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S.C. Supreme Court

STATE OF SOUTH CAROLINA

IN THE SUPREME COURT

Appeal from Charleston County

Roger M. Young, Circuit Court Judge

BROOKE JEWELL,

PETITIONER,

V.

STATE OF SOUTH CAROLINA,

RESPONDENT

Appellate Case No. 2013-000898

SUPPLEMENTAL APPENDIX

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Science that benefits humanity

ATTACHMENT A

DNA DRUG SENSITIVITY TEST (DST) RESULTS
Cytochrome P450 2D6 Test

Genelex Laboratory #	CRM 15776	Report Date:	June 17, 2010
Patient Name:	Brooke A. Jewell	Collection Date:	6/1/2010
Date of Birth:	11/3/1973	Sample Type:	Buccal Swab
Cytochrome P450 2D6 Genotype	DST- CYP 2D6 *4 / *4 (Poor Metabolizer)		
(Phenotype) Interpretation:			

Laboratory Director: Teresa H. Aulinskas, Ph.D.

Laboratory Test Interpretive Comments:

Normal metabolizers represent the norm for metabolic capacity. In general normal metabolizers can be administered drugs which are substrates of the CYP2D6 enzyme following standard dosing practices. Genotypes consistent with the normal metabolizer phenotype include two active CYP2D6 alleles or one active and one partially active CYP2D6 allele. Increased caution may be appropriate for individuals having one partially active allele.

Intermediate metabolizers may require lower than average drug dose for optimal therapeutic response to medications with the exception of prodrugs. For the majority of drugs consider decreased dosage. For prodrugs, like tamoxifen, that require activation by CYP2D6, an alternative treatment or increased dose should be considered. Genotypes consistent with the intermediate metabolizer phenotype are those with one active and one inactive CYP2D6 allele, one inactive and one partially active CYP2D6 allele, or two partially active CYP2D6 alleles.

Poor metabolizers are at increased risk of drug-induced side effects due to diminished drug elimination or for prodrugs, like tamoxifen, lack of therapeutic effect resulting from failure to generate the active form of the drug. Alternative treatment should be considered. Genotypes consistent with the poor metabolizer phenotype are those with no active CYP2D6 alleles.

Ultra metabolizers exhibit higher than average rates of metabolism. Ultra metabolizers are at increased risk of therapeutic failure due to increased drug elimination and thus may require an increased dose of drugs that are inactivated by CYP2D6. For prodrugs, ultra metabolizers may also be at increased risk of drug-induced side effects due to increased exposure to active drug metabolites, in which case they may require lower than average doses. Genotypes consistent with ultra metabolizer phenotype include three or more active CYP2D6 alleles due to duplication of an active allele.

Co-administration of other drugs. Genotype results should be interpreted in context of the individual clinical situation including co-administration of other drugs, hepatic and renal function. In all cases monitor for co-administration of CYP2D6 inhibitors which may convert patients to poor metabolizer status. Potential adverse outcomes included overdose toxicity or treatment failure particularly for prodrugs. For more information see GeneMedRx drug-drug and drug-gene interaction software and Cytochrome P450 Metabolism Inhibitor/Inducer Tables. Access GeneMedRx via the patient access code provided at www.GeneMedRx.com/DNAlogin.

DNA Drug Sensitivity Test (DST) Cytochrome P450 CYP2D6 alleles tested:

Active alleles: CYP2D6 *1 or *2

Partially active alleles: CYP2D6 *9 or *10 or *17 or *41

Inactive alleles: CYP2D6 *3 or *4 or *5 (deletion) or *6 or *7 or *8 or *11 or *12 or *14 or *15

Gene Duplication: CYP2D6 *1 or *2 or *4 or *10 or *41

Analytical specificity and sensitivity for detection of these mutations are 99%. Other known variants not listed are not detected (< 5% of the population for Caucasians).

Note: This is a list of all tested markers and is no indication of your genetic profile. Your genotype is in the box above.

For more detailed information visit our website at www.healthandDNA.com

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Science that benefits humanity

DNA DRUG SENSITIVITY TEST (DST) RESULTS
Cytochrome P450 2D6 Test

Clinical Indication for Testing:

For individuals with a personal or family history of adverse drug reactions to medications metabolized by CYP2D6. Confirm presence of genotypes that affect metabolism of tamoxifen and any drugs that are metabolized by cytochrome CYP2D6.

Methodology:

This assay detects all common and most rare CYP2D6 variants with known clinical significance. Laboratory specimens were analyzed for 17 nucleotide variants and two gene rearrangements using PCR based technologies. The performance of this assay was validated by Genelex Corporation. Rare CYP2D6 variants may not yet have been observed at Genelex (<1% of the population). This test does not detect polymorphisms other than those listed. Other polymorphisms in the primer binding regions can affect the testing, and ultimately, the genotyping assessments made. Rare diagnostic errors may occur due to primer site mutations. Drug metabolism may be affected by non-genetic factors. DNA testing does not replace the need for clinical and therapeutic drug monitoring. As with all laboratory testing there is a possibility of error. Genelex Corporation is certified by the Clinical Laboratory Improvement Amendments (CLIA No. 50D0980559) and as Washington State Medical Test Site No. MTS-39190 is qualified to perform high complexity clinical testing. Genetic counseling is recommended.

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For more detailed information visit our website at www.healthandDNA.com

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CURRICULUM VITAE

David T. Kurtz Ph.D.

Born: November 11, 1951, Akron Ohio

Home address:

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Department of Pharmacology
Room 319F BSB
Medical University of South Carolina

EDUCATION:

Princeton University, N.J.	A.B.	1973	Biochemistry
Columbia University, N.Y.	M.A.	1975	Biochemistry
Columbia University, N.Y.	Ph.D.	1978	Biochemistry

PROFESSIONAL EXPERIENCE:

Columbia University, Institute of Cancer Research
Research Associate, January 1978 - December 1978

Cold Spring Harbor Laboratory
Staff Investigator, January 1979 - December 1980

Cold Spring Harbor Laboratory, Senior Staff Investigator, Head,
Section on Hormonally Regulated Genes, January 1981 - August, 1986

Medical University of South Carolina, Department of Pharmacology
Associate Professor January 1994-2000
Professor 2001-present

GRANT SUPPORT**As principal Investigator:**

R01 DK46446-01 Transcription factors and secondary steroid response.
(04/01/93 - 03/31/96) Total direct costs, \$371,883

NIH R01 AM 26969-01-06 (1980 – 1986) DNA sequences involved in the hormonal regulation of rat α 2u globulin. Total direct costs, \$389,226

NIH P01 CA29569 (1981 – 1985) Section on hormonal control of gene expression.
Total direct costs, \$509,783

As Co-investigator:

NIH 1 R01 CA69598-02 (09/01/97 – 06/30/02) Induction and Analysis of Murine Prostate Cancer (10% time and effort) with Dr. James Norris. Annual direct costs, \$167,895

DOE DE-FC02-98CH10902 (10/1/98-9/30/99) Environmental Hazards Assessment Program/Environmental Biosciences Program (20% time and effort) Dr. Lawrence. Mohr, P.I. \$ 71,243

NIH R01 CA78887-01 (04/01/00 – 03/31/05) Inhibition of IFG Mediated Carcinogenesis (5% time and effort) with Dr. Steven Rosenzweig, \$900,000

NIH R01 GM27673 (07/01/00 – 06/30/05) Role of Eicosanoids in shock (10% time and effort) with Dr. James A. Cook, \$1,250,000

R01 HL 42040 (12/1/90-11/30/95) Sodium/Calcium Exchange Across Cardiac Sarcolemma. Co-investigator (20% time and effort) with Dr. George Lindenmayer. Annual direct costs, \$146, 503

R01 HL 36838 (7/1/86-3/31/95) Thromboxane A2 receptors in health and disease. Coinvestigator (10% time and effort) with Dr. Perry Halushka. Annual direct costs, \$164,214

R01 HL44671 (5/1/91-4/30/95) Kinins and Epithelial Ion Transport Mechanisms. Coinvestigator (10% time and effort) with Dr. Harry Margolius. Annual direct costs, \$123,869

NIH 1 R01 CA69598-02 (07/01/98-06/30/99) Induction and Analysis of Murine Prostate Cancer (10% time and effort) with Dr. James Norris. Annual direct costs; \$167,895

PUBLICATIONS

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Feigelson, P. and Kurtz, D.T. (1977). Hormonal modulation of α 2u globulin: sequence measurements using a specific cDNA probe. *Cold Spring Harbor Symp. Quant. Biol.* Volume XLII pp. 659-663.

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Scholarly Books and Monographs

Watson, J.D., Tooze, J. and Kurtz, D.T. *Recombinant DNA: a Short Course.* Scientific American Books, New York, 1984.

Chapters in Scholarly Monographs and Books

Kurtz, D.T. and Feigelson, P. (1978). Multihormonal control of the messenger RNA for the Hepatic protein α 2u globulin in "Biochemical Actions of Hormones" (G. Litwack, ed.) Vol. 5 pp. 433-435.

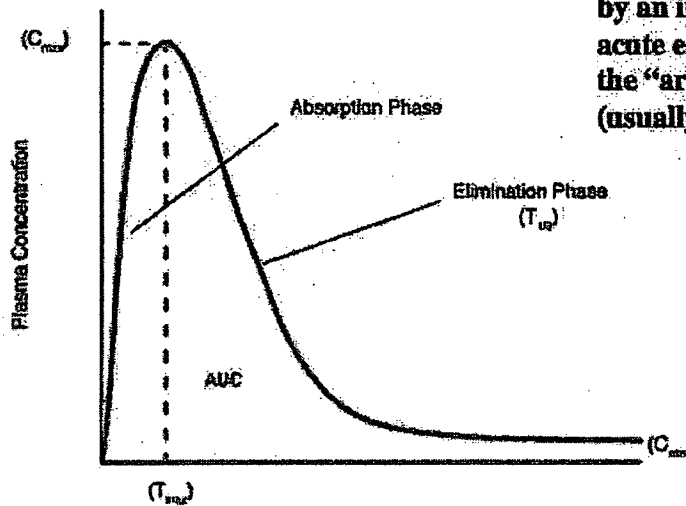
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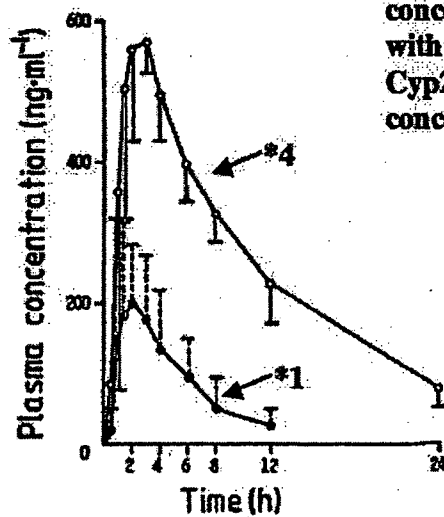
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The length of time that an active drug remains in the body is based on its rate of breakdown and its rate of excretion. A typical example is shown:



Excess side effects may be caused by an increase in C_{max} (usually acute effects) or by an increase in the "area under the curve" (AUC) (usually more chronic side effects)

In an individual that breaks down the drug more slowly (such as Mr. Jewell), both the peak concentration and the AUC will be increased, which increase the likelihood of side effects.



A hypothetical comparison between the blood concentrations of Paxil in an individual with Cyp2D6*1 (the "normal" gene) and one with Cyp2D6*4. Note that both the peak blood concentration and the AUC are increased.

In Moore et al. (2010) Prescription Drugs Associated with Reports of Violence Towards Others. PLoS ONE 5(12): e15337. doi:10.1371/journal.pone.0015337, it was reported that:

" Acts of violence towards others are a genuine and serious adverse drug event associated with a relatively small group of drugs. Varenicline, which increases the availability of dopamine, and antidepressants with serotonergic effects were the most strongly and consistently implicated drugs."

Paxil (paroxetine) is in the category of " antidepressants with serotonergic effects".

The authors further state:

" Violence cases as defined here were infrequently reported, accounting for 0.25% of all serious adverse drug events, and confined to a relatively small number of drugs.

This analysis shares many limitations common to studies based on spontaneously reported adverse drug events. The submission of an individual adverse event report does not itself establish causality, only that a reporting individual suspected a relationship existed."

The conclusion of this peer-reviewed manuscript is that violence is indeed a very rare side effect of Paxil, but specific cases have been reported.

HOU 2000-08-03476

WITNESSES

JOHN BURNETT AND/OR

KEITH HAIR

BUNCUM, CCSSO

2000-017589-B

DOCKET NO. 2000-GS-10-0747

The State of South Carolina

County of Charleston

COURT OF GENERAL SESSIONS

OCTOBER TERM 2000

THE STATE

vs.

BROOKE ALEXANDER JEWELL

ARREST WARRANT NUMBER

G432365

JULY 17, 2000

ACTION OF GRAND JURY

FORFEITURE

OCT 09 2000

Forfeiture of Grand Jury

VERDICT

BURGLARY FIRST DEGREE

Indictment for

Foreperson of Petit Jury

Date:

HOU 2000-08-03476

WITNESSES

JOHN BURNETT AND/OR

KEITH HAIR

BUNCUIM CCSSO

2000-017589-B

DOCKET NO. 2000-GS-10-6748

The State of South Carolina

County of Charleston

COURT OF GENERAL SESSIONS

OCTOBER TERM 2000

THE STATE

VS.

BROOKE ALEXANDER JEWELL

ARREST WARRANT NUMBER

G432366

JULY 17, 2000

ACTION OF GRAND JURY

RETURN

OCT 9 2000

Foreperson of Grand Jury

VERDICT

Indictment for

**CRIMINAL SEXUAL CONDUCT IN THE
FIRST DEGREE**

Foreperson of Petit Jury

Date:

STATE OF SOUTH CAROLINA)
)
COUNTY OF CHARLESTON)

INDICTMENT FOR
CRIMINAL SEXUAL CONDUCT IN THE FIRST
DEGREE

At a Court of General Sessions, convened on October 9, 2000 the Grand Jurors of Charleston County present upon their oath:

That Brooke Alexander Jewell did in Charleston County on or about July 12, 2000, while using aggravated force and/or during the commission of a burglary, commit a sexual battery against Jennifer Anne Simon, without her consent and against her will. This is in violation of §16-3-652 of the South Carolina Code of Laws (1976) as amended.

Against the peace and dignity of the State, and contrary to the statute in such case made and provided.



ASSISTANT SOLICITOR