maternal-Fetal, 2605
Inherited Disease, 1860
Neurologic, 561
Cardiovascular, 334
OUR GOAL

2016 750 exomes → 2020 50,000 exomes
Barriers to Deployment

- Public Wariness - Insurance
- Physician Acceptance
- Proof of Value = Payment
- Data Visualization
- Storage and the EHR
- Validity and Re-Interpretation
- Genetic Counseling
Mayo Clinic NGS Data Volumes; 96,000 Datafiles: 12,000 clinical tests

<table>
<thead>
<tr>
<th></th>
<th>Clinical</th>
<th>Research</th>
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<tr>
<td></td>
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<td>External (N/A)</td>
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<td>External</td>
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<td>2016</td>
<td>8,552</td>
<td>3,400</td>
<td>24,882</td>
<td>6,350</td>
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<tr>
<td>Total</td>
<td>11,845</td>
<td>3,400</td>
<td>74,207</td>
<td>6,350</td>
<td>95,802</td>
</tr>
</tbody>
</table>

mForge at NCSA – UIUC
8PB Storage (4 PB consumed at Go live)
Return of Genomic Results: Information Overload!

**Data exchange**
- Printed lab reports
- Entered into EHR as static scanned image
- EHRs do not support discrete genomic results

**Provider utilization**
- Uncertain how to apply data to treatment decisions
- Lack of Clinical Decision Support capabilities
- Lack of patient/provider education
- Shortage of Genetic Counselors
“Tonight I’m launching a new Precision Medicine Initiative to bring us closer to curing diseases like cancer and diabetes. And to give us all access to the personalized information we need to keep ourselves and our families healthier.”

President Barack Obama
2015 State of the Union Address 1 January 20, 2015
Mayo Clinic BioBank

55,000 Primary Care Mayo Clinic patients
8 million legacy disease specific samples
35 million samples for National ‘All of US’
Direct to Consumers: Mayo App Powered by Helix

Welcome to the dawn of genetics.

Join the journey of genetic understanding
So Much To Learn!