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PharmGenEd™: Bridging the Gap Between Science & Practice

Train-the-Trainer Session for Asthma

Tuesday, November 2nd, 2010

Train-the-Trainer Agenda

1. Introduction
   • Objective of PharmGenEd™ program
   • Shared curriculum and format
   • Introduction of author

2. Review of educational content for selected therapeutic area

3. Future webinar dates
   • Program implementation
   • Other therapeutic areas

4. Contact information

5. Survey instruments
   • Post training survey for trainers

6. Question & Answer (Q & A) session

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Overall Objective of PharmGenEd™ Program

- The “Pharmacogenomics Education Program: Bridging the Gap between Science and Practice” (PharmGenEd™) is an evidence-based pharmacogenomics education program designed for pharmacists and physicians, pharmacy and medical students, and other healthcare professionals.

- The overall objective of the PharmGenEd™ program is to increase awareness about current knowledge of the validity and utility of pharmacogenomic tests and the potential implications of benefits and harms from use of the tests.

Shared Curriculum

- Educational Materials (each 1 hour)
  - Asthma
  - Cardiology I (warfarin & statins)
  - Cardiology II (clopidogrel & beta blockers)
  - Concepts and clinical applications
  - Economic issues
  - Oncology I (solid tumors)
  - Oncology II (hematologic malignancies)
  - Psychiatry I (depression)
  - Psychiatry II (antipsychotics)

- Future webinar dates for these sessions will be provided later

Therapeutic Area Discussion

- Format
  - Patient case
  - Gene/Allele of interest
  - Functional effect
  - Population prevalence
  - Clinical relevance (dosing/selection, efficacy, and toxicity)
  - Genomic test and testing recommendation
  - Patient case summary

Author

Alice Gardner, PhD
Associate Professor of Pharmacology
Massachusetts College of Pharmacy and Health Sciences School of Pharmacy - Worcester
Learning Objectives

• Upon completion of this program, participants will be able to:
  – Identify specific drug therapies used in asthma in which pharmacogenomic testing can be applied in the clinical setting
  – Summarize evidence-based recommendations for pharmacogenomic testing
  – Using patient case scenarios, formulate a plan for pharmacogenomics testing based upon available scientific evidence

Presentation Outline

• Select pharmacogenomic effects in patients with asthma
  – β2-agonists
    • Adrenergic beta-2-receptor, surface (ADRB2)
  – Glucocorticoids (GCs)
    • Corticotropin-releasing hormone receptor (CRHR1)
    • Fc fragment of immunoglobulin E, low affinity II (FCER2)
  – Leukotriene modifiers
    • Arachidonate 5-lipoxygenase (ALOX5)

Therapeutic Area Discussion

• Format
  – Patient case
  – Gene/Allele of interest
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  – Population prevalence
  – Clinical relevance (dosing/selection, efficacy, and toxicity)
  – Genomic test and testing recommendation
  – Patient case summary

Case Presentation

A 49-year-old African-American female presents to the ER with acute shortness of breath. Patient history reveals she had multiple hospitalizations for asthma. She denies non-adherence to her asthma medications. She reports very frequent use of her short-acting β2-agonist (SABA) (Metzger et al 2008)

Physical examination: BP 133/92 mm Hg, HR 137, respiratory rate 24 breaths/min, 81% O2 Sat
Past medical history: asthma, hypertension, community-acquired pneumonia, obstructive sleep apnea, bilateral pulmonary emboli, deep vein thrombosis
Labs: blood glucose 234 mg/dL, calcium 8.2 mg/dL, phosphate 2.2 mg/dL

(Metzger et al 2008)
Case Presentation – cont’d

- **Asthma Meds**: albuterol, fluticasone/salmeterol, montelukast, levalbuterol, and ipratropium (doses unknown)
- **Allergies**: NKDA
- **Questions to consider**:
  - Why is the patient not responding to beta agonists?
  - What polymorphisms may impact use of beta agonists?
  - Recommendations for therapy?

(Metzger et al 2008)

Gene/Allele: **ADRB2**

- **Gene/Allele**: ADRB2
- ADRB2 gene found on chromosome 5q31-33 and encodes $\beta_2$-adrenergic receptor ($\beta_2$AR) (Caron et al 1988)
  - Region has linkage to asthma and related phenotypes (Postma et al 1995)
- $\beta_2$AR is a G-protein coupled receptor (GPCR) (Johnson et al 1998)
  - Gs activation coupled to increased cAMP and bronchodilation
  - Stimulation of $\beta_2$AR results in rapid and potent relaxation of airway smooth muscle
- Short- and long-acting $\beta_2$-adrenergic agonists target the G-protein coupled $\beta_2$AR

Asthma

1) **What is Asthma?**
   - An inflammatory disease of the airways

2) **Pathophysiology**
   - Inflammation
   - Reversible bronchospasms
   - Bronchial hyperresponsiveness
   - Airway remodeling

3) **Signs and symptoms**
   - Wheezing, coughing
   - Bronchoconstriction
   - Mucus hypersecretion
   - SOB
   - Intercostal retractions

4) **Treatment of Asthma?**
   - Bronchodilators
   - Anti-inflammatory
   - Antibodies
Gene/Allele: **ADRB2**

- The β2-adrenergic receptor encoded by the ADRB2 gene is **HIGHLY** polymorphic (Hall 2006).

- Single nucleotide polymorphisms (SNP’s) of ADRB2 most studied *in vitro* or *in vivo* include (Hall 2006):
  - Arg/Arg16, Gln/Gln27, Thr/Thr164 are wild type alleles
  - Arg/Gly16, Gln/Glu27, Thr/Ile164 are heterozygote alleles
  - Gly/Gly16, Gln/Glu27, Ile/Ile164 are homozygote variant alleles

### Functional Effect: ADRB2

<table>
<thead>
<tr>
<th>ADRB2 alleles</th>
<th>Polymorphism allele frequency</th>
<th>In vitro effects</th>
<th>Functional effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arg/Arg16 (wild type)</td>
<td>N/A</td>
<td>~78% reduction in receptor expression with agonist stimulation</td>
<td>Decreased β2AR agonist-induced down regulation/desensitization</td>
</tr>
<tr>
<td>Gly/Gly16 (variant)</td>
<td>0.61</td>
<td>~96% reduction in receptor expression with agonist stimulation</td>
<td>Enhanced β2AR agonist-induced down regulation/desensitization</td>
</tr>
</tbody>
</table>


<table>
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<td>N/A</td>
<td>~78% reduction in receptor expression with agonist stimulation</td>
<td>Decreased β2AR agonist-induced down regulation/desensitization</td>
</tr>
<tr>
<td>Gly/Glu27 (variant)</td>
<td>0.43</td>
<td>~29% reduction in receptor expression with agonist stimulation</td>
<td>Minimal β2AR agonist-induced down regulation/desensitization</td>
</tr>
<tr>
<td>Thr/Thr164 (wild type)</td>
<td>N/A</td>
<td>Enhanced binding affinity of β2AR agonist</td>
<td>Enhanced Gs-coupling and adenylate cyclase activation</td>
</tr>
<tr>
<td>Thr/Ile164 (variant)</td>
<td>0.05</td>
<td>Decreased binding affinity of β2AR agonist</td>
<td>Reduced Gs-coupling and adenylate cyclase activation</td>
</tr>
</tbody>
</table>

Population Prevalence: ADRB2

<table>
<thead>
<tr>
<th>ADRB2 alleles</th>
<th>Caucasian (C)</th>
<th>African-American (A-A)</th>
<th>Asian (A)</th>
<th>Hispanic (H)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arg/Arg16 (wild type)</td>
<td>11-20%</td>
<td>24-31%</td>
<td>28-35%</td>
<td>18%</td>
</tr>
<tr>
<td>Gly/Gly16 (variant)</td>
<td>30-53%</td>
<td>22-31%</td>
<td>18-21%</td>
<td>30%</td>
</tr>
<tr>
<td>Glu/Glu27 (wild type)</td>
<td>24-53%</td>
<td>59-69%</td>
<td>80-90%</td>
<td>64-80%</td>
</tr>
<tr>
<td>Gly/Glu27 (variant)</td>
<td>12-32%</td>
<td>3-13%</td>
<td>0-0.7%</td>
<td>3%</td>
</tr>
<tr>
<td>Thr/Thr164 (wild type)</td>
<td>95%</td>
<td>98%</td>
<td>99%</td>
<td>97%</td>
</tr>
<tr>
<td>Thr/Ille164 (heterozygote variant)</td>
<td>4%</td>
<td>2-4%</td>
<td>0–1%</td>
<td>3%</td>
</tr>
</tbody>
</table>


Clinical Relevance: ADRB2

- Dosing/selection: No literature, to date, to suggest changes in dosing or selection of beta-2 agonists
- Toxicity: No literature related to ADRB2 polymorphism and beta-2 agonist side effects

Population Prevalence: ADRB2

- Differences exist in allelic frequencies among ethnic groups
- Allelic frequencies for Arg16Gly and Gln27Glu are significantly different among groups
- Arg/Arg16 polymorphism has an increased occurrence in African-Americans and Asian populations (Taylor 2007)
  - In vivo and clinical studies have focused on this polymorphism
- Thr/Ille164 polymorphism has a low frequency among ethnic groups, and the Ile/Ile164 has not been found in an individual to date
  - Polymorphism under evaluation with unknown clinical significance

Clinical Relevance: Efficacy/response

<table>
<thead>
<tr>
<th>Gene/Allele</th>
<th>Study Design</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Arg/Arg16</td>
<td>Randomized, double blind, placebo controlled, 3-way crossover study of 157 adult patients with mild to moderate asthma. Primary endpoint: Asthma exacerbations, PEFRmax.</td>
<td>Arg/Arg16 patients observed increased frequency of major and total asthma exacerbations with albuterol vs placebo (p&lt;0.005). No significant difference in PEFRmax with Arg/Gly16 and Gly/Gly16 patients vs. placebo. No significant increase in asthma exacerbations with long-acting beta agonist salmeterol.</td>
</tr>
<tr>
<td>Arg/Gly16</td>
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<tr>
<td>Gly/Gly16</td>
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Metzger et al 2008; Taylor et al 2000
Clinical Relevance: Efficacy/response

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<tr>
<th>Gene/Allele</th>
<th>Study Design</th>
<th>Conclusions</th>
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</thead>
<tbody>
<tr>
<td>Arg/Arg16</td>
<td>Retrospective study included 190 adult patients with mild asthma (defined as FEV₁ ≥ 70% predicted) who were in a previous randomized, double blind, multicenter study. Primary endpoint: PEFR&lt;sub&gt;AM&lt;/sub&gt;</td>
<td>Arg/Arg16 patients with regular albuterol use had a greater decline in PEFR&lt;sub&gt;AM&lt;/sub&gt; (p=0.012)</td>
</tr>
<tr>
<td>Arg/Gly16</td>
<td>BARGE trial was a randomized, placebo controlled, cross over study in 78 adults with mild asthma. Primary endpoint: PEFR&lt;sub&gt;AM&lt;/sub&gt;</td>
<td>Arg/Arg16 patients had decreased PEFR&lt;sub&gt;AM&lt;/sub&gt; (p=0.0209)</td>
</tr>
<tr>
<td>Gly/Gly16</td>
<td>Gly/Gly16 patients had increased PEFR&lt;sub&gt;AM&lt;/sub&gt; (p=0.0175)</td>
<td></td>
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</table>

Clinical Relevance: Efficacy/Toxicity

<table>
<thead>
<tr>
<th>Gene/Allele</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Arg/Arg</td>
<td>Randomized, double-blind, placebo controlled study that included 173 adult patients with moderate asthma (defined as FEV₁ ≥ 40% predicted; or ≥ 50% if using regular ICS) to determine whether the response to LABA's plus ICS therapy is genotype specific. Primary endpoint: PEFR&lt;sub&gt;AM&lt;/sub&gt;</td>
<td>Arg/Arg16 and Gly/Gly16 patients with combination treatment of LABA + ICS improved PEFR&lt;sub&gt;AM&lt;/sub&gt; compared to ICS alone. Increased PEFR&lt;sub&gt;AM&lt;/sub&gt; was not significant between genotypes (p=0.99)</td>
</tr>
<tr>
<td>Gly/Gly</td>
<td>Ethnicity specific difference observed in PEFR&lt;sub&gt;AM&lt;/sub&gt; in African-American: Gly/Gly16 patients showed benefit with treatment (p=0.013) but not Arg/Arg16 patients (p=0.57)</td>
<td></td>
</tr>
</tbody>
</table>

Clinical Relevance: Toxicity

• Regular use of SABA’s have demonstrated adverse treatment effects in Arg/Arg 16 homozygotes
• LARGE trial indicated that lung function is not significantly different between Arg/Arg16 or Gly/Gly16 homozygotes when LABA’s are added to ICS therapy
  – African-Americans may not benefit from addition of LABA’s to ICS therapy

Pharmacogenomic Test and Testing Recommendations

• Genomic Testing
  – $\beta_2$AR genotyping: Arg/Arg16 confers risk for asthma exacerbations (Kelly 2005)
  – Currently no FDA approved test
• Testing recommendations
  – A pharmacogenetic predictive test is currently under development (Wu et al 2010)

Case Presentation Summary

• Due to patient’s asthma history, self-reported adherence, and ethnicity, she was tested for the $\beta_2$-adrenoreceptor genotype
  – Genotype indicated she was Arg/Arg16
  – Application of the Naranjo probability scale revealed probable causality between uncontrolled asthma in patient and SABA use
• Recommendations for Therapy
  – $\beta_2$-Agonists were discontinued
  – Tiotropium for maintenance therapy and ipratropium as primary rescue therapy were initiated
• Patient Outcome:
  • Patient followed in outpatient pulmonary clinic
  • To date, not been admitted to hospital for asthma-related events
(Metzger et al 2008, Small et al 2003; Hall, 2007; Martinez, 1997; Israel, 2000)

Inhaled corticosteroids (ICS) and CRHR1
Inhaled corticosteroids (ICS)

- ICS are a mainstay of asthma therapy
  - Mechanism of action is via binding to the glucocorticoid (GC) receptor
  - GC-GC dimer functions as transcription factors via activating or repressing gene transcription
    - GCs can inhibit pro-inflammatory gene expression
    - GCs can stimulate anti-inflammatory gene expression
  - In asthma ICS pharmacotherapy decreases airway inflammation and airway hyperresponsiveness (AHR)
  - ICS resistance has been demonstrated in asthmatics treated with ICSs

(Gen/Allele: CRHR1)

- Functional Effect
  - Heterogeneity exists in the response to ICS among asthmatics (Tantisira et al 2004)
  - Identified SNPs associated with CRHR1 gene in three clinical trial populations
  - Specific CRHR1 genotypes and haplotypes have been studied:
    - Example 1: rs242941
      - CRHR1 G/G (wild type genotype), CRHR1 G/T (heterozygous), CRHR1 T/T (homozygous variant)
    - Example 2: rs1876828
      - CRHR1 G/G (wild type genotype), CRHR1 A/G (heterozygous), CRHR1 A/A (homozygous variant)

Gene/Allele: CRHR1

- Gene/Allele: Corticotropin-releasing hormone receptor (CRHR1)
- CRHR1 gene found on chromosome 17q21-22 and encodes CRHR (Polymeropoulos et al 1995, Tantisira et al 2004)
- CRHR is a G-protein coupled receptor (GPCR) (Eckart et al 2002, Kageyama et al 2009)
  - Gs activation coupled to adenylate cyclase activation and increased cyclic AMP (cAMP)
  - Endogenous ligand is corticotropin-releasing factor (CRF)
  - CRF stimulates adrenocorticotropic hormone (ACTH) production via CRHR Gs-coupled signaling pathway in HPA-axis
  - ACTH stimulates GC synthesis
- CRHR1 has been shown to be a major regulator of GC synthesis (Weiss et al 2006)

Clinical Relevance: CRHR1

- Dosing/selection: No literature related to CRHR1 polymorphism impacting ICS dosing or selection
- Efficacy/response:
  - Specific variants in the CRHR1 gene demonstrate enhanced lung function to short-term ICS treatment (Tantisira et al 2004)
  - Decreased lung function associated with CRHR1 polymorphism during long-term ICS treatment (Rogers et al 2009)
- Toxicity: No literature related to CRHR1 polymorphism and ICS side effects
## Clinical Relevance: Efficacy/response

<table>
<thead>
<tr>
<th>Gene/Allele</th>
<th>Study Design</th>
<th>Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRHR1</td>
<td>Evaluated 3 independent studies of mild-moderate asthmatic populations who were on various ICS. Primary endpoint: change in FEV₁ from baseline</td>
<td>Specific genetic variants in the CRHR1 gene demonstrate enhanced lung function (FEV₁) to short-term ICS treatment in childhood and adult asthma (P-values ranged from 0.006 to 0.025) Individuals with these variants were more likely to positively respond to ICS therapy</td>
</tr>
</tbody>
</table>

Tantisira et al 2004

<table>
<thead>
<tr>
<th>Gene/Allele</th>
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<th>Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRHR1</td>
<td>Evaluated mild to moderate asthmatics in CAMP study for long-term effects of ICS Primary endpoint: change in FEV₁ from baseline; number of asthma exacerbations</td>
<td>CRHR1 allele variant confers increased risk of poor lung response (FEV₁) during long-term ICS treatment (P = 0.05) Patients with these variants had lower bronchodilator response to albuterol during ICS therapy Poor long-term responses to ICS are genetically and phenotypically distinct when outcomes are defined</td>
</tr>
</tbody>
</table>

Rogers et al 2009; Tantisira et al 2004

### Pharmacogenomic Test and Testing Recommendations for CRHR1

- **Genomic Testing**
  - Currently no FDA approved test
- **Testing recommendations**
  - No recommendation in asthma guidelines for routine use (National Asthma Education and Prevention Program Expert Panel Report 2 2007)

### Inhaled corticosteroids (ICS) and FCER2
**FCER2**

- Gene/Allele: Fc fragment of immunoglobulin E, low affinity II (FCER2)
- Functional Effect and Population Prevalence:
  - **FCER2** encodes for the low affinity IgE receptor
  - Presence of variant confers higher levels of IgE and differential expression of **FCER2** (Tantisira et al 2007)
    - **FCER2 2206TT** (wild type genotype)
    - **FCER2 2206CT** (heterozygous genotype)
    - **FCER2 2206CC** (homozygous genotype)
      - 26% in Caucasians, 44% in African-Americans

**Clinical Relevance: FCER2**

- Dosing/selection: No literature related to **FCER2** polymorphism impacting ICS dosing or selection
- Efficacy/response: Presence of a **FCER2** polymorphism confers an increased risk for severe asthma exacerbations and poor lung function while being treated with ICS (Tantisira, 2007; Rogers, 2009)
- Toxicity: No literature related to **FCER2** polymorphism impacting ICS side effects

**Clinical Relevance: Efficacy/response**

<table>
<thead>
<tr>
<th>Alleles</th>
<th>Study Design</th>
<th>Conclusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>FCER2 2206T and 2206C</td>
<td>Randomized, double blind, longitudinal, placebo controlled study in children (5-12 years of age) with mild-moderate asthma. Primary endpoint: Severe asthma exacerbations (ER or hospitalization over 4 years); poor lung function (decline in FEV₁). Secondary endpoint: IgE levels.</td>
<td>Patients who are homozygous for the 2206C variant allele had a significantly greater risk for severe asthma exacerbations while on ICS. 2206C variant allele contributed to both recurrent exacerbations and poor lung function (p=0.046). Presence of the 2206C variant allele confers higher levels of IgE and differential expression of <strong>FCER2</strong>.</td>
</tr>
</tbody>
</table>

Tantisira et al 2007; Rogers et al 2009

**Pharmacogenomic Test and Testing Recommendations for FCER2**

- Genomic Testing
  - Currently no FDA approved test
- Testing recommendations
  - No recommendation in asthma guidelines for routine use (National Asthma Education and Prevention Program Expert Panel Report 2 2007)
Leukotriene Pathway

- Multiple genes are involved in the leukotriene signaling pathway
- Patients receiving leukotriene modifiers for asthma have a variable response to therapy (Malmstrom et al, 1999)
- Multiple polymorphisms related to the leukotriene pathway genes have been identified
  - ALOX5, LTA4H, LTC4S, MRPI, CYSLTR2 and CYSLTR1 (Drazen et al 1999; Lima et al, 2006; Wechsler et al 2002; Telleria et al 2008)
  - Heterogeneity in response to treatment with leukotriene modifiers may result from genetic variations (Langmack et al 2010)

ALOX5

- Gene/allele: ALOX5
- Functional Effect:
  - ALOX5 encodes for 5-lipoxygenase (5-LO), which is involved in leukotriene synthesis (Hall 2006)
  - Presence of variant confers variability in FEV1 response when treated with leukotriene modifiers (Currie et al 2003, Drazen et al 1999)
  - Transcription factor binding motif in promoter region of ALOX5 was analyzed for tandem repeats of the Sp1-binding motif (Drazen et al 1999)
  - ALOX5 SNP’s have been analyzed for response to leukotriene modifiers (Fowler 2002; Lima 2006)
### Clinical Relevance: Efficacy/response

<table>
<thead>
<tr>
<th>Gene/Allele</th>
<th>Study Design</th>
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</tr>
</thead>
<tbody>
<tr>
<td>ALOX5</td>
<td>Randomized, double blind, placebo controlled study in adults with mild-moderate asthma treated with 5-LO inhibitor</td>
<td>ALOX5 variant demonstrated decreased response (p &lt; 0.05)</td>
</tr>
<tr>
<td></td>
<td>Additionally, independent studies on ALOX5 polymorphisms were studied in moderate persistent asthmatics treated with LT-receptor antagonist</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Primary endpoint: change in FEV₁ from baseline; asthma exacerbations</td>
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</table>

Patients with 1 or 2 ALOX5 wild-type alleles on a LT-receptor antagonist had improved FEV₁, and fewer asthma exacerbations compared to ALOX5 variant genotype (P=0.0006 and 0.001, respectively). Polymorphisms in ALOX5 are associated with changes in FEV₁ and asthma exacerbations.


### Clinical Relevance: Efficacy/response

<table>
<thead>
<tr>
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</tr>
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<tbody>
<tr>
<td>ALOX5</td>
<td>Study of poorly controlled mild-to-moderate adult asthmatics treated with LT-receptor antagonist plus theophylline</td>
<td>ALOX5 heterozygous variant carriers had a 73%; reduced risk for asthma exacerbations versus the wild type who had a higher risk (p&lt;0.045)</td>
</tr>
<tr>
<td>MRP1</td>
<td>Primary endpoint: change in FEV₁ from baseline; asthma exacerbations</td>
<td>MRP1 heterozygous variant carriers had a 76% reduced risk for asthma exacerbations (p=0.023) compared to variants</td>
</tr>
</tbody>
</table>

Drazen et al 1999; Lima et al, 2006; Telleria et al 2008

### Clinical Relevance: Efficacy/response

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<tr>
<td>ALOX5</td>
<td>Data from adolescents and adults with a history of persistent asthma treated with LT-receptor antagonist</td>
<td>Changes in FEV₁ and PEF₉₄ associated ALOX5 (p=0.01 and p=0.01, respectively) and CYSLTR2 (p=0.02 and p=0.02) polymorphisms</td>
</tr>
<tr>
<td>CYSLTR2</td>
<td>Primary endpoint: change in FEV₁ from baseline; PEF₉₄</td>
<td>ALOX5 and CYSLTR2 variant alleles had a higher PEF₉₄ response</td>
</tr>
<tr>
<td></td>
<td>A small subset of the population with ALOX5 and CYSLTR2 polymorphisms confers a distinct phenotype whereby they respond positively to leukotriene modifiers</td>
<td></td>
</tr>
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</table>

Klotsman et al, 2007

### Clinical Relevance: Efficacy/response

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<tbody>
<tr>
<td>ALOX5</td>
<td>Study in children with mild or moderate-severe asthma</td>
<td>ALOX5 variant genotype more likely to have moderate to severe asthma (p=0.008)</td>
</tr>
<tr>
<td></td>
<td>Primary outcome: LTC₄ secretion Secondary outcome: severity of asthma</td>
<td>The ALOX5 genotype predicts asthma severity</td>
</tr>
</tbody>
</table>

Kalayci et al 2006; Lima et al 2008
Clinical Relevance Summary:  
**ALOX5**

- Heterogeneity in the treatment response to leukotriene modifiers exist
- The heterogeneity may be the result of the combination of polymorphisms in the key genes regulating leukotriene synthesis

Pharmacogenomic Test and Testing Recommendations for  
**ALOX5**

- Genomic Testing
  - Currently no FDA approved test
- Testing recommendations
  - No recommendation in asthma guidelines for routine use (National Asthma Education and Prevention Program Expert Panel Report 2 2007)

Acknowledgements

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References


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References


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Future Webinar Dates
(all times are PST)

- **Oncology II: Hematologic Malignancies**
  - Tuesday, Aug. 10, 2010 10am-12pm – COMPLETED
- **Concepts and Clinical Applications**
  - Wednesday, August 11, 2010 – COMPLETED
- **Psychiatry II: Antipsychotics**
  - Tuesday, Aug. 24, 2010 10am – 12pm – COMPLETED
- **Oncology I: Solid Tumors**
  - Thursday, Aug. 26, 2010 10 am – 12 pm – COMPLETED
- **Cardiology I: Warfarin and Statins**
  - Tuesday, Sept. 21, 2010 10am –12 pm – COMPLETED
- **Cardiology II: Clopidogrel and Beta Blockers**
  - Thursday, Sept. 23, 2010 10 am – 12 pm – COMPLETED
- **Economic Issues**
  - Tuesday, Oct. 5, 2010 9:30 am – 11:30 am – COMPLETED
- **Psychiatry I: Depression**
  - Thursday, Oct. 21, 2010 10am – 12pm – COMPLETED

Please register at www.pharmacogenomics.ucsd.edu to download materials prior to the scheduled webinar

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Survey Instruments: Evaluation

- Faculty trainers will complete a Post-Training Survey
  - Evaluate knowledge, attitudes, and self-efficacy
- All survey materials will be mailed after completion of all webinars in November 2010

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