HILO*met* PhyzioType System:

Personalizing Patient Care with Gene-based Decision Support for Prescribing Neuro-Psychiatric + Cardio-Metabolic Drugs

The **HILO*met* Phyziotype® System** offers clinicians the ability to personalize drug therapy and increase safety and compliance in the most challenging cases:

- Patients experiencing drug intolerance, side effects, treatment resistance or therapeutic failure to medications
- Patients treated with combinations of medications or medical devices
- Children, adolescents, the elderly and the infirm
- Patients hospitalized or with multiple medical conditions

The assays are non-invasive and require only a blood sample or buccal swab.

The **Personalized Health Portal©** provides clinicians access to real-time information for gene-guided prescription of 250 drugs widely used in medicine:

- **130 Neuro-Psychiatric**
  Drugs: antidepressants, pain, antipsychotics, stimulants, addiction, anticonvulsants, neurodegenerative, anxiolytics, sleep
- **120 Cardio-Metabolic**
  Drugs: hypertension, cholesterol, diabetes, gastric reflux, asthma, erectile dysfunction, angina, antithrombotics, heart failure

Personalized Medicine in Real-time

- Timesaving, user friendly, password protected, interactive web interface for decision support
- Benchmarking of innate drug metabolism function for each patient with comparisons to the population using 4 quantitative indices
- Drug interactions assessed via interactive display
- Clinician-customized archive of patient reports and drug selections + dosing
- Objective results, evidence-based predictive analyses and rapid turnaround of 3 business days

TO ORDER: **Test Requisitions + Sample Reports available at *www.genomas.com/LPH***

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The HILO*met* PhyzioType System.

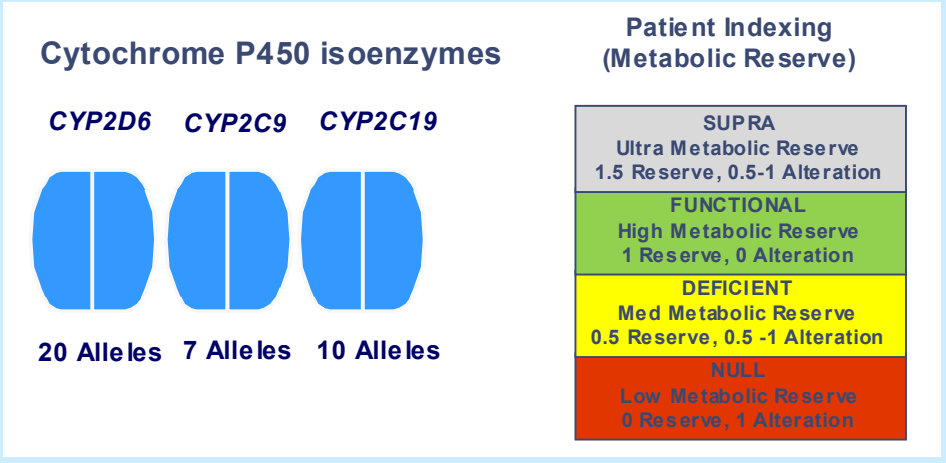
Deployment of the HILO*met* PhyzioType allows personalized management of drugs to treat mental illness, neurological disorders, diabetes, and heart disease. Based on Genomas clinical studies and case reports, the HILO*met* PhyzioType offers interpretative guidance to assess the functional status of a patient's drug metabolism in order to establish functionalities and deficiencies. Clinicians are then guided to make prescribing decisions based on knowledge of those metabolic capabilities and deficits. The HILO*met* PhyzioType System enables clinicians to select the drug with the least risk and superior efficacy based on data derived from the patient's own genome.

GPS

GENETIC PRESCRIPTION SYSTEM

Similar to Global Positioning Systems (GPS) used in vehicles today to help us reach our intended destinations, the HILOmet PhyzioType System enables a Genetic Prescription System to be implemented from correlations of gene variation and drug response outcomes. This drug GPS leads clinicians and patients to their desired treatment goal, resulting in effective and individualized healthcare.

Using the HILO*met* PhyzioType's combinatorial genotyping, the innate metabolic capacity of the patient can be predicted and diagnosed simply from a blood sample or buccal swab. Patients intolerant to these drugs or refractory to treatment can be benchmarked for their drug metabolism function and innate reserve. Therapy can be directed to drugs whose primary metabolic pathway is functional, while avoiding drugs with the most risk, whose primary metabolic pathways are deficient, null or ultra-rapid.



The genes coding for CYP2D6, CYP2C9 and CYP2C19 isoenzymes are critical for metabolism of neuro-psychiatric and cardio-metabolic drugs and polymorphic resulting in highly diverse metabolism function among individual patients.

The guidance provided by the HILOmet PhyzioType markedly improves the safety and efficacy of drug therapy by providing:

- High-resolution combinatorial genotyping of a total of 37 variants in genes *CYP2D6, CYP2C9* and *CYP2C19* (20, 7, and 10 alleles, respectively)
- Well-characterized ultra-rapid promoter alleles for genes *CYP2D6* and *CYP2C19* (**2a* and **17*, respectively) conferring gain of metabolic function in carriers
- Objective Indices for Metabolic Reserve and Alteration , Allele and Gene Alteration
- Interactive Drug Interactions utility allowing the clinician's review of other medications jointly prescribed with recalculation of the therapeutic guidance

Personalized Health Portal (PHP). The PHP integrates the patient's innate drug metabolism capacity as determined by the HILO*met* PhyzioType with pharmacokinetic information available from Genomas clinical studies, the FDA, drug manufacturers and pharmacogenetic databases. It guides clinicians to prescribe the drugs most beneficial for that patient and provides that guidance through an on-line, interactive secure portal.

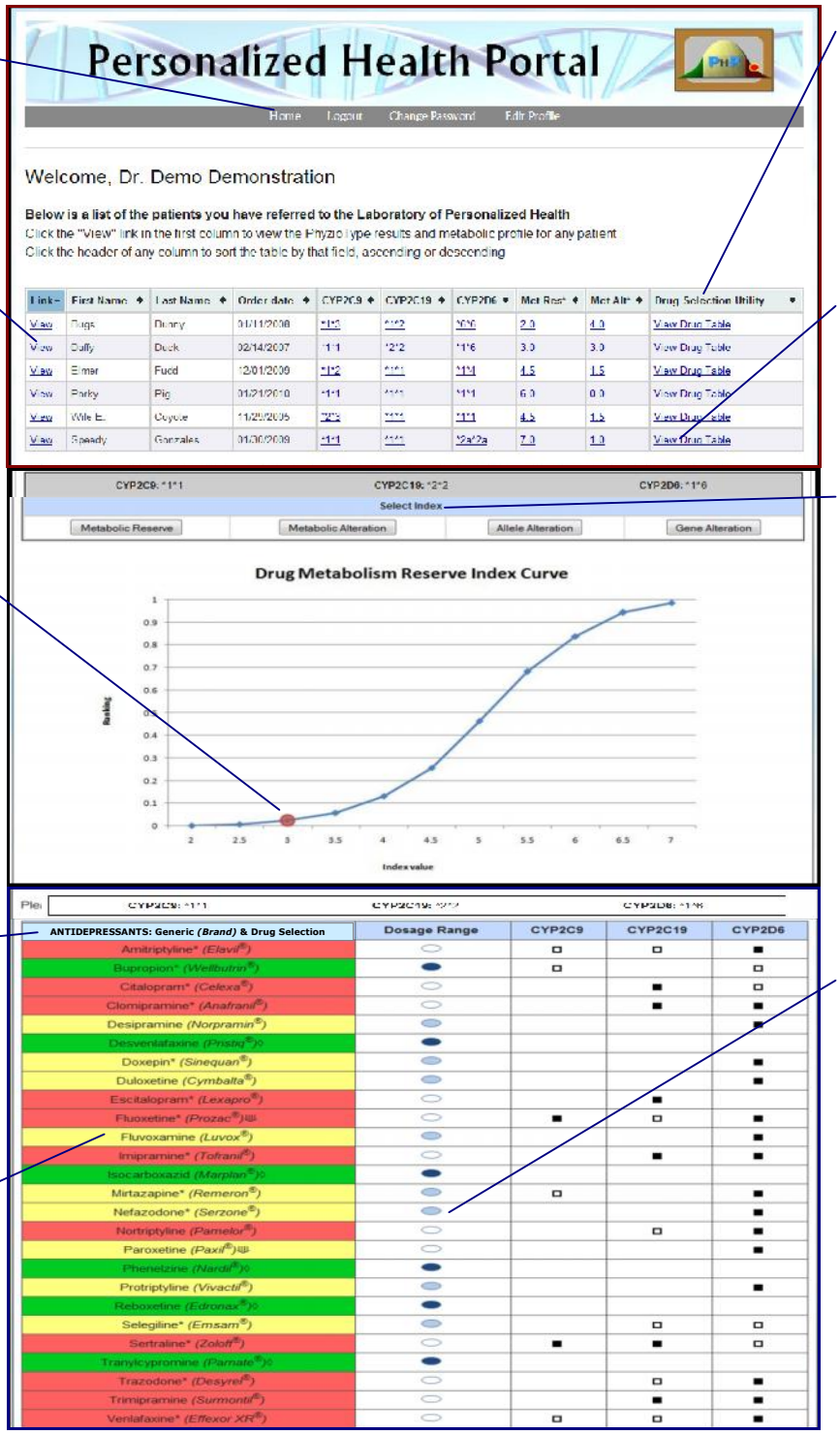
Password protected, interactive web interface for decision support

Secure on-line access to all of your patient's reports

Benchmarking of innate drug metabolism function for each patient

Intuitive format display guides drug selection by therapeutic class

Red denotes *Modify* drug choice; Yellow, *Monitor;* Green, *Use*



Gene Guidance for 250 Drugs: *130 Neuro-Psychiatric, 120 Cardio-Metabolic*

Provides guidance on Drug Interactions

Profile of patient's ability to metabolize drugs: Null, *No reserve*; Deficient, *Low reserve*; Functional *High reserve*; Supra, *Ultra high reserve*

Guidance on Dosing: empty ovals, *Below Normal* dosing; shaded, *Low Normal;* solid, *High Normal;* double solid, *Above Normal*

Laboratory of Personalized Health (LPH). Established in 2005 as a Division of Genomas, LPH is a high-complexity clinical DNA testing center. LPH is certified by the Centers for Medicare and Medicaid Services (CMS) under CLIA (Clinical Laboratory Improvement Amendments, ID #07D1036625) and licensed by the Connecticut Department of Public Health (license #CL-0644) and by the Rhode Island Department of Health (license #LCO-00591). HILO*met* PhyzioType has been used by more than 400 clinicians in Connecticut who have referred nearly 4,000 patients (as of September 2012).

Extensive Research and Publications. Genomas technology has been developed in partnership with the Institute of Living and Hartford Hospital, a major research-based New England medical center. The HILO*met* PhyzioType has been extensively published and presented at professional meetings. The Personalized Health Portal is copyrighted. A patent is pending on the HILO*met* PhyzioType.

GENOMAS PUBLICATIONS: *Selected Research Articles, Case Reports, Presentations, Patent, Copyright*

1. Ruaño *et al.* High Prevalence and Significant Pharmacokinetic Implications of the *CYP2C19* Gain-of-Function Allele **17* in Psychotropic-treated Patients. *American Psychiatric Association, Annual Meeting,* 2012
2. Rai *et al. CYP2C19* Genotype-Guided Antiplatelet Therapy in a Patient with Clopidogrel Resistance. *Connecticut Medicine,* 76 (5): 267-272, 2012
3. Windemuth *et al.* Validation of Candidate Genes Associated with Cardiovascular Risk in Psychiatric Patients. *Progress in Neuro-Psychopharmacology & Biological Psychiatry,* 36 (2): 213-219, 2012
4. Villagra *et al.* Novel Drug Metabolism Indices for Pharmacogenetic Functional Status Based on Combinatorial Genotyping of *CYP2C9*, *CYP2C19* and *CYP2D6* Genes. *Biomarkers in Medicine,* 5 (4): 427-438, 2011
5. Ruaño *et al.* Physiogenomic Analysis of *CYP450* Drug Metabolism Correlates Dyslipidemia with Pharmacogenetic Functional Status in Psychiatric Patients. *Biomarkers in Medicine,* 5 (4): 439-449, 2011
6. Landino *et al.* Guidance of Pharmacotherapy in a Complex Psychiatric Case by *CYP450* DNA Typing. *Journal of the American Academy of Nurse Practitioners,* 23 (9):459-463, 2011
7. Ruaño *et al.* Dyslipidemia in Psychotropic-treated Patients correlates with Combinatorial CYP450 Drug Metabolism Indices. *American Psychiatric Association, Annual Meeting,* 2011
8. Ruaño G *et al.* Physiogenomic Method for Predicting Antidepressant and Anxiolytic Drug Metabolic Risk. *U.S. Patent Application Publication US 2011/0098186A1, 2011*
9. Ruaño G *et al.* Longer Hospitalization Associated with Combinatorial CYP450 Metabolism Deficiencies. *American Psychiatric Association, Annual Meeting,* 2010
10. Namerow *et al.* Antidepressant-induced Mood Dysregulation: Association with CYP450 Alterations. *American Academy of Child and Adolescent Psychiatry, Annual Meeting, 2010*
11. Seip *et al.* Implementing genotype-guided antithrombotic therapy. *Future Cardiology*, 6 (3): 409-424, 2010
12. Ruaño. *Personalized Health Portal.* Copyright Registration Number VA 1-797-692, 2010
13. Ruaño *et al.* Utilization of Psychiatric Services is Associated with Pharmacogenetic Variation and Metabolic Deficiencies. *American Psychiatric Association, Annual Meeting,* 2009
14. Ruaño *et al.* Combinatorial CYP450 for Depressed Patients. *American Psychiatric Association, Annual Meeting,* 2008
15. Ruaño *et al.* Increased Carrier Prevalence of Deficient *CYP2C9, CYP2C19* and *CYP2D6* Alleles in Depressed Patients Referred to a Tertiary Psychiatric Hospital. *Personalized Medicine*, 5 (6): 579-587, 2008
16. Ruaño *et al.* High carrier prevalence of combinatorial *CYP2C9* and *VKORC1* genotypes affecting warfarin dosing. *Personalized Medicine*, 5 (3): 225-232, 2008
17. LaSala *et al.* Integrating Genomic Based Information into Clinical Warfarin (Coumadin®) Management: An Illustrative Case Report. *Connecticut Medicine,* 72 (7): 399-403, 2008
18. Ruaño *et al.* CYP Genotyping in Patients Treated for Depression. *American Psychiatric Association, Annual Meeting,* 2007
19. Ruaño *et al.* Somatic Complications of Psychotropic Medications in a Patient with Multiple CYP2 Drug Metabolism Deficiencies. *Connecticut Medicine,* 71: 197-200, 2007
20. Ruaño *et al.* Physiogenomic Comparison of Weight Profiles of Olanzapine- and Risperidone-Treated Patients. *Molecular Psychiatry,* 12: 474- 482, 2007
21. Ruaño *et al.* Physiogenomic Association of Statin Myalgia to Serotonin Receptors. *Muscle & Nerve,* 36: 329-335, 2007
22. Ruaño *et al.* High carrier prevalence of deficient and null alleles of CYP2 genes in a major USA hospital: Implications for personalized drug safety. *Personalized Medicine*, 3 (2): 131-137, 2006