Volume 4

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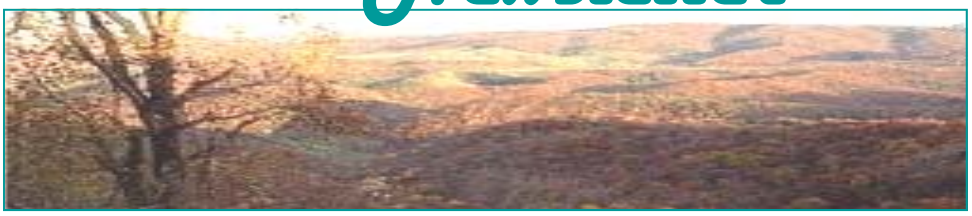
Newsletter



WV-INBRE Holds Summer Research Symposium
Research!America President Featured Speaker

As the culmination of the 2004 summer research program, the WV-INBRE held its third annual Summer Research Symposium on August 5, 2004, at the Robert C. Byrd Health Sciences Center of West Virginia University. The day was highlighted by oral and poster presentations by summer student interns and faculty fellows describing the projects they conducted during the nine-week program. Thirty-nine poster presentations were on display with authors discussing research with faculty and students from around the state.

Mary Woolley, President of **Research!America** gave the keynote address entitled "A Career in Medical Research: The Challenge of Meeting a Public Priority."

Ms. Woolley emphasized that the American public is very supportive of basic biomedical research; Americans rank scientists as the most prestigious occupation. She encouraged the audience to become advocates for science and told the student interns that a career in science serves the public's interest.

Research!America is a not-for-profit, membership-supported public education and advocacy alliance founded in 1989. Their 475 member institutions represent the voices of more than 40 million Americans striving to make medical and health research—including research to prevent disease, disability and injury and to promote health—a higher national priority. Research!America's work, including advocacy-related materials and programs, focuses on educating decision makers and opinion leaders about the critical need to increase the nation's investment in medical and health research. In addition to her position at Research!America, Ms. Woolley serves on several boards and committees, including the National Council for Johns Hopkins nursing and the Overseers of the Harvard School of Public Health. She is a member of the Institute of Medicine and a fellow of the American Association for the Advancement of Science.

Supported by: National Center for Research Resources, National Institutes of Health

Institutions of the WV-INBRE

Lead Universities

Marshall University
West Virginia University

Network Research Institutions (NRIs)

Fairmont State University
West Liberty State College
West Virginia State University
Wheeling Jesuit University
Bluefield State College (transitional)

Network Outreach Institutions (NOIs)

Alderson-Broaddus College
Davis & Elkins College
Shepherd University
West Virginia Wesleyan College

Inside this issue:

Poster Presentations at the 2004 Summer Research Symposium

2004 Participants	Mentor	Project Title
Dr. Jarrett Aguilar West Liberty State College	Dr. Peter Gannett	-Molecular Modeling Study of CYP2C9 Using the INSIGHT II Software Package
Abra Bates Wheeling Jesuit University	Dr. Albert Berrebi	-Immunocytochemistry of the Cochlear Nucleus in Developing Prenatal Mice
Corey Baxter Wheeling Jesuit University	Dr. Beverly Delidow	-B-Catenin Localization in Retinoic Acid-Treated B16 Mouse Melanoma Cells
Dane Campbell West Virginia State University	Dr. Laura Richardson	-Expression of Co-Repressor SMRT in Male Germ Cells
Dr. Yi Charlie Chen Alderson-Broaddus College	Dr. Bing-Hua Jiang	-Novel Mechanism of Hypoxia-Inducible Factor 1A
Brandi Connors West Liberty State College	Dr. Leah Hammer	-Oxidative Stress in Skeletal Muscle of Aged Rats
Jennifer Crum Alderson-Broaddus College	Dr. Bernie Schreurs	-Changes in the PQ Interval of an Electrocardiogram Resulting from Heart Rate Conditioning and Conditioning-Specific Reflex Modification in Rabbits
Holly Dudash Wheeling Jesuit University	Dr. Steve Alway	-Injury Fails to Induce Apoptosis in Tibialis Anterior Muscles of Young Adult Rats
Renee Ellis Bluefield State College	Dr. Kathy Brundage	-Analysis of the Effect of Pesticides on Cytokine Production by T Cells and Macrophages
Dr. Mark Flood Fairmont State University	Pilot Grant Recipient	-Analysis of SNPS in APO-A1, -A4, and –A5 Genes and Their Relationship to Obesity -Analysis of SNPS in CETP and APOB and Their Relationship to Obesity -Homocysteine and BHMT, MTR and PON Genotypes in an Obese WVa Population -Analysis of SNPS in Lipase Genes and Their Relationship to Obesity -Homocysteine and CBS Geneotypes in an Obese WVa Population -Analysis of SNPS in Apoliproprotein and Scavenger Receptor Genes and Their Relationship to Obesity -Analysis of SNPS in LDLR Genes and Their Relationship to Obesity
Daniel Gallagher Wheeling Jesuit University	Dr. Nilay Mukherjee	-The Effects of Mechanical Stimulation At Varying Frequencies on CITED2 mRNA Levels in Chondrocytes
Dr. Ethel Gordon Bluefield State College	Pilot Grant Recipient	- Graft Tolerance and Wound Healing in Mouse Model of Type I and Type II Diabetes
Dr. Thomas Guetzloff West Virginia State University	Dr. Monica Valentovic	-The Effect of S-Adenosyl-L-Methionine on Glutathione Reductase Activity Following Acetaminophen Treatment in C57BL/6 Mice
Miranda Hanson Wheeling Jesuit University	Dr. Daniel Flynn	-AFAP-110 as a Potential Binding Partner for the P85 Alpha Subunit of P13K
Daniel Hodges Bluefield State College	Dr. Todd Green	-Neuronatin Expression in Rat Vascular Smooth Muscle Cells
Dr. Robert Kreisberg West Liberty State College	Pilot Grant Recipient	-Single Nucleotide Polymorphisms Assay Development for the Detection of Genetic Markers of Cardiovascular Disease

Dr. Huey Miin Lee Salem International University	Pilot Grant Recipient	-Obesity-Associated Cardiovascular Disease Study
Dr. Albert Magro Fairmont State University	Pilot Grant Recipient	-Evidence for C-MYB Being a Transcription Factor for Beta Integrin In CRL-2610 Glioblastoma Cells
Justin Morgan Fairmont State University	Dr. Stan Hileman	-Ataxia Telangiectasia Mutated and RAD3-Related as a Potential Link Between Obesity and Cancer
Melissa Morton-Fishman West Virginia State University	Dr. Mike Moore	-The Effect of Dexamethasone on BCL-2 In MDA-MB-231 Human Breast Cancer Cells
Ben O'Kelly West Virginia State University	Dr. Gary Wright	-Response of Smooth Muscle to Static Versus Cyclic Stretch
Brian Phlegar Bluefield State College	Dr. Gary Wright	-Changes in Signaling and Morphology in A7R4 Cells with Mechanical Stretch
Dr. Harold Pinnick West Virginia State University	Dr. Gary Rankin	- Studies on the Synthesis of Nephrotoxic Compounds
Rebecca Reindel Wheeling Jesuit University	Dr. Monica Valentovic	- The Effect of S-Adenosyl-L-Methionine on Mitochondrial Depletion of Glutathione by Acetaminophen Treatment in C57BL/6 Mice
Dr. Jiben Roy Salem International University	Dr. Pat Callery	-Modern Medicines from Traditional Sources: Investigation on a Traditional Herbal Medicine Containing Garlic and Black Cumin; Acetaminophen Toxicity: Investigations Using ESI Mass Spectrometry; The Effect of Sunlight on Ciprofloxacin Eye Drops
Justin Sanders Salem International University	Dr. Peter Gannett	-Synthesis of Staphlococcal Protein A Inhibitors
Dr. Robert Shurina Wheeling Jesuit University	Pilot Grant Recipient	-Creating a Recombinant AFAP Fusion Protein to Monitor the Role of AFAP in Angiogenesis
Kimberly Snodgrass West Virginia State University	Dr. Elsa Mangiarua	-Development of 2-Kidney, 1-Clip Renovascular Hypertension in the Obese Zucker Rat
Jessica Stone Alderson-Broaddus College	Dr. Richard Dey	-Localization of Excitatory Amino Acid Carrier 1 in the Nodose and Jugular Ganglia of Rat
Sabrena Thomas West Virginia State University	Dr. Hongwei Yu	-Sequencing and Functional Analysis Of the Transposon Vector pED1 in *Pseudomonas Aeruginosa* Genomics
Nissa Thomsen Shepherd University	Dr. Rob Haining	-Drug Interactions and CYP2C9: An Inquiry into the Mechanism of Hetero-Activation
Melinda Varney West Liberty State College	Dr. Hongwei Yu	-Genetic Basis of Complement Factor 5 in *Pseudomonas Aeruginosa* Lung Infections in Mice
Chelsea Walton West Liberty State College	Dr. Will McCumbee	-The Production of Vasoactive Metabolites In Diet-Induced Hypertension in the Obese Zucker Rat
Dr. Yi Wang Fairmont State University	Dr. Ping He	-Confocal Image Processing
Dr. Robert Warburton Shepherd University	Pilot Grant Recipient	-Proteomics of H-2K^{b} & H2-K^{bm19} Antigenic Peptides

2005 Summer Research Program Announcement

The WV-INBRE is sponsoring a Summer Research Program to be held June 6 through August 5 at West Virginia University Health Sciences Center and Joan C. Edwards School of Medicine at Marshall University. The program is open to students from the NRIs and students and faculty members from the NOIs. In addition, students from the Extended Outreach Institutions (EOIs – Bethany College, Concord University, Glenville State College, Mountain State U, Salem International University, and the University of Charleston) are eligible to apply. Student applicants must have at least one semester of school remaining after completion of the program to be eligible. Application forms and a copy of the Mentors Directory are available at www.wv-inbre.net. The deadline for applications is February 21, 2005. Contact Dr. Mark Reasor at mreasor@hsc.wvu.edu or (304) 293-2418 for more information.

Travel Awards

Three students from Alderson-Broaddus College received travel awards to attend the 19th National Conference on Undergraduate Research to be held April 20-23, 2005 in Lexington, Virginia, where they will present research they conducted as part of the WV-INBRE program. **Jennifer Crum** and **Jessica Stone** were 2004 summer research interns and **Monica Chroussis** was supported by a Pilot Grant Award to Dr. Yi Charlie Chen of Alderson-Broaddus College. The citations are: Jennifer M. Crum and Bernard G. Schreurs, "Changes in the PQ Interval of an Electrocardiogram Resulting from heart Rate Conditioning and Conditioning-specific Reflex Modification in Rabbits"; Jessica K. Stone, Thomas Batchelor, Dawn Hunter and Richard D. Dey, "Localization of Excitatory Amino Acid Carrier 1 (EAAC1) in the Nodose and Jugular Ganglion of Rat"; and Monica Chroussis and Yi Charlie Chen, "The Effect of H_2O_2 on HIF1–alpha in Ovarian Cancer Cells".

WV-INBRE Summer Intern Research to be Presented at National Meetings

The summer research conducted by **Corey Baxter** (Wheeling Jesuit University) was presented at the Melanoma Research Conference in Phoenix, Arizona, held November 13-16, 2004. The citation of the presentation was: Corey M. Baxter, Shannon Kern, Margaret McFarland, Chris Barry and Beverly C. Delidow, "Localization of B-Catenin is Altered in B16 Mouse Melanoma Cells Exposed to Retinoic Acid". The research conducted by **Renee Ellis** (Bluefield State College) will be presented at the Annual Meeting of the Society of Toxicology to be held in New Orleans, March 6-10, 2005. The citation of the presentation is: Kathleen M. Brundage and Renee Ellis, "Alterations in Cytokine Production in the Presence of the Pesticides, Bentazon, Isoxaflutole and Terbufus".

WV-INBRE Research Investigator Co-Authors Presentations at National Meeting

Dr. Robert Harris, West Virginia State University, and one of the WV-INBRE research investigators, is a co-author on three presentations to be made at the annual meeting of the American College of Sports Medicine that will be held in Nashville, Tennessee, beginning on June 6, 2005. The citations of the presentations are 1) "ERK-1/2 and p38 MAPK Signaling in the A7R5 Cell Line Following Fluprostenal Stimulation", Kevin M. Rice, Sreevani Uddemaari, Devashish Desai, Randy S.. Kinnard, Robert Harris, G. L. Wright, and E. R. Blough; 2) "Comparison Between Stretch-induced p42/44 MAPK Signaling in Rat Aortic Smooth Muscle and A7R5 Vascular Cells", Devashish H. Desai,, Robert T. Harris, Gary L. Wright, Kevin M. Rice, Deepak B. Mylabathula, Eric R. Blough; 3) "The PGF2a Analog Fluprostenal Activates mTOR and GSK-3a in the A7R5 Smooth Muscle Cell Line", Sreevani Uddemaari1, Kevin M. Rice, Randy S. Kinnard, Robert Harris, G. L. Wright, and E. R. Blough.

WV-INBRE Pilot Grant Recipient Presents Research

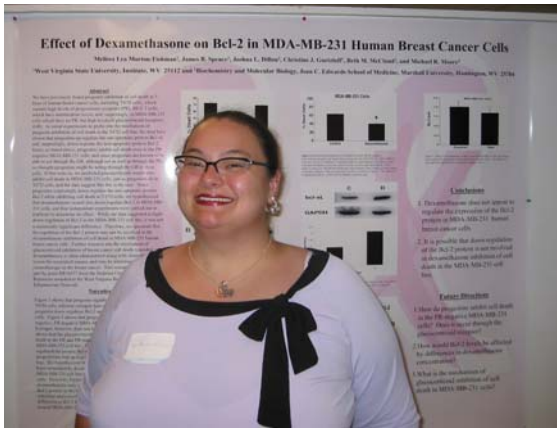
Dr. Mark Flood, Fairmont State University, presented a poster at the American Society of Human Genetics meeting in Toronto, Canada which was held October 26-30. The title of the presentation was "Genetics and Homocysteine in Obese West Virginians". The co-authors were J.M. Chappell, C. Clark, S. Hesson, B. Hill, J. Jeong, J. Nash, M. Ramey, J. Roth, P. Sekar, B. Kahle, G. Wright, T. Green, M. Studney, P. Wehner, and E.E. Murray.

Pilot Research Awards

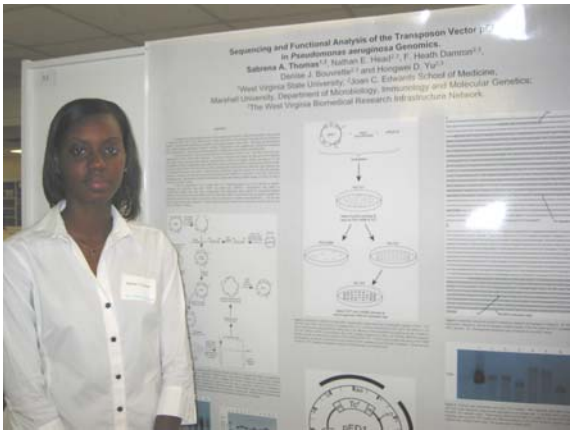
The WV-INBRE Outreach Core awarded the following pilot research grants for 2004-2005:

Investigator	Affiliation	Project Title	Award
Dr. Yi Charlie Chen	Alderson-Broaddus College	Role of P13K, AKT and ERK in ROS-Induced Cancer Cells	$30,000
Dr. Robert Warburton	Shepherd University	Proteomics of Murine H-K2b Mutant Antigenic Peptides	$30,000
Dr. Ben Whitlock	West Virginia Wesleyan College	Modulation of Survival Pathways During Differentiation in a Neutrophil-Like Cell Line	$10,000

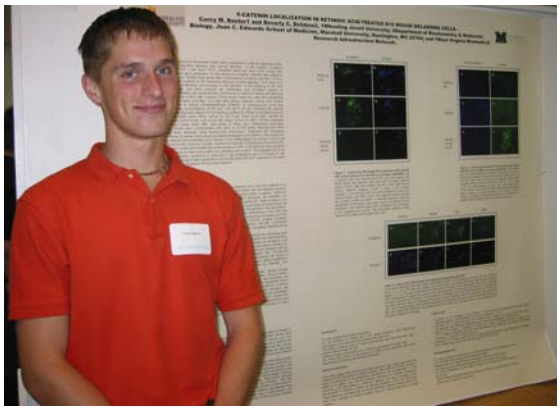
Summer Symposium Poster Presentations August 5, 2004



Melissa Morton-Fishman—West Virginia State University



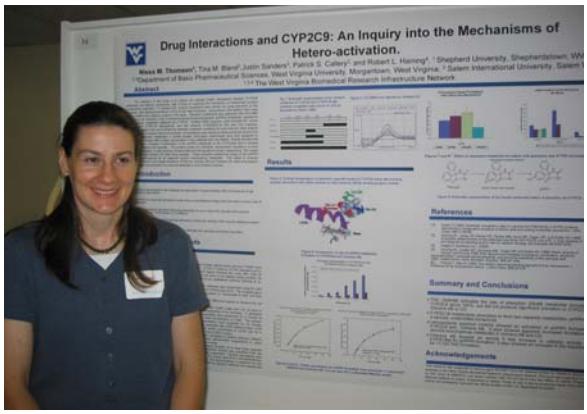
Sabrena Thomas—West Virginia State University



Corey Baxter — Wheeling Jesuit University

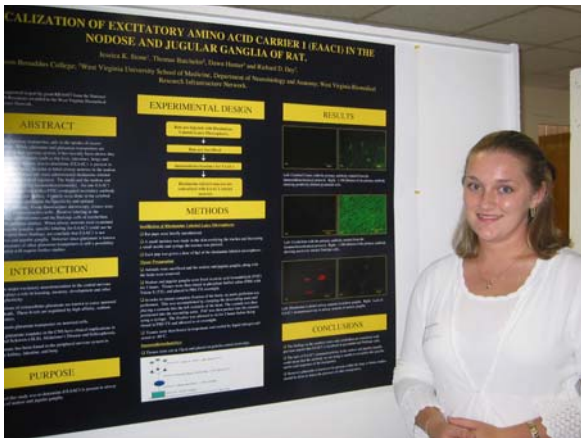
Brandi Connors—West Liberty State College

Summer Symposium
Poster Presentations
Continued

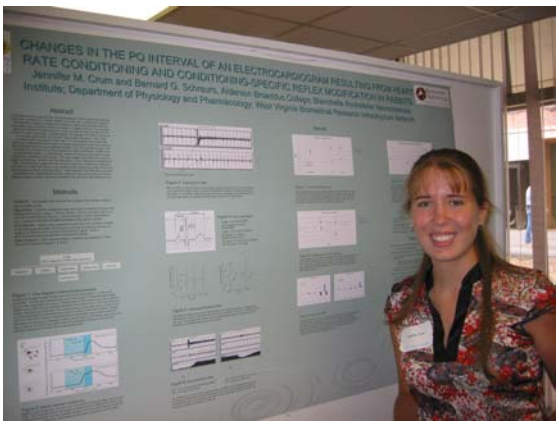


Nissa Thomsen—Shepherd University

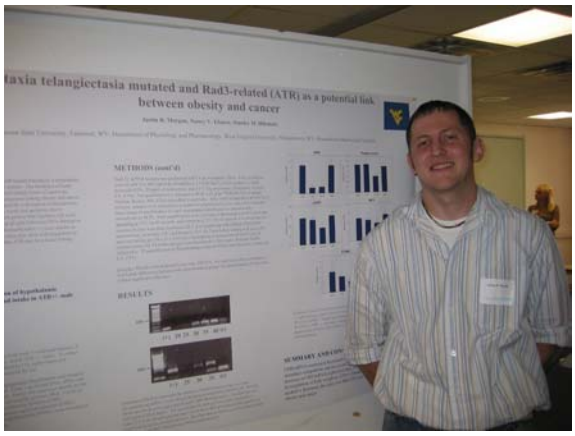
Dr. Tom Guetzloff—West Virginia State University



Jessica Stone—Alderson-Broaddus College



Jennifer Crum—Alderson-Broaddus College



Justin Morgan—Fairmont State University

Daniel Hodges—Bluefield State College

Research Overview of WV-INBRE

A major focus of the overall research plan for the *West Virginia IDeA Network of Biomedical Research Excellence (WV-INBRE)* is directed towards identifying and understanding risk factors for cardiovascular disease and their potential application to disease management. Using cellular and molecular biology approaches to determine how these risk factors might be associated with increased cardiovascular disease susceptibility, the WV-INBRE supports six full (and one transitional) research projects, distributed among five undergraduate network research institutions (NRIs), that are either directly or indirectly connected with establishing an association of certain genetic and biological markers with an increased cardiovascular disease risk.

The first project, entitled "Genetic Basis for Familial Combined Hyperlipidemia (FCHL)", is directed by Mark Flood, Ph.D. of Fairmont State University. The overall objective of this project is to identify gene(s) that predispose to FCHL using family-based linkage analysis and population-based association methods. The central hypotheses are that (i) there are specific genes that confer susceptibility to FCHL, and (ii) there is genetic heterogeneity (i.e. more than one gene or set of genes) that can give rise to the disease. In the first specific aim Dr. Flood and his colleagues will identify FCHL susceptibility loci by linkage analysis on a genome-wide set of makers and on a small set of previously identified FCHL candidate loci. In the second aim they will obtain a genetic fine map of the susceptibility loci in order to narrow the region of interest.

The second project, entitled "Genetic Basis for Familial Hypertriglyceridemia (FHTG)", is directed by Robert Kreisberg, Ph.D. of West Liberty State College. Individuals with FHTG have elevated levels of triglycerides and normal total cholesterol. FHTG affects about 1% of the US population and is one of the most common genetic lipid disorders in patients with coronary artery disease. FHTG is thought to segregate as an autosomal dominant disorder but the single segregation analysis has not been conclusively replicated. The long-term objective of this project is to identify gene(s) that predispose individuals to FHTG using family-based linkage analysis and determine how elevated levels of serum triglycerides and lipids predispose these individuals to atherosclerosis. The results of these two studies will further our understanding of the pathogenesis of vascular disease and identify susceptibility genes that represent new targets for preventive and therapeutic intervention.

These two projects are closely linked with the research and clinical programs of the Appalachian Cardiovascular Research Network (ACoRN), which is a major programmatic focus of the WV-INBRE. Under the guidance of the ACoRN Director, Don Primerano, Ph.D., these two projects directly address the overall objectives of ACoRN to enhance our understanding of cardiovascular disease susceptibility risks and markers. In addition to the faculty and students involved in these two research projects, the overall research team for the ACoRN program includes researchers from both Marshall University and West Virginia University, as well as research and clinical staff from Charleston Area Medical Center (CAMC) and several rural health clinics (Lincoln Primary Care Center, Tri-County Clinic, Tug River Clinic, and Valley Health Systems). Other projects addressing the WV-INBRE research emphasis on cardiovascular disease include the following: (i) "Response of vascular smooth muscle cells to stretch" by Robert Harris, Ph.D. of West Virginia State University, (ii) "AFAP-110 as a regulator of angiogenesis", by Robert Shurina, Ph.D. of Wheeling Jesuit University, and (iii) "Therapeutic Interventions to accelerate wound healing in diabetic mice", by Ethel Gordon, Ph.D. of Bluefield State College. Dr Harris' project focuses on how mechanical forces can affect the regulation of smooth muscle cell function. By examining how mechanical stretching, such as occurs in hypertensive states, alters smooth muscle cell reorganization and cell signaling, he will obtain important information on vascular function under such conditions. Dr. Shurina's project studying factors important for angiogenesis has important implications for the revascularization of occluded areas and mechanisms that may be altered in hypertensive states. Lastly, Dr. Gordon's project involving examining wound healing in diabetes may also provide insights into cardiovascular issues, as diabetics have numerous cardiovascular problems, and the origin of many of these problems are unclear.

Finally, information gleaned from two projects using cellular and molecular approaches to understand biological mechanisms in normal and disease states could indirectly impact on the cardiovascular disease focus of the WV-INBRE. These two projects supported by WV-INBRE are: (i) "Integrin regulation of cell death in cancer cells", by Albert Magro, Ph.D. of Fairmont State University, and (ii) "Dapsone activation of CYP2C9: A molecular modeling study", by Jarrett Aguilar, Ph.D. of West Liberty State College. The primary focus of Dr. Magro's project is directed toward understanding the development of cancer chemotherapy resistance by providing information on the pro-apoptotic and anti-apoptotic machinery of focal adhesions. However, his research also has implications for angiogenesis research. As indicated above, angiogenesis is an important process in vascular disease. Dr. Aguilar's project will provide basic information on how dapsone activates CYP2C9. He will utilize dapsone and a number of non-steroidal anti-inflammatory agents as substrates to model the active site of the enzyme. The information obtained in this study will form the basis for studies examining other P450 isoforms and will help predict drug-drug interactions. Since cardiovascular drugs may also be a target for biotransformation by CYP2C9 and other P450 isoforms, modeling the interactions of various drugs with the active site of the enzymes has widespread implications.

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