CYP2D6 in Ibero American Populations

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San Juan de Puerto Rico 13.05.2010
Terminology: HISPANICS

The term *Hispanic* is derived from *Hispanicus*, which derived from *Hispania* (Iberian Peninsula), both of them Latin terms.

*Hispanic* is used to refer to modern Spain, to the Spanish language, and to the Spanish-speaking nations of the world and particularly the *Americas*.

Prior to the marriage of Queen Isabella I of Castile and King Ferdinand II of Aragon in 1469, the four Christian kingdoms of the Iberian Peninsula, namely the Kingdom of Portugal, the Crown of Aragon, the Crown of Castile, and the Kingdom of Navarre, were collectively referred to as *Hispania* - the Roman name for the Iberian Peninsula.

The expansion of the *Spanish Empire* between 1492 and 1898 brought thousands of Spanish migrants to the conquered lands, who established settlements, mainly in the Americas but also in other distant parts of the world, producing a number of multiracial populations.

http://upload.wikimedia.org/wikipedia/commons/.pn

In October 1469 Isabella I and Ferdinand II, heir to the throne of Aragon, married in secret in the *Palacio de los Vivero* in Castilian Valladolid.
• **Hernando de Soto** or (c.1496/1497 - 1542) was a Spanish explorer and conquistador who, while leading the first European expedition deep into the territory of the modern-day United States, was the first European documented to have discovered the Mississippi River.
Cabeza de Vaca

Cabeza de Vaca was born into the Spanish nobility in 1492.

Francisco Pizarro

He was an illegitimate son of Gonzalo Pizarro Rodríguez de Aguilar who as colonel of infantry served in the Italian campaigns under Gonzalo Fernández de Córdoba, and in Navarre, with some distinction.

Francisco was second cousin to Hernán Cortés, the famed conquistador of Mexico.

Marta Montañez Martínez

Enrique Martín Morales
Latino / Hispanics
Definitions in the United States

The terms *Hispanic* and *Latino* tend to be used interchangeably in the United States for people with origins in Spanish speaking countries.

Today the term *Hispanic* is typically applied to the varied populations of these places, including those with insignificant or no Spanish ancestry.

The U.S. Office of Management and Budget currently defines "Hispanic or *Latino*" as "a person of Mexican, Puerto Rican, Cuban, South or Central American, or other Spanish culture or origin, regardless of race". This definition excludes people of Portuguese origins, such as Portuguese Americans or Brazilian Americans. However, they are included in some government agencies' definitions.

*Hispanic and Latino Americans* are Americans with origins in the *Hispanic* countries of *Latin America* or in *Spain*.
Spanish speaking countries

Para ver esta película, debe disponer de QuickTime™ y de un descompresor.
Ibero-America is a term used since the second half of the 19th century to refer collectively to the countries in the Americas which were formerly colonies of Spain or Portugal.

Para ver esta película, debe disponer de QuickTime™ y de un descompresor.
Fármacos

Xenobióticos

P450

Endobióticos

Cáncer, neurotoxicidad, etc

Metabolismo endógeno

Variabilidad en la respuesta terapéutica
Variabilidad en los efectos adversos
1. Interindividual variability in drug response
2. CYPs pheno and genotyping in Spaniards
Debrisoquine hydroxylation phenotype (CYP2D6) in the Spanish Population (n=633) (LLerena et al 1988)

**CYP2D6 phenotype**

- Test substrate: DBQ
- 4-OH-debrisoquine

**Metabolic ratio**

\[
\frac{\% \text{ debrisoquine}}{\% \text{ 4-OH-debrisoquine}}
\]

**Ultrarapids**

- \(? \%\)

**5-7%**

**Extensive Metabolizers**

**Poor Metabolizers**

Número de individuos

Debrisoquina/4-OH debrisoquina (log₁₀)
1. Interindividual variability in drug response
2. CYPs pheno and genotyping in Spaniards

pheno/ genotypes
VARIABILITY IN DRUG RESPONSE: GENE-ENVIRONMENTAL INTERACTION Phenotype

- Occupation Exposure
- Smoking
- Diet
- Alcohol
- Drugs
- PVCs
- Drug metabolism
- Age
- Sex
- Pregnancy
- Exercise
- Starvation
- Infection
- Circadian Rhythm
- Cardiovascular Function
- G.I. Function
- Renal Function
- Hepatic Function

Adrián LLerena 2008
Gene-environmental interaction: CYP2D6 Pheno/ genotype

Ultrarrapids: DBQ Phenotypes

CYP2D6 Genotypes

(Dorado et al, 2005)

(LLerena et al, 1993)
Debrisoquine Metabolic Ratio in 925 Spanish Healthy Volunteers (LLerena et al., 1993)
CYP2D6
URs
Interethnic distribution of individuals with CYP2D6 gene duplicated
**CYP2D6 allelic frequency in the Spanish Population (n=142)**  
(LLerena et al 2007)

<table>
<thead>
<tr>
<th>Genotype</th>
<th>Predicted phenotype</th>
<th>Number of subjects</th>
<th>Genotype frequencies % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>wt/wtxN</td>
<td>UM</td>
<td>7</td>
<td>4.93 (2.23-10.0)</td>
</tr>
<tr>
<td>wxN/*4</td>
<td>EM or UM</td>
<td>2</td>
<td>1.41 (0.06-5.31)</td>
</tr>
<tr>
<td>wxN/*10</td>
<td>EM or UM</td>
<td>2</td>
<td>1.41 (0.06-5.31)</td>
</tr>
<tr>
<td>wt/*4xN</td>
<td>EM</td>
<td>2</td>
<td>1.41 (0.06-5.31)</td>
</tr>
</tbody>
</table>

**CYP2D6 duplication/multiplication among 142 Spanish healthy volunteers**  
(LLerena et al 2007)
Percentage of Spaniards with multiplication of $CYP2D6$

Llerena et al., (2007) → 9%

- IM (1 $CYP2D6$ act. gene) 1.4% (n=2)
- EM (2 or >2 $CYP2D6$ act. gene) 2.8% (n=4)
- UM (>2 $CYP2D6$ act. gene) 4.9% (n=7)

Percentage of $CYP2D6$ gene multiplications among Spanish healthy volunteers (n=13)
Interethnic variability: CYP2D6 gene multiplication and ultrarapid metabolism
(Reviewed by Dorado et al, 2006; LLerena et al 2007)
Debrisoquine hydroxylation phenotype (CYP2D6) in the Spanish Population (n=923) (LLerena et al 1993)

Debrisoquine hydroxylation polymorphism among 923 Spaniards (LLerena et al 1993)
Distribution of urinary debrisoquine/4'-OH log ratios in 925 Spanish Healthy Volunteers

Genes CYP2D6 activos:

- >3-20
- 1-2
- 0

Fenotipos:

- Ultrarápidos: 7-10%
- Rápidos (normales): 83-88%
- Lentos: 5-7%
CYP2D6

- **CYP2D6*2xN**
  - Gene multiplication
  - Incremento actividad

- **CYP2D6*4**
  - Defecto sitio splicing
  - Enzima inactiva

- **CYP2D6*5**
  - Deletion
  - No hay enzima

- **CYP2D6*10**
  - Pro34Ser Ser486Thr
  - Enzima inestable

- **CYP2D6*17**
  - Thr107Ile Arg296Cys Ser486Thr
  - Afinidad por el sustrato reducida

**PMs**

<table>
<thead>
<tr>
<th>CYP2D6 Allele</th>
<th>Caucasians</th>
<th>Asians</th>
<th>Black African</th>
<th>Ethiopians and Arabs</th>
</tr>
</thead>
<tbody>
<tr>
<td>CYP2D6*2xN</td>
<td>1-5</td>
<td>0-2</td>
<td>2</td>
<td>10-16</td>
</tr>
<tr>
<td>CYP2D6*4</td>
<td>12-21</td>
<td>1</td>
<td>2</td>
<td>1-4</td>
</tr>
<tr>
<td>CYP2D6*5</td>
<td>2-7</td>
<td>6</td>
<td>4</td>
<td>1-3</td>
</tr>
<tr>
<td>CYP2D6*10</td>
<td>1-2</td>
<td>51</td>
<td>6</td>
<td>3-9</td>
</tr>
<tr>
<td>CYP2D6*17</td>
<td>0</td>
<td>ND</td>
<td>34</td>
<td>3-9</td>
</tr>
</tbody>
</table>

*RIBEF - Adrián Llerena, Pedro Dorado 2004*
1. Interindividual variability in drug response
2. CYPs pheno and genotyping in Spaniards
3. Interethnic differences
4. CYP2D6 in Hispanics
CYP2D6 phenotypes
CYP2D6 genetic polymorphism: Interethnical variability

Debrisoquine hydroxylation phenotype (Cubans and Spaniards n=633)

- Cubanos
  - URs: 3.8%
  - MRs: 4.6%

- Españoles
  - URs: 7.2%
  - MRs: 4.9%

Idilio González, Med Clin 2007
Percentage of PMs of CYP2D6 in different populations phenotyped with debrisoquine

Figure 3. Percentage of debrisoquine PM in different populations. PM: Poor metabolizers.
Cuban-Caucasians 5.3%
Cuban-Mestizos 3.9%
Nicaraguan-Amerindians 6.0%
Spaniards 5.2%

Unpublished, (A. LLerena)
Iberogen consortium 2010

LLerena y cols., Datos no publicados
### MRs of debrisoquine among EMs individuals in Nicaraguan, Cuban and Spanish studied populations

<table>
<thead>
<tr>
<th>Population</th>
<th>N*</th>
<th>debrisoquine/4-OH debrisoquine</th>
<th>p†</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nicaraguans</td>
<td>118</td>
<td>1,5±1.6</td>
<td>--</td>
</tr>
<tr>
<td>Cuban-Mestizos</td>
<td>124</td>
<td>1.0±1.3</td>
<td>0.0001</td>
</tr>
<tr>
<td>Cuban-Caucasians</td>
<td>124</td>
<td>0.7±1.0</td>
<td>0.0001</td>
</tr>
<tr>
<td>Spaniards</td>
<td>880</td>
<td>0.9±1.3</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

N*=number of EMs  
†Compared with Nicaraguans by using t-test.

Unpublished, (A.LLerena)  
Iberogen consortium 2010

LLerena y cols., Datos no publicados
<table>
<thead>
<tr>
<th>CYP2D6 alleles</th>
<th>Cuban-Caucasians (n=260)</th>
<th>Cuban-Mestizos (n=252)</th>
<th>Nicaraguan-Amerindian (n=196)</th>
</tr>
</thead>
<tbody>
<tr>
<td>wt (*1 or *2)</td>
<td>0.754</td>
<td>0.663</td>
<td>0.761</td>
</tr>
<tr>
<td>*3</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>*4</td>
<td>0.146</td>
<td>0.143</td>
<td>0.142</td>
</tr>
<tr>
<td>*5</td>
<td>0.019</td>
<td>0.016</td>
<td>0.046</td>
</tr>
<tr>
<td>*6</td>
<td>0.008</td>
<td>0.012</td>
<td>0</td>
</tr>
<tr>
<td>*10</td>
<td>0.004</td>
<td>0.008</td>
<td>0.031</td>
</tr>
<tr>
<td>*17</td>
<td>0.027</td>
<td>0.102</td>
<td>0</td>
</tr>
</tbody>
</table>

**Duplications**

| wt (*1 or *2)xN | 0.038                    | 0.047                  | 0.020                       |
| *4xN           | 0.004                    | 0                      | 0                           |

n= number of alleles.
<table>
<thead>
<tr>
<th>País</th>
<th>Grupo</th>
<th>N</th>
<th>% PMs **</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cuba</td>
<td>Blanco</td>
<td>131</td>
<td>5.3 (DBQ)</td>
<td>González y cols., 2007</td>
</tr>
<tr>
<td>Cuba</td>
<td>Mestizo</td>
<td>129</td>
<td>3.9 (DBQ)</td>
<td>González y cols., 2007</td>
</tr>
<tr>
<td>España</td>
<td>Español</td>
<td>925</td>
<td>4.9 (DBQ)</td>
<td>LLerena y cols., 1993</td>
</tr>
<tr>
<td>Nicaragua</td>
<td>Nicaragüense</td>
<td>125</td>
<td>5.6 (DBQ)</td>
<td>LLerena y cols., unpub.</td>
</tr>
<tr>
<td>Panamá</td>
<td>Cuna</td>
<td>89</td>
<td>0 (DBQ)</td>
<td>Jorge y cols., 1990</td>
</tr>
</tbody>
</table>
CYP2D6 GENOTYPES
Unpublished, (P. Dorado)
Iberogen consortium 2010
CYP2D6 alleles in different geographic populations

(Sistonen, 2008)
CYP2D6 alleles in different geographic populations

(Sistonen, 2008)
Frequency of CYP2D6 alleles

- Spain10 White
- Colombia2 Mestizo
- Nicaragua9 Mestizo
- Cuba4 Mestizo
- Cuba4 White
- Colombia-Panama3 Ngawbe
- Mexico5 Mestizo
- Colombia-Panama3 Embera
- Mexico Mestizo
- Mexico-USA8 Mestizo
- Mexico6 Mestizo
- Chile1 Mapuche
- Mexico7 Tepehuano

Dorado 2009

Unpublished, (P.Dorado)
Iberogen consortium 2010
CHAPTER

Pharmacogenetics of Cytochrome P450 in Hispanic Populations

Pedro Dorado, Guilherme Suarez-Kurtz and Adrián LLerena*
Variabilidad en la respuesta terapéutica
Variabilidad en los efectos adversos
1. Interindividual variability in drug response
2. CYPs pheno and genotyping in Spaniards
3. Interethnic differences: UR in Spaniards
4. CYP2D6 in Hispanics

5. CYP2D6 and endogenous metabolism: personality
Nevertheless, further studies should be done to standardise the selection procedures for healthy volunteers participating in clinical trials. Otherwise, the results obtained would be very difficult to extrapolate to the general population.

Department of Pharmacology,
Medical School,
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A. LLERENA
J. COBALEDA
J. BENÍTEZ

Llerena et al. Lancet 1987
Llerena et al, Acta Psych Scand 1993
1. Relationship between CYP2D6 polymorphism and profession (LLerena, 1988)

2. Association between the participation like healthy volunteer in clinical trials and debrisoquine Poor Metabolizer (LLerena et al., 1989).

3. Relationship between CYP2D6 activity and personality in a Swedish population (Bertilsson et al., 1989)
6. Relationship between CYP2D6 activity and personality (KSP – TCI) psychopathology and Nerocognition (Peñas-LLedó et al., 2009 July)


2008. Personality (KSP) in Cubans (González I et al 2008)

1. Psychological factors in Healthy Volunteers

2. Association between the participation like healthy volunteer in clinical trials and debrisoquine Poor Metabolizer (LLerena et al., 1989).

DEBISOQUEINE HYDROXYLATION PHENOTYPES IN HEALTHY VOLUNTEERS

Sir,—Dr Bertilsson and colleagues (March 11, p 555) report differences in personality between poor and extensive hydroxylators of debrisoquine in a previously phenotyped Swedish population.1 We also had the impression that poor hydroxylators differ in personality from extensive hydroxylators in two Spanish populations studied by us.2,3

We have recently done a phase I clinical trial to study the kinetics of a non-steroid anti-inflammatory agent for which we had to recruit six healthy volunteers. We offered the chance to participate in the study to thirteen medical students, of whom seven accepted. However, one could not be included because of a skin disease. Before the trial the volunteers were phenotyped, three of them being poor hydroxylators of debrisoquine (urinary ratio of debrisoquine greater than 12:6 after administration of 10 mg of the drug). Although the numbers of students contacted and agreeing to participate are small we find it remarkable that half the participants were poor hydroxylators of debrisoquine. This contrasts with the 25 (6:6%) poor metabolisers found among 377 Spaniards previously studied.4 Whether this is due to “ease of decision making”, claimed by Bertilsson and colleagues to be associated with the poor hydroxylator phenotype, or is merely fortuitous is difficult to say.

Nevertheless, further studies should be done to standardise the selection procedures for healthy volunteers participating in clinical trials. Otherwise, the results obtained would be very difficult to extrapolate to the general population.

Department of Pharmacology, Medical School, University of Extremadura, 06071 Badajoz, Spain

A. LLerena

Relationship between CYP2D6 activity and personality in a Spanish population (LLerena et al., 1993):

**Hypothesis**

Fig. 1. Illustration of two possible connections between debrisoquine hydroxylation phenotype and personality. Hypothesis 1: the liver or brain debrisoquine hydroxylase metabolizes an unknown endogenous substance of importance for central nervous system activity and personality. Hypothesis 2: there might be a linkage between the debrisoquine hydroxylase gene (CYP2D6) on chromosome 22 and a gene regulating an unknown enzyme (or receptor etc.) of importance for personality.

**Methods**

Fig. 2. Distribution of the urinary metabolic ratio (MR) of debrisoquine:4-hydroxydebrisoquine in 925 healthy Spanish subjects. The KSP inventory was distributed to all 83 poor metabolizers (PM) (MR > 12:1) and to 100 age- and sex-matched extensive metabolizers (EMs) of debrisoquine. The 225 subjects participating in the study are indicated as dark bars. The EM subjects were divided into EM1 (very rapid EMs), EM2 (intermediate EMs) and EM3 (slow EMs).

PMs were more anxiety-prone and less successfully socialized than EMs.
4. Relationship between CYP2D6 activity and personality in a Spanish population (LLerena et al., 1993)

**Relationship between personality and debrisoquine hydroxylation capacity**

Suggestion of an endogenous neuroactive substrate or product of the cytochrome P4502D6


We administered the Karolinska Scales of Personality to 225 healthy subjects in Spain selected from a group of 925 individuals previously phenotyped with regard to their capacity to hydroxylate debrisoquine. A significant relationship was found between the scores in as many as 4 of the 15 subscales (psychic anxiety, psychasthenia, inhibition of aggression and socialization) and the debrisoquine hydroxylation capacity. Poor metabolizers were more anxiety-prone and less successfully socialized than extensive metabolizers of debrisoquine. This and a previous study among subjects in Sweden suggest that there may be a relationship between personality and the activity of the enzyme hydroxylating debrisoquine (cytochrome P4502D6). This polymorphic enzyme may have an endogenous neuroactive substrate or product, such as a biogenic neurotransmitter amine.

Key words: pharmacogenetics; debrisoquine; personality

Lof Bertilsson, Department of Clinical Pharmacology, Karolinska Institute, Huddinge Hospital, S-14186 Huddinge, Sweden

Accepted for publication August 27, 1992
Relation between CYP2D6 phenotype and genotype and personality in healthy volunteers

**CYP2D6 & SNC amines**

- **Dopamine**
  - Bertilsson et al, 1989
  - LLerena et al, 1989
  - LLerena et al, 1993

- **Serotonin**
  - Ozdemir et al, 2006

**Neurocognition**

- Peñas-LLedó et al, 2009

**Personality**

- Pacheco-Puig, 2008

**Metabolites**

- Miksys and Tyndale, 2004

**Drugs**

- LLerena et al, 1993


**Endobiotics**

- 2008-09
Relation between CYP2D6 genotype, personality, neurocognition and overall psychopathology in healthy volunteers.

Peñas-LLedó EM, Dorado P, Pacheco R, González I, LLerena A.

CYP2D EXPRESSION IN THE HUMAN BRAIN

(Miksys and Tyndale, 2004)
Psychiatric Patients: *CYP2D6* PMs & Schizophrenia

CYP2D6 has been suggested to be functionally similar to the dopamine transporter. The present study was aimed at analyzing the frequency of CYP2D6 alleles and genotypes among schizophrenic patients compared to healthy volunteers. CYP2D6 *CYP2D6* *CYP2D6* alleles were identified in 101 unrelated schizophrenic patients and 142 unrelated white European volunteers. The frequency of the CYP2D6 active allele was lower in psychiatric patients than in healthy volunteers. The hypothesis of a potential role of CYP2D6 in the vulnerability to schizophrenia was supported by the lower frequency of PMs in schizophrenic patients compared to healthy volunteers.

<table>
<thead>
<tr>
<th>CYP2D6 Genotype (no. active genes)</th>
<th>CYP2D6 genotypes</th>
<th>Schizophrenic patients (n=101)</th>
<th>Healthy Volunteers (n=142)</th>
</tr>
</thead>
<tbody>
<tr>
<td>UM (&gt;2)</td>
<td>wt/wtxN</td>
<td>5 (5%)</td>
<td>7 (4.9%)</td>
</tr>
<tr>
<td>EM (2)</td>
<td>wt/wt; wtxN/*4; wt/*10; wtxN/*10</td>
<td>69 (68,3%)</td>
<td>76 (53,5%)</td>
</tr>
<tr>
<td>IM (1)</td>
<td>wt/*4; wt/*4xN; wt/*6; wt/*5; *5/*10</td>
<td>24 (23,7%)</td>
<td>47 (33%)</td>
</tr>
<tr>
<td>PM (0)</td>
<td>*4/*4; *4/*6; *5/*6; 6/*6</td>
<td>3 (3%)</td>
<td>12 (8,5%)</td>
</tr>
</tbody>
</table>

(LLLerena A et al., The Pharmacogenomics Journal 2007).
CYP2C9*3 as a risk factor for major depression. (LLerena A et al., The Pharmacogenomics Journal 2004).

The CYP2C9*3 allele frequency was higher (p<0.01) among the depressive patients than in the population of schizophrenic patients (odds ratio=3.3) and healthy volunteers (odds ratio=2.8).
### CYP2C9 genetic polymorphism: Interethnical variability

<table>
<thead>
<tr>
<th>Population</th>
<th>n</th>
<th>CYP2C9 *1</th>
<th>CYP2C9 *2</th>
<th>CYP2C9 *3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spanish</td>
<td>276</td>
<td>0.78</td>
<td>0.14</td>
<td>0.08</td>
</tr>
<tr>
<td>White-Americans</td>
<td>280</td>
<td>0.83</td>
<td>0.13</td>
<td>0.04</td>
</tr>
<tr>
<td>White-Americans</td>
<td>200</td>
<td>0.86</td>
<td>0.08</td>
<td>0.06</td>
</tr>
<tr>
<td>Swedish</td>
<td>860</td>
<td>0.82</td>
<td>0.11</td>
<td>0.07</td>
</tr>
<tr>
<td>British</td>
<td>200</td>
<td>0.79</td>
<td>0.13</td>
<td>0.09</td>
</tr>
<tr>
<td>Italians</td>
<td>314</td>
<td>0.80</td>
<td>0.11</td>
<td>0.09</td>
</tr>
<tr>
<td><strong>Total caucasians</strong></td>
<td>2444</td>
<td>0.80</td>
<td>0.12</td>
<td>0.08</td>
</tr>
<tr>
<td>Indo-europeans</td>
<td>1812</td>
<td>0.80</td>
<td>0.11</td>
<td>0.08</td>
</tr>
<tr>
<td>Africans</td>
<td>740</td>
<td>0.96</td>
<td>0.03</td>
<td>0.01</td>
</tr>
<tr>
<td>Asians</td>
<td>2494</td>
<td>0.97</td>
<td>---</td>
<td>0.03</td>
</tr>
<tr>
<td><em>Mexican-Americans</em></td>
<td>98</td>
<td>0.86</td>
<td>0.08</td>
<td>0.06</td>
</tr>
</tbody>
</table>

*LLerena et al, 2005. The Pharmacogenomic Journal
Center for Pharmacogenomics and Clinical Pharmacology. UCLA, USA.*

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University of Extremadura, Spain
University of Beira Interior, Portugal

Center for Pharmacogenomics & Clinical Pharmacology
David Geffen School of Medicine. Neuropsychiatric Institute

UCLA
Para ver esta película, debe disponer de QuickTime™ y de un descompresor.
Chapter 5

Pharmacogenetics of Cytochrome P450 in Hispanic Populations

Pedro Donadio, Guillermo Suarez-Kurtz and Adrián LLerena

Abstract

The present review focuses on the pharmacogenetics of the cytochrome P450 (CYP) enzymes in Hispanic populations, encompassing the people living in Spanish-speaking countries in Latin America as well as those originating or Hispanic in the United States. We acknowledge the diversity of these peoples by their country of origin or residence, nature, and genetic composition, the latter resulting from genomics of different origins of between American, European, and African. This diversity is reflected in the frequency distribution of polymorphisms of the CYP genes that code for the main CYP enzymes involved in the metabolic formation of xenobiotics, namely CYP2D6, CYP2C19, CYP3A4, CYP1A1, CYP1B1, CYP2C9, CYP2C8, and CYP3A5. Our review of the literature disclosed that for all these CYPs, only in Mexicans or Puerto Ricans American. For other populations, including several American groups, scattered information was processed on individual CYPs. For several Latin American countries, no information could be retrieved on any of these enzymes or related other pharmacogenetics.

With the purpose of filling this information gap and to promote collaborative pharmacogenetics research in Spanish- and Portuguese-speaking peoples in the Americas and the Hispanic population, a network—the Hispanic American Network of Pharmacogenetics and Pharmacogenomics—was recently created. This initiative represents a promising step towards the inclusion of Latin American populations among those who will benefit from the implementation of pharmacogenetic principles and tailoring therapy.
La globalización obligará a cambiar la idea del sistema sanitario internacional

El curso de verano sobre salud global concluye con una jornada dedicada a las implicaciones éticas y sociales del desarrollo biotecnológico

Badajoz 9 de Julio de 2007
RED IBEROAMERICANA DE FARMACOGENETICA: IMPACTO EN SALUD PUBLICA

GRUPOS PARTICIPANTES
Existen una amplia representacion de la comunidad Iberoamericana, 12 grupos de 16 países, que van de norte a sur (desde la Patagonia chilena hasta Dunango en Mexico) y de este a oeste (desde Lima en Peru hasta Rio de Janeiro en Brasil), incluyendo Leon (Nicaragua), Bogota (Colombia) y la Habana (Cuba), además de la Peninsula Ibérica (Portugal y España).

| Genetab. Universidad Nacional de La Plata (GENELAB) | Buenos Aires, ARGENTINA |
| Hospital Psiquiatrico y Centro de Salud Mental de la Habana Vieja (HPS) | La Habana, CUBA |
| Instituto Nacional de Cancer (INCA) | Rio de Janeiro, BRASIL |
| Instituto Politecnico Nacional (INP) | Mexico City, MEXICO |
| Pontificia Universidad Javeriana (PUJ) | Bogota, COLOMBIA |
| Universidad Austral de Chile (UACh) | Puerto Montt, CHILE |
| Universidad de Extremadura (UEX) | Badajoz, ESPAÑA |
| Universidad del Rosario (UR) | Bogota, COLOMBIA |
| Universidad Nacional Autonoma de Nicaragua (UNAN-MANAGUA) | Leon, NICARAGUA |
| Universidad Nacional Mayor de San Marcos (UNMSM) | Lima, PERU |
| Universidad de la Beira Interior (IBI) | Coimbra, PORTUGAL |
| Universidad de Algarve (UALG) | |

Pending:
- Bolivia
- Paraguay

RESEARCH:
01. Argentina (2)
02. Brasil
03. Chile
04. Colombia (2)
05. Cuba (2)
06. España
07. México (2)
08. Nicaragua
09. Perú (2)
10. Portugal (2)
11. Ecuador
12. Uruguay

Rep.
- Dominicana
- Guatemala
- El Salvador
- Costa Rica
- Venezuela

Pendiendo:
- Bolivia
- Paraguay
Área geográfica de la Red RIBEF CYTED206RT0290 (2006-2009)

Movilidad
- RCA 2007
- RCA 2006
- RCA 2009

Docencia
- RCA 2008

Investigación

Coordinación

Europa
- España
- Portugal

Norteamérica
- México

Caribe
- Cuba
- R.Dominicana

Centroamérica
- Guatemala
- El Salvador
- Honduras

América del Sur
- Ecuador
- Colombia
- Venezuela
- Perú
- Brasil
- Bolivia
- Paraguay
- Uruguay
- Chile
- Argentina

RCA 2006
RCA 2007
RCA 2008
RCA 2009
Actividades del RIBEF

Cursos y Simposios
Conf y Sem
Talleres
Pasantías
DEA, Maestrías y Doctorados

número
Cursos y Simposios por año
Conferencias y Seminarios por año
Pasantías por año

![Bar chart showing the number of pasantías per year from 2006 to 2009-10. The number of pasantías increases from 2006 to 2007, remains steady in 2008, and significantly increases in 2009-10.](chart.png)
Talleres por año

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Actividades por año

![Bar graph showing the number of activities by year from 2006 to 2009-10.]
Actividades por año
CYP2D6 genotypes in Iberoamerica
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<td>Negros</td>
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<td><strong>2689</strong></td>
</tr>
</tbody>
</table>
Unpublished, (A.LLerena)
Iberogen consortium 2010
Para ver esta película, debe disponer de QuickTime™ y de un descompresor.
This research is devoted to all patients participating in the studies; their suffering is our main motivation.
Hospital Universitario Infanta Cristina

Alcazaba árabe de Badajoz. Siglo IX

allerena@unex.es