Clinical Genomics in a Children’s Hospital

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*with help from Kejian Zhang, MD & Sander Vinks, PhD

Cincinnati Children’s Hospital Medical Center
Cincinnati

Genomic Medicine 4
Dallas
Tuesday, January 29, 2013
Cincinnati Children’s Hospital
Medical Center
Cincinnati &
Cincinnati Children’s Hospital
Cincinnati Children’s Hospital Medical Center

- 1,144,858/y Patient Visits
- 70,000/New Patients
- 5,000/y NICU Admissions
- 6,365/y I/P Surguries
- 27,000/y O/P Surgeries
- 550 Liver Transplants Procedures (>400 survivors)
- 3,500/y Adenoidectomies
- 3,000 Peña Procedures
- 250 Nuss Procedures (76 in 2012)
- 822 Faculty
- 13 Off-site Outpatient Clinics
- 512 Inpatient Beds
- 13,000 Employees
- $1.4 Billion Gross Income
- $173 Million Research Funding (13% Increase over 2011) ($107 Million from the NIH)
- Epic Electronic Record
- Cerner Lab Record
- 24 heart transplants with 100% survival (2011 & 2012)
Genomic Medicine at CCHMC

• **Existing**
  – Individual gene sequence
  – Infectious disease Dx
  – Cytogenetics
  – Pharmacogenomics

• **Underway**
  – Targeted gene sequencing
  – Whole exome sequencing

• **Probable Future...**
  – Gene expression -- Methylation
  – DNAse sensitivity -- Histone marks
  – Genome sequence -- ChIP sequence
2012 Genomic Medicine Financing

CCHMC Human Genetics
• Bill: $11 million
• Collect: $7 million

CCHMC Cytogenetics
• Bill: ~$4 million
• Collect: ~$2.4 million

Other Service Providers
• Cost: $2 million
  – Athena Diagnostics
  – Prometheus
  – Gene DX
  – Baylor Genetics
  – Ambry Genetics
  – Others
Genetic Pharmacology Service, Psychiatry Panel

Adult and Pediatric Psychiatry Panels Available

The Genetic Pharmacology Service for children and adults at Cincinnati Children's Hospital Medical Center offers drug panels for many commonly prescribed psychiatry medications.

The table below lists the panels currently available through the Genetic Pharmacology Service at Cincinnati Children's.

View List of Drugs Tested

Psychiatry Panel

<table>
<thead>
<tr>
<th>Amitriptyline</th>
<th>Fluoxetine</th>
<th>Moclobemide</th>
<th>Sertraline</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aripiprazole</td>
<td>Flupentixol</td>
<td>Nefazadone</td>
<td>Thioridazine</td>
</tr>
<tr>
<td>Atomoxetine</td>
<td>Fluvoxamine</td>
<td>Nortriptyline</td>
<td>Trazadone</td>
</tr>
<tr>
<td>Bupropion</td>
<td>Haloperidol</td>
<td>Olanzapine</td>
<td>Trimipramine</td>
</tr>
<tr>
<td>Citalopram</td>
<td>Imipramine</td>
<td>Paroxetine</td>
<td>Venlafaxine</td>
</tr>
<tr>
<td>Clomipramine</td>
<td>Levomepromazine</td>
<td>Perazine</td>
<td>Zotepine</td>
</tr>
<tr>
<td>Clozapine</td>
<td>Maprotiline</td>
<td>Perphenazine</td>
<td>Zuclopenthixol</td>
</tr>
<tr>
<td>Desipramine</td>
<td>Mianserin</td>
<td>Pimozide</td>
<td></td>
</tr>
<tr>
<td>Doxepin</td>
<td>Mirtazapine</td>
<td>Risperidone</td>
<td></td>
</tr>
</tbody>
</table>
Included in the patient report

- Test performed
- Genotype (allelic information)
- Predicted phenotype (e.g. Poor Metabolizer, etc.)
- Dosing recommendation(s)
- List of drugs that cause serious drug-drug interaction
- Test limitations
- Location of supplemental information
- How to order a GPS consult

Meta-analysis of published research from 1970-2003 on the relevance of PG effects of CYP2D6 and CYP2C19 on 36 antidepressants and 38 antipsychotics
What's Inside

The Genetic Pharmacology Service web site includes information about:

- Why Choose Us
- Drugs Tested / Panels
- Meet the Team
- Request a Consult
- Order a Test
- Shipping Instructions
- Education
- Frequent Questions
- Other Resources
- Contact Us
PG linked to inpatient medication ordering
Genetic Pharmacology Service

- Order by drug name – not by specific gene
- Rapid turn around time: 2 business days
- Report includes
  - Dosing recommendations based on genotype
  - Identification of other drugs that induce, inhibit or interact with drug in question
- Provide consultative service if needed
- Provide educational materials for health care professionals, families and patients
Experience to Date – Lessons learned

- Used in > 8,000 pediatric patients
- Most commonly used for:
  - inpatient and outpatient pediatric psychiatry patients
  - children with autism
- Marked differences between physicians regarding knowledge about impact of genetic variation on drug metabolism
  - Some want gene name
  - Some drug name
  - Some want panel to cover potential drugs
Methods: Weight-Free Behavioral Intervention Score (BIS)

• Behavioral interventions: $x_1$: seclusions or timeouts [summed], $x_2$: holds, and $x_3$: restraints.

• Improved approach: minimize variability effect, place equal emphasis on each variable by using a weight-free index:
  
  $BIS = \log(x_1+1) + \log(x_2+1) + \log(x_3+1)$

R.C. Elston. A weight-free index for the purpose of ranking or selection with respect to several traits at a time. The Biometric Society, Vol.19(1), March 1963.
## Study Population

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Children on CYP12D6/CYP2C19 psychotropics (n=305)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, median (25, 75 percentile)</td>
<td>13 (11,15)</td>
</tr>
<tr>
<td>Gender, female n (%)</td>
<td>147 (48%)</td>
</tr>
<tr>
<td><strong>Primary Diagnosis</strong></td>
<td></td>
</tr>
<tr>
<td>Mood disorders</td>
<td>161 (53%)</td>
</tr>
<tr>
<td>Psychotic disorders</td>
<td>16 (5%)</td>
</tr>
<tr>
<td>Disruptive behavior disorders</td>
<td>34 (11%)</td>
</tr>
<tr>
<td>Anxiety disorders</td>
<td>58 (19%)</td>
</tr>
<tr>
<td>Impulse control disorders</td>
<td>14 (5%)</td>
</tr>
<tr>
<td>Adjustment disorders</td>
<td>3 (1%)</td>
</tr>
<tr>
<td>Eating disorders</td>
<td>1 (0%)</td>
</tr>
<tr>
<td>Pervasive developmental disorders</td>
<td>14 (5%)</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>4 (1%)</td>
</tr>
</tbody>
</table>
Results: Genotype – Behavioral Intervention Score (BIS) Relationship (adjusted for age, sex, admitting GAF, diagnoses)

N=305, Patients on any 2D6/2C19 drugs, p=0.02
Results: Genotype – Behavioral Intervention Score (BIS) Relationship (adjusted for age, sex, admitting GAF, diagnoses)

N=305, Patients on any 2D6/2C19 drugs, p=0.02

N=64, Patients not on 2D6/2C19 drugs, p=0.90

Not a disease effect
Relative Successes to date

- NeuroPsych drugs – CYP2D6, CYP2C19
- Codeine – CYP2D6 (Surgical/Pain service)
- Irinotecan – UGT-1A1 (CBDI)
- 6-mercaptopurine, azathioprine – TPMT (CBDI, GI)
- Warfarin – CYP2C9, VCOR1

Other (not pediatrics/CCHMC)
- Clopidogrel – CYP2C19, ABCB1
- Pharmacogenomic Resource for Enhanced Decisions in Care and Treatment (PREDICT)
- Tamoxifen – CYP2D6

Next steps at CCHMC – Translational PGx projects

Building on our EMR - Decision Support tools and outcomes studies with the Anderson Center

- Immunosuppressive drugs – CYP3A5*3, ABCB1
  - As proposed as part of our Genomic Medicine RFA application
- Immunomodulating drugs – UGT 2B7, 1A8/9
  - Mycophenolates PGx in Transplantation and cSLE
- Morphine - OPRM1, COMT and ABCB1 (OPRD1, TRPV1, 5HTT)
- Voriconazole – CYP2C19 (CYP3A4)
  - There is an ongoing pilot with our BMT group
- Technology: Affymetrics DMET or Illumina VeraCode ADME Core
Factors mediating tacrolimus disposition; Previous findings

TAC, tacrolimus; TAC-Ms, tacrolimus metabolites; POR, P450 oxidoreductase
Factors mediating tacrolimus disposition; Other pathways

TAC, tacrolimus; TAC-Ms, tacrolimus metabolites; POR, P450 oxidoreductase
Next steps at CCHMC – Expansion of neuropsych drug panel

<table>
<thead>
<tr>
<th>Gene</th>
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<tbody>
<tr>
<td>5HT2C</td>
</tr>
<tr>
<td>ANK3-ANKRIN3</td>
</tr>
<tr>
<td>CACNAIC</td>
</tr>
<tr>
<td>COMT</td>
</tr>
<tr>
<td>CYP3A4</td>
</tr>
<tr>
<td>DRD2</td>
</tr>
<tr>
<td>MTHFY</td>
</tr>
<tr>
<td>SLC6A4</td>
</tr>
</tbody>
</table>

There is a small explosion of labs offering other tests in addition to CYP2D6 and 2C19. But it is unclear at this point what the correct interpretation should be.
Decision Support for Visit Planning

- **Organize** data for *complex patients* in a way that facilitates *efficient* and *reliable* clinical decision making

- **Risk stratify** patients for individual and *population management*

- **Automatically** suggest indicated testing and therapies to providers
# Immunosuppression

- Race: Black/African American
- Donor Type: LRD
- # HLA Mismatch: 0
- Rejct’n Episode: Type Date
- Last Four Levels: Sirolimus
  - 2/4/2012: 6.1
  - 12/10/2011: 3.1
  - 10/19/2011: 5.1
  - 9/16/2011: 7.2

## Cardiovascular Disease

- Cholesterol: NO
  - Target: <200
  - Current: 147
- BP: NO
  - Target: <130/80
  - Current: 129/73
- Lipid Panel:
  - Total Cholesterol: 147
  - HDL: 98
  - LDL: 26
  - Triglycerides: 117

## Behavior Management

- Self Mgmt: Last SMA 12/12/11
- Adhere: Ctr: 21
- Diet Plan:
  - Exercise Plan:

## Chronic Kidney Disease

<table>
<thead>
<tr>
<th>Test</th>
<th>Result</th>
<th>Date</th>
<th>Suggested Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyst. C GFR</td>
<td>56 ml/min</td>
<td>12/10/2011</td>
<td>Monitoring up to date</td>
</tr>
<tr>
<td>Proteinuria</td>
<td>300</td>
<td>12/12/2011</td>
<td></td>
</tr>
<tr>
<td>Creatinine</td>
<td>1.4</td>
<td>10/19/2011</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.4</td>
<td>12/10/2011</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.4</td>
<td>2/4/2012</td>
<td></td>
</tr>
</tbody>
</table>

## General Information/Care Items

- Labs:
  - Test: Echo
  - Test: Testosterone
  - Test: CK
  - Test: Cyst. C
  - Test: Uric Acid
  - Test: Lipids
  - Test: Renal Ultrasound
  - Test: LH
  - Test: 25-OHD
  - Test: Hep B
  - Test: Fe Studies
  - Test: FSH
  - Test: BK
  - Test: DSAs
  - Test: Liver Profile
  - Test: PTH
  - Test: EBV

- Others:
  - Monitoring up to date

- MD/RN Notes:
  - Flw’d? Helpfl? Comments Date

- Area of Focus:
  - Suggested Action: YES/ NO YES/ NO YES/ NO

- BP Mgmt:
  - Test: Target: 12/10/2011
  - Cholesterol: <200
  - LDL: <130
  - HDL: >45
  - Triglycerides: <200

- Cardiovascular Disease Mgmt:
  - Below target w/ Rx

- Immunosuppression:
  - Last Four Levels: Sirolimus
  - Target: 2/4/2012: 6.1
  - Current: 12/10/2011: 3.1
  - 10/19/2011: 5.1
  - 9/16/2011: 7.2

- Cardiovascular Disease:
  - Cholesterol: NO
  - BP: NO

- Behavior Management:
  - Self Mgmt: Last SMA 12/12/11
  - Adhere: Ctr: 21

- Chronic Kidney Disease:
  - Cyst. C GFR: 56 ml/min
  - Proteinuria: 300
  - Creatinine: 1.4

- DK Hooper, 2011
### Risk

- **Patient:**
- **Provider:** Hooper
- **Location:** BASE
- **Diagnoses:**
  - Last Four levels
  - Immunosuppression: NO
- **Infectious Disease:**
  - Bacterial 1/28/2012
  - EBV 8/27/2001
- **Immunologic Risk:** Low
- **Cardiovascular Disease:**
  - Latest SBP: 12/10/2011
  - Latest DBP: 12/10/2011
  - BP Mgmt: 12/10/2011
  - Test: Cholesterol 147
  - Test: LDL 98
  - Test: Triglycerides 26
  - Test: LDL/Trig Mgmt: Dyslipidemia
  - Test: CV Stratification: None RF controlled
- **Behavior Mgmt:**
  - Test: SMA 12/12/11
  - Test: Adhere Ctr:
  - Test: Behavior Mgmt Risk: Low

### Current Therapy

- **Last Four levels**:
- **Drug**:
  - Tacrolimus
  - Sirolimus
  - MMF
  - Azathioprine
  - Prednisone
- **Target or Protocol**:
  - Total Daily Dose (mg):
    - Tacrolimus
  - Current target or Protocol:
    - Target dose
  - Protocol:
    - Target dose

### Suggested Action

- **Provider Response**
- **Note:**
  - MD/RN Notes:
  - Provider Response:
  - Provider Response:

### Risk

- **Current Therapy**
- **Suggested Action**
- **Provider Response**

DK Hooper, 2011
# Color Coded Risk Stratification

## Patient:

<table>
<thead>
<tr>
<th>MRN:</th>
<th>Overall Risk</th>
<th>Moderate</th>
</tr>
</thead>
</table>

| Race: | Black/African American |
| Donation Type: | LRD |
| # HLA Mismatch: | 0 |
| Reject'n Episode: | Type Date |

| Immunologic Risk: | Low |

<table>
<thead>
<tr>
<th>Date</th>
<th>Systolic</th>
<th>Diastolic</th>
<th>Systolic%ile</th>
<th>Diastolic%ile</th>
<th>BP Medications</th>
<th>Dose</th>
<th>Suggested Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>12/12/2011</td>
<td>127</td>
<td>64</td>
<td>80.5</td>
<td>25.2</td>
<td>Cozaar 50 mg q24h</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10/19/2011</td>
<td>105</td>
<td>55</td>
<td>1.6</td>
<td>8.1</td>
<td>Procacid XL 30 mg q24h</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| BP Mgmt: | Below target w/ Rx |

## Cardiovascular Disease

### Test:

- Cholesterol: <200
- LDL: <130
- HDL: >45
- Triglycerides: <200

**CV Stratification:** Only one RF controlled

## Color Coded Suggested Actions

- **Suggested Action:** Transition F/U with Sondra

---

**DK Hooper, 2011**
Limitations

• Outside of the EMR (distribution requires email, photocopies, etc…)

• Requires manual data input (dual entry) from the EMR (time, resources, human error)

• Does not incorporate pharmacokinetic data

• Limited information on adherence
What if we had…

...pharmacokinetic data
and...

...adherence data
and...

...protocol recommended drug level targets
and...

...patient reported outcomes (side effects)
and...

...passive patient reported outcomes...

...all in the same place?
Research Questions

• How does visit planning with decision support impact outcomes?
  – Adherence
  – Rejection of transplanted kidney
  – Survival of transplanted kidney
  – Cost
Research Questions

• Can we also incorporate patient reported outcomes (social networking, smart phone apps etc…)? Yes & underway…

• How can these same principles be applied to other chronic disease populations (adults and children)?
  – Other solid organ transplant
  – Diabetes
  – Hypertension
  – Any chronic condition
Genetic Pharmacology Service

- Vision: To improve the management of childhood disorders by:
  - Systematic integration of genotypic, phenotypic, biologic, psychosocial, and environmental variables
  - Identify patients genetically predisposed to
    - Toxicity & Non-response
    - Treat these patients with different doses alternative medications
  - Multidisciplinary approach to analyze impact of these different factors on clinical outcome and educate health care providers in their use
Clinical Services (Human Genetics):

Technology Available:
- Targeted DNA genotyping
- RT-PCR
- Quantitative PCR
- Southern Blot analysis
- Sanger Sequencing
- AB Low Density Array
- Affymetric resequencing array
- NextGen Platforms
  - Raindance Target Enrichment
  - HiSeq2500 & MiSeq

>60 tests offered:
- Primary Immunodeficiencies
- Hearing Loss
- Pharmacology Genetic Services
- Fatty Acid Oxidation Disorders
- Inherited Liver Diseases
- Lysosomal Storage Diseases
- Oncology Services
- Thrombophilic Condition
- Mitochondrial diseases
- Hemoglobin defects
Clinical NextGen Tests* Offered at CCHMC

- **OtoSeq** Hearing Loss Panel
  - 23 genes, sensorineural hearing loss

- **MetaboSeq** Fatty Acid Oxidation Disorder Panel
  - 19 genes, fatty acid oxidation metabolic pathway

* Any results reported are 1st confirmed by Sanger sequencing
Clinical NextGen Tests for 2013

Immunodeficiency Panels

- Severe Combined Immunodeficiency (SCID)-30 genes
- Hemophagocytic Lymphohistiocytosis (HLH)- 14 genes
- Autoimmune Lymphoproliferative Syndrome (ALPS)-5 genes
- Severe Congenital Neutropenia (SCN)-6 genes
- Mendelian Susceptibility to Infection panel (MSI)-19 genes
- Common Variable Immunodeficiencies (CVID)- 15 genes
- Autoimmune Disorders (IBD/IPEX/AIRE)- 7 genes
- Chronic Granulomatous Disease (CGD)- 7 genes
- Familial Periodic Fever (PFP)- 6 genes
- Hyper-IgM Syndrome (HIGM)- 14 genes
- Hyper IgE Syndrome (HIGE)- 3 genes
Clinical NextGen Tests for 2013

• Hematology/Oncology
  – Fanconi Anemia (14 genes)
  – Diamond-Blackfan Anemia (DBA)-10 genes
  – Bone Marrow Failure syndrome (BMF)- 25 genes
  – Chromosomal Breakage Disorders (CBD)- 7 genes
  – Erythrocyte Cytoskeleton Disorders (ECD)- 24 genes
  – TMA-aHUS panel- 15 genes
  – Platelet disorder panel- 36 genes

• Dermatology
  – Dyskeratosis Congenita (DKC)- 7 genes
  – Epidermolysis Bullosa (EB)- 24 genes

• Ophthalmology
  – Eye disorder panel (EyeSeq)- 40 genes
Next Steps -- **Whole Exome Sequencing** as a clinical test.

• Greater **Cost** of targeted sequencing will lead to whole exome sequencing.

• More accurate, highly redundant coverage will make **Confirmation** by Sanger sequencing unnecessary.

• When target negative, **Query** the exome.

• Best practices for **Incidental Results**.
CCHMC 2012 Exome Sequencing: Discovery &/vs. Clinical Utility

366 subjects from 122 trios

- Systemic Lupus Erythematosus (SLE) (38)
- Juvenile Idiopathic Arthritis (JIA) with Macrophage Activation Syndrome (MAS) (48)
- Eosinophilic Esophagitis (18)
- Diaphragmatic Hernia (9)
- Disseminated Staphylococcus after Osteomyelitis (4)
- Tracheal Ring Deformity (3)
- Congenital Neutropenia (1)
- Situs Inversus (1)
- Idiopathic Liver Failure, Cloacal Extrusion, Esophageal Atresia, Microgyria, Early Childhood Severe Obesity
Baraitser Winter Syndrome

*Riviere et al., Nature Genetics, 2012*

**Intellectual Disability**
**Hearing Loss**
**Seizures**
**Short Stature**
**Microcephaly (postnatal)**
**Pachygyria (lissencephaly)**
**Facial Dysmorphia**
**Ocular Colobomata**

- 18 of 18 *de novo variants* (or rare variants) in actin genes: *ACTB* (10) or *ACTG1* (8)
- 11 proven *de novo*
- Neural cell migration defect
Parallel “next generation” Sequencing

• **Advantage:** Massive amounts of sequence
  - Exome: 2 Gb 60,000 variants
  - Genome: 100 Gb 3,000,000 variants

• **Problems:**
  - Unreliable sequence
    • Error in the sequence & alignment
    • Interference across replicated regions
    • Incomplete sequence
  - Analysis is a nightmare
    • Too much sequence and way too many variants
  - Too expensive
Exome Sequencing: Critical Infrastructure

• Genetic Counseling... *(expertise)*
• Technical capacity... *(expertise)*
  – Next generation sequencing
  – Confirmation
• Informatics... *(expertise)*
  – Processing to annotated file
  – Preparation of files for interpretation
  – Preservation
• Interpretation ... *(expertise)*
  – Return of results (phenotype & incidental)
  – Future re-use
• Financing... *(courage)*

Efficiency & Iterative Improvement
Whole Exome Sequencing
Clinical Application

Begin – Phenotypes with literature support

• Severe Intellectual Disability (20-40%)
• Autism (~15%)

• Then...
  – ...many, many rare conditions.
  – ...many uncharacterized common conditions.
Clinical Whole Exome Sequencing at CCHMC

Plans
### Diagnostic & Prognostic Genomics

<table>
<thead>
<tr>
<th>Past</th>
<th>Present</th>
<th>Future</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sanger</td>
<td>Sanger</td>
<td>? Sanger</td>
</tr>
<tr>
<td>Array</td>
<td>? Array</td>
<td>? Targeted NG</td>
</tr>
<tr>
<td>Targeted NG</td>
<td>? Targeted NG</td>
<td></td>
</tr>
<tr>
<td>- Gene Sets</td>
<td></td>
<td></td>
</tr>
<tr>
<td>- almost Exome</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exome</td>
<td></td>
<td>Whole GENOME</td>
</tr>
</tbody>
</table>

**other genomics**

*Epigenetics, Expression, Metabolomics, ChIP-Seq, Proteomics, Chromatin Conformation, etc...
Epigenome-wide association data in RA

• Causal Inference Test for methylation of peripheral blood mononuclear cells in Rheumatoid Arthritis.

• Single nucleotide polymorphism (SNP) (p<10E-14) (DRB1_A104_E2_326559926_AE)
  Differentially Methylated Place (DMP)
  (cg16609995 – PBX2) (p<10E-8)

CIT p<10E-15
Rheumatoid arthritis (RA)
Causal Inference Test
Acknowledgements

Ken Kaufman, PhD
Beth Cobb, MBA
Sara Lazaro, MBA
Kejian Zhang, MD, MBA
Alexander A. Vinks, PharmD, PhD

Thank you
Plan Notes:

**CURRENT THERAPY**

**Blood Pressure Meds**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Daily Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diuretics</td>
<td>Dose1</td>
</tr>
<tr>
<td>captopril (Capoten)</td>
<td>Dose2</td>
</tr>
</tbody>
</table>

**Exercise Plan:**

New exercise effective 9/1/2012. Increase daily activity time to 30 minutes.

**Diet Plan:**

A healthy food plan.

**Cholesterol Meds:**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Daily Dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lipitor (atorvastatin)</td>
<td>10mg once daily</td>
</tr>
<tr>
<td>colestid (colesticol)</td>
<td>2-16 grams</td>
</tr>
</tbody>
</table>

**SUGGESTED ACTIONS**

**Blood Pressure Medication**

<table>
<thead>
<tr>
<th>Drug</th>
<th>Suggested Action</th>
</tr>
</thead>
<tbody>
<tr>
<td>Enalapril 5 mg q24h</td>
<td>Accept?</td>
</tr>
<tr>
<td>Norvasc 10 mg q24h</td>
<td>Accept?</td>
</tr>
<tr>
<td>Atenolol 25 mg q24h</td>
<td>Accept?</td>
</tr>
</tbody>
</table>

**Cholesterol Medication**

Other Suggested Actions:

Require regular physical check up.
Outline

• Intro
• Patient population / special characteristics
• Existing Genomic Services
  – Sanger sequencing
    • CYP2D6 & pharmacogenomics
    • How many? What do we send out?
  – Cytogenetics
• Adapt targeted gene analysis to next generation sequencing
  – Kejian’s plans
• Whole exome sequencing
  – Intellectual disability
  – Idiopathic severe disease
• What are we missing?
  – Expression analyses
  – DNA methylation
  – Histone marks
  – Any manner of ChIP-Seq analyses.
WHAT WOULD IT LOOK LIKE?
### DEMOGRAPHICS

<table>
<thead>
<tr>
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### VISIT INFORMATION

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**Risk Level:**
- **Immunosuppression**
- **Cardiovascular Disease**
- **Chronic Kidney Disease**
- **Behavior Management**

**Legend:**
- Low
- Standard
- High