

Doris M. Benbrook, PhD
CURRICULUM VITAE

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EDUCATION: *Bachelor of Arts*, majors in Biology and Chemistry, minor in German. North Central College, Naperville, IL, 1981; *PhD* in Biochemistry, Loyola University Medical Center, Maywood, IL Mentor: Robert V. Miller, PhD 1985.

POSTDOCTORAL EXPERIENCE: *La Jolla Cancer Research Foundation (Currently The Burnham Institute)*, La Jolla, CA, Mentor: Magnus Pfahl, PhD, Subject: Nuclear Receptors in Cancer (1985-1988); *Imperial Cancer Research Fund*, London, England, U.K. Mentor: Nicholas C. Jones, PhD Subject: Interaction of CREB and JUN Transcription Factors (1988-1991).

OUSHC FACULTY APPOINTMENTS: *Department of Obstetrics and Gynecology, Gynecologic Oncology Section:* Tenured Professor and Director of Research (2004-present) Associate Professor (1997-2004), Assistant Professor (1991-1997), Director of Research, Gynecologic Oncology (1993-present); *Graduate College:* Associate Member (1993-present); *Department of Pharmaceutical Sciences:* Adjunct Professor (2013-present); *Department of Biochemistry and Molecular Biology:* Adjunct Professor (2005-2013), Adjunct Associate Professor (1997-2005), Adjunct Assistant Professor (1993-1997); *Department of Genetic Counseling:* Adjunct Professor (2011-present).

AWARDS AND HONORS: Endowed Chair in Gynecologic Oncology (2009-present), North Central College Sesquicentennial Medal (2011); First Place for best business plan in Oklahoma Governors Cup Competition. Submitted by a team of OU undergraduate internsto commercialize Dr. Benbrook's Flex-Het drugs for polycystic kidney disease (2009); Second Place for best businesss plan in the W. Reynolds Tri-State Collegiate Business Plan competition. Submitted by Renephron to commercialize Dr. Benbrook's Flex-Het drugs for polycystic kidney disease (2009); Innovator of the Year On the Brink Award, *The Journal Record* (2005); Oklahoma Scientist of the Year awarded by the Oklahoma Academy of Science (2004); Woman of the Year Nominee awarded by the *Journal Record* (2004).

EDITOR-IN-CHIEF: *Biologics: Targets & Therapy*, Dove Medical Press, 2008-present

CHAIR OF NATIONAL COMMITTEES: AREA R15 Review Panels 2008-2015 (one to two panels per year), SBIR/STTR Review Panels 2009; NCI Chemoprevention Committee, Subcommittee E, Cancer Epidemiology, Prevention and Control 2003-2005 (This involved multiple site visits per year).

PERMANENT MEMBER SERVICE ON NATIONAL COMMITTEES: Drug Discovery and Molecular Pharmacology (DMP) 2019-2013; Cancer Biomarkers Study Section (CBSS), 2004–2008; NCI Chemoprevention Subcommittee E 2000-2005 (This involved multiple site visits per year).

ADVISORY BOARDS: Native Americans in Biological Sciences Advisory Board (NABS), Oklahoma State University 2005-07; New Mexico Cancer Center 2009.

EDITORIAL BOARDS: *Cancer Research*, 2010 – 2012, *Journal of Cell Death*, 2008- present, *Open Access Journal of Clinical Trials*, 2008-present, *Biochemical Journal and Biochemical Society Transactions*, 2007-present, *Open Medicinal Chemistry Journal*, 2007-present, *Bioinformatics and Biology Insights*, 2007-present, *Open Reproductive Science Journal*, 2007-present, *Current Medicinal Chemistry*, 2006-present, *Cancer Epidemiology, Biomarkers & Prevention*, 2002-2009

CONSULTANCIES: Expert Scientific Witness to Patent Litigation Case, Haynes and Boone, LLP, 2012-2013, Consultant to Procter & Gamble, 1999-2002

SESSION CHAIR OF NATIONAL CONFERENCES: Retinoids and Cancer, FASEB Retinoid Meeting, 2006; Translational Research Session of the Ovarian Cancer State of the Art Meeting, sponsored by CTEP and GOG 2005.

SESSION CHAIR OF INTERNATIONAL CONFERENCES: “Functional Genomics, Proteomics and Signalomics in Cancer” at the International Cancer Research Symposium 2010: Defining & Translating Science Behind Disease. Rajiv Gandhi Centre for Biotechnology, Thiruvananthapuram, Kerala, India, December 21, 2010; Stephenson Cancer Center Ovarian Cancer Symposium 2014. “Recent Trends in Biotechnological Therapeutic Applications”. 2nd International BAU Drug Design Congress, Istanbul, Turkey, April 17-19, 2014.

REVIEWER ON NATIONAL COMMITTEES: NCI Specialized Programs of Research Excellence (SPORE) Grants Panel 2005, 2014; DMP Special Emphasis Panel 2014;CDMRP/DOD 2002-2004, 2014; Cancer Detection, Diagnosis, and Treatment Technologies for Global Health 2014; NCI AREA R21 Grant Review Panels 2005; DMP Study Section 2006, 2008-2009; Oak Ridge Associated Universities (ORAU) Center of Excellence Award Reviews 2007 – present; CDC Improving Public Health Practice through Translation Research (R18) 2007; U.S. Civilian Research & Development Foundation (CRDF) Cooperative Grants Program (CGP) 2007; Phillip Morris External Research Program, 2003-2007; SBIR/STTR Study Section 2006; NCI Chemoprevention Subcommittee E 2006; Substitute Chair and Reviewer for Early Detection Research Network, Clinical Epidemiology and Validation Centers 2004; Eppley NCI-Designated Cancer Center Site Visit 2004; Department of Veterans Affairs’ Medical Research Branch Grant Reviews 1992-1995 (nominated for their National Advisory Committee 2002); Clinical Nutrition Research Units Review Panel 2001; NCI Molecular Target Drug Discovery 2000; NCI Early Detection Research Network (EDRN) - Clinical and Epidemiologic Centers 2000; NCI Chemoprevention in Genetically-Identified High-Risk Groups Interactive Research and Development Projects 2000; NCI Chemoprevention Subcommittee E (as ad hoc, site visits involved) 1999-2000; American Society of Clinical Oncologists (ASCO), Cancer Genetics Trainer.

OTHER NATIONAL COMMITTEES: Gynecological Oncology Group (GOG), Member of the Experimental Medicine Committee (CEM) (1992-2010) and Member of Chemoprevention Committee (2000-2009); Chair of Developmental Therapeutics Subcommittee of the GOG CEM Committee 2006-2008; American Association for Cancer Research (AACR), Chairman of State Legislative Committee in the 1990’s.

NATIONAL WORKSHOPS: NCI Clinical Development of Small Molecules Workshop 2008; NCI Phase 0 Trials in Oncologic Drug Development 2007; Reviewer on Mock Study Section in Grant Writing Workshop for Clinicians, American Association for Cancer Research (AACR) Professional Advancement Series Section 2006, 2009; Co-Chair of Chemoprevention Workshop for the GOG Gynecologic Cancer Translational Research Retreat II 2000;

INTERNATIONAL GRANT REVIEWS: Italian Research Council 2002 – present; World Cancer Research Fund International 2010-11; University Grants Committee, University of Hong Kong 2006; Biotechnology and Biological Sciences Research Council (BBSRC – United Kingdom) 2006; Cancer Research UK (United Kingdom), 2002

AD HOC REVIEW: Over 75 Journals.

STEPHENSON CANCER CENTER (PREVIOUSLY OUCI) APPOINTMENTS: Scientific Review Committee 2002- present; Gynecologic Cancer Biospecimen Core Committee 2006-present; Co-Leader, Women’s Cancer Program 2011-2014; Co-Chair, Scientific Advisory Committee 2006-2009; Director, Women’s Cancer Program 2007-2009; Co-Director, Gynecologic Cancer Program 2001-2006.

UNIVERSITY OF OKLAHOMA CLINICAL AND TRANSLATIONAL SCIENCE AWARD (CTSA): CTSA P20 Planning Grant was Awarded; Co-Director, “Med into Grad” PhD Specialization Program 2009; Member, CTSA Grant Planning Committee 2006-2008; Chancellor of the Clinical and Translational Science Society (CTSS) 2007-2008; Member of the Clinical and Translational Science MS Program Executive Committee 2007-2008; Co-Chair of the Translational Working Group 2005

UNIVERSITY OF OKLAHOMA HEALTH SCIENCES CENTER COMMITTEES: Faculty Senate Appeals Committee 2014- present; Faculty Advisory Committee for the Core Laboratories 2006; Chair of Research and Graduate Student Affairs Committee 2006-2009; Clinical and Translational Science (CTS) Executive Committee 2006-present; Search Committee of Deputy Directory of the Basic and Translational Cancer Research Center 2007; Recruitment Committee, College of Pharmacy, Pharmaceutical Sciences Department Chair 2007; Vice Chair of the Institutional Biosafety Committee (IBC) 1995-2006; Chair of the Internal Review Committee of the Biostatistics and Epidemiology Graduate Program 2006; Clinical & Translational Science (CTS) Degree and Curriculum Committee 2006; Search Committee for Cancer Genetics Endowed Chair 2005-2006; Search Committee for Children’s Medical Research Institute Endowed Chair 2005-2006; Faculty Affair Liaison 2002; Outstanding Thesis/Dissertation Committee 2000-2010.

DEPARTMENTAL COMMITTEES: *Obstetrics and Gynecology:* Director of Research, Gynecologic Oncology 1995-present; Promotions Committee 2003-2014; Environmental Health and Safety Training Coordinator 1995-2003; Tuberculosis Coordinator 1996- 2003; Research Administration Liaison 1994-2003; *Biochemistry Department:* PhD Qualifying Exam Committees (1-2 per year, 1992-2014); Graduate Student Awards Committee 2007-2013; Faculty Search Committee 2008-2010; Student Admissions and Recruitment Committee 2004-2007; Dental/Pharmacy Course Curriculum Committee 2003-2004; Student Admissions and Advisory Committee 2002-2003; Student Advisory Committee 2001-02; General Examination Committee 2001-02; Graduate Program Curriculum/Review Committee 1995-97; Adjunct Faculty Review and Evaluation Committee 1997-2000; Student Recruitment Committee 2000-01

EDUCATIONAL ADMINISTRATION: Prepared grant applications to fund Translational Research Certificate for PhD Degrees (Director of Program); Served on committee to revise curriculum for systems based learning approach for Medical Students 2007 – 2008; Assisted in development of “Clinical and Translational Science Course 2005.

COURSE DIRECTOR: Foundations in Translational Research 2015-present.

TEACHING: Integrated Graduate Student Curriculum (2007-present) “Cellular Systems, Integration of Cell Death and Survival Pathways” (3 hrs); “Current Topics in Cancer Research Journal Club” (4 hrs) CTS Summer Scholar Program Lectures (2007-2013) “Clinical and Translational Science” (2 hrs, 2007-2013) and “The University of Oklahoma Cancer Institute” (1 hr); Clinical Bioinformatics (6 hrs, 2005); Biochemistry Department (2000-2006) prior to Integrated Curriculum “Laboratory Rotations” (20 hrs, 2 students/year) “Carcinogenesis and Chemoprevention” (2 hrs), “Molecular Mechanisms of Cancer” (1 hour), “Cancer Genetics/Biomarkers” (1.5 hrs), “Regulation of Gene Expression” (4.5 hours), “Oncogenes and Tumor Suppressor Genes” (4 hrs); “RNA Splicing Mechanisms” (4 hrs), “Current issues in Biomedical Research: Clinical Trials” (2 hrs), “Glycobiology (1.5 hrs); Biochemistry Curriculum (1992-2000) “DNA tumor viruses and Chemical Carcinogenesis” (4 hours), “DNA Sequencing and EMSA” (2 hrs), 7 week laboratory rotations for Graduate Students, “Advanced Topics in Human Molecular Genetics” (2 hrs); Dental Biochemistry (1999-2001) “Carcinogenesis” (1 hr); Departments of Pathology and Radiological Sciences (1993-2004) “ Oncogenes and Tumor Suppressor Genes” (1 hr).

CHAIR OF THESIS/DISSERTATION COMMITTEES: Five PhD students and two MS students (2001-2014)

TRAINING OF POSTDOCTORAL FELLOWS: Three Fellows trained, one currently faculty in academia, one a member of the NCI and another a Phase I Trial Director in Industry.

GYN ONCOLOGY CLINICAL FELLOWS MENTORED: (Over 24 fellows trained since 1994, over 40% currently in Academia)

SERVICE ON OTHER DISERTATION/THESIS COMMITTEES: Twentyfive PhD Committees (Four current), Three Masters Committees(Two Current) and Two PharMD Committees.

CLINICAL FACULTY MENTORED: Seven Assistant Professors mentored (1999-2013) each achieving national grant awards, peer-reviewed publications and academic advancement.

RESIDENT RESEARCH PROJECTS MENTORED: Four Residents (1997- 2003).

MEDICAL STUDENT RESEARCH PROJECTS MENTORED: Eleven Medical Students (1992-2013).

UNDERGRADUATE STUDENT RESEARCH PROJECTS MENTORED: Nine Students, two State-level awards (2003-2008).

HIGH SCHOOL STUDENT/TEACHER RESEARCH PROJECTS MENTORED:Twelve students and one teacher mentored. Three regional awards.

PATENTS: “Heteroarotinoids containing urea or thiourea linker” US Patent No. 6,586,460 issued 07/01/2003, Co-inventors: K. Darrell Berlin, PhD, Doris M. Benbrook, PhD, Eldon C. Nelson, PhD; “Treatment and Inhibition of Disease Conditions Using Flexible Heteroarotinoids” US Patent No. 7,612,107 issued 11/03/2009, Co-Inventors: Doris M. Benbrook, PhD, Suresh Guruswamy, PhD, Martin Turmin, MD

CURRENT FUNDING

MD Anderson Moonshot Program Contract, “Development of a Vaginal SHetA2 Formulation for Cervical Cancer and Dysplasia”, 2015, \$30,000.

Presbyterian Health Foundation Bridge Grant, “Sensitization of Ovarian Cancer to DR5 Agonists” Role: PI, 2014-2015, Total direct costs: \$75,000.

Presbyterian Health Foundation Seed Grant, “Inhaled SHetA2 dry powder aerosols as novel treatment for tuberculosis” Role: Co-I, 2014-02015, Total direct costs: \$45,000.

Presbyterian Health Foundation Bridge Grant, “Optimizing targeting strategy for delivering NIR-activatable prodrugs to peritoneally metastasized ovarian cancers” Role: Co-I, 2014-2015, Total direct costs: \$75,000

Chapman Foundation Collaboration Grant, “Autophagy in Ovarian Cancer Therapeutics and Tumor Microenvironment” Role: Co-PI, Other Co-PI: Bulent Ozpolat, PhD at MD Anderson Cancer Center, 2013-2014, Total direct costs to Dr. Benbrook: \$45,000.

Reynolds Center of Geriatric Nursing Excellence Interdisciplinary Seed Grant, “Correlates of Quality of Life, Biomarkers, and Physical Activity in Older Women with Ovarian Cancer who Experience Chemotherapy-Induced Peripheral Neuropathy Pain (CIPN)” Role: Co-I, PI: Elana Cuaderes, PhD, R.N., 2014-2015, Total Direct Costs \$30,000.

Reynolds Center of Geriatric Nursing Excellence Interdisciplinary Seed Grant, “Descriptive Study of Cognitive Disturbances in Older Breast Cancer Survivors” Role: Co-I, PI: Melisa Craft, PhD APRN-CNS AOCN, 2014-2015, Total direct costs: \$30,000.

Vice President for Research Seed Grant, “Memory Consolidation and Cerebral Oxygenation in Elders with Mild Cognitive Impairment” Role: Co-I, PI: Barbara Carlson, R.N., PhD, 2014-2015, Total direct costs: \$29,884.02.

Norman Faculty Investment Program, Norman Research Council, “Memory Consolidation and Cerebral Oxygenation in Elders with Mild Cognitive Impairment”, Role: Co-I, PI: Michael J. Wegner, PhD, 2014-2015, Total direct costs: \$15,000.

NCI U10 National Clinical Trials Network (NCTN), This project funds our participation in national clinical trials and translational research. Dr. Benbrook may be asked to perform translational research on some of the trials. Role: Co-I, PI: Robert Mannel, MD, Direct costs variable depending on contracts, 2014-2019.

PAST FUNDING:

National Research Grants as Principal Investigator

National Cancer Institute, National Institutes of Health (R01), “Mechanism of SHetA2 in Ovarian Cancer” Role: PI, 2005-2010, Total direct costs: \$987,500.

NCI Small Research Grant Program (R03), “Steroids and Stem Cells in Carcinogenesis” Role: PI, 2004-2006, Total direct costs: \$100,000.

Mary Kay Ash Charitable Foundation, “Mechanism of ER Activation in Thyroid Hormone Administration in Breast Cancer Survivors” Role: PI, 2004-2006, Total direct costs: \$100,000.

NCI R01 Grant, “Mechanism & Potential of Retinoid & DNA Damage Therapy” Role: PI, 1999-2004. Total direct costs: \$310,555.

Mary Kay Ash Charitable Foundation, "Development of Retinoids and Response Biomarkers for Ovarian Cancer" Role: PI, 1998-2000, Total direct costs: \$90,864.

American Institute of Cancer Research (AICR), 94A63, "Carotenoid Effects on Transcription and Growth in Tumors" Role: PI, 1994-1996, Total direct costs: \$100,000.

National Science Foundation, MCB-9209479, "DNA Binding Specificities of cJun Dimers" Role: PI, 1992-1994, Total direct costs: \$16,200.

Milheim Foundation for Cancer Research, 92-14, "Retinoids, cJun and Cervical Cancer" Role: PI, 1992-1993, Total direct costs \$14,000.

Translational Drug Development Program Grants as Principal Investigator

Rapid Access to Preventive Intervention Development (RAPID), “Flexible Heteroarotinoids for Chemoprevention” Role: PI, 2007-2011, funded preclinical development of SHetA2 >\$2 billion.

Rapid Access to Intervention Development (RAID), “SHetA2 will Inhibit Cancer Recurrence Without Retinoid-Associated Toxicities.” Role: PI, 2003-2006, funded preclinical development of SHetA2 >\$2 billion.

National Grants as Mentor

Oklahoma INBRE (IDeA Network of Biomedical Research Excellence) NIH/NCRR (P20RR016478), Role: Mentor of Wei-Qun Ding’s Junior Faculty Award, PI: Darrin Akins, Ph.D, 2009-2014, Total direct costs \$13,312,160.

Cancer Research Foundation of America (CRFA) Fellowship, “Human Papillomavirus and Epidermal Growth Factor Receptor as Biomarkers of Retinoid Cervix Cancer Chemoprevention”, Role: Mentor, Postdoctoral Fellow: Shennan Lu, PhD, 2000-2003, Total direct costs: \$60,000.

NIH Center Planning Grants

NCI Program Planning Grant for NCI Cancer Research Centers (P20), “Cancer Center Planning Grant.” Role: Co-Director of the Women’s Cancer Program, PI: Howard Ozer, MD, PhD, 2002-2008, Total direct and indirect costs: \$925,084.

NIH CTS Grant (P20) “Oklahoma Planning Grant for Clinical and Translational Medicine”. Role: Executive Planning Committee. Total direct and indirect costs: \$418,536

Local Research Grants as Principal Investigator

University of Oklahoma Health Sciences Center Vice President of Research Bridge Grant Program, “Heat Shock Proteins and Stress in Cancer Prevention” Role: PI, 2012-2013, Total direct costs: \$60,000.

Stephenson Cancer Center Experimental Therapeutics Program Grant, “Therapeutic Targeting of HSP70 Chaperones in Cancer Drug Discovery” Role: Co-PI, Other Co-PI: Franklin Hays, PhD, 2012-2013, Total direct costs: \$25,000.

University of Oklahoma Growth Fund, “Flex-Het Treatment for Polycystic Kidney Disease” Role: PI, 2009-2011: Total direct costs: \$50,000.

The Presbyterian Health Foundation, “Radiation and Retinoid Effects on Cervical Cancer”, Role: PI, 1994-1995, Total direct costs \$25,000.

Oklahoma Medical Alumni Association, “Retinoids, cJun and Cervical Cancer” Role: PI, 1992-1993, Total direct costs of \$20,000 awarded, \$11,000 accepted due to overlap with other funding.

National Research Grants as Co-Investigator

Gynecologic Cancer Foundation, “The Role of Ribonucleotide Reductase Regulatory Subunit 1 (RRM1) and Excision Repair Cross Complementation Group 1 (ERCC1) in Determining Chemosensitivity for Advanced Ovarian Cancer” Role: Co-I, PI: Kathleen Moore, MD, 2007-2008, Total direct costs: \$50,000.

American Cancer Society, “Search for the Potential Targets for the Prevention of Carcinogenesis” Role: Collaborator, Parent Grant PI: Marie Hanigan, PhD, PI of Project: Igor Dozmorov, PhD 2008-2009, \$25,000.

NCI R01 Grant, “A Murine Model of Endometrial Tumorigenesis.” Role: Co-I, PI: Paul Goodfellow, PhD., at Washington University in Saint Louis, IL, 2004-2007, Subcontract to Dr. Benbrook: \$74,996.

NCI R21 Grant, “Genetic Regulation of Glycan Antigens in Cancer Cells” Role: Collaborator, PI: Richard Cummings, PhD at OUHSC, 2005-2007, Total direct costs: \$253,598.

NCI R01 Grant, “Biological Activity of Heteroarotinoids” Role: Co-I, PI: Eldon C. Nelson, PhD at Oklahoma State University, 1996-1999, Total direct costs: \$981,456 direct.

American Institute for Cancer Research (AICR), “Ligand Activation of Peroxisome Proliferator-Activated Receptors in Rodent Mammary Tumor Models”, Role: Collaborator, PI: Stephen Glore, PhD at OUHSC, Total direct costs: \$100,000.

National Research Contracts as Principal Investigator

Haynes and Boone, LLC Consultancy Fees, Role: Consultant, 2012-2015, over \$100,000 was generated in the 2013 fiscal year from this consultancy to support Dr. Benbrook’s salary and research.

Gynecologic Oncology Group (GOG) NIH/NCI, “Translational Research of GOG229I Phase II trial of Brivnab for Persistent or Recurrent Endometrial Cancer” Role: PI, 2012-2013, Total direct costs: \$20,000.

NCI, Gynecologic Oncology Group (GOG), “A Phase II Evaluation of Enzastaurin in the Treatment of Persistent or Recurrent Epithelial Ovarian or Primary Peritoneal Carcinoma” Role: PI, 2007, Total direct costs: \$17,279.

NCI, Gynecologic Oncology Group, “Lab Analysis for GOG0207 Phase II Trial of Celecoxib for CINIII” Role: PI, 2005-2007, Total direct costs: \$64,028.

NCI, Gynecologic Oncology Group, “Analysis for GOG229-B, GOG230-B, GOG-231-B Stage I”, Role: PI: 2002-2004, Total direct costs: \$25,290.

Proxima Concepts LTD, London, England, UK, “Agreement Using Proxima Technology to Screen Libraries of Recombinant Probes”, Role: PI, 2004-2005, Total direct costs: \$6,078.

Novartis Pharmaceutical through PRA International, “Phase II Trial of Gleevec (Imatinib Mesylate Formerly Known as STI571) in Patients with CD1q17(+) Gynecologic Malignancies”, Role: Co-I, PI: D. Scott McMeekin, MD 2002-2004, Total direct costs: \$65,882.

Procter & Gamble, “Determination of Retinoid X Receptor Ligand Structure-Function Properties” Role: PI, 2002, Total direct costs: \$48,000.

NeoPharm, “Develop and Perform ELISA’s for Neo-MS-02 Clinical Trial”, Role: PI, 2000-2002, Total direct costs: \$72,000.

Procter & Gamble, “Determination of Retinoid Receptor Transactivation Properties” Role: PI, 1999, Total direct costs: \$8,890.

Local Equipment Grants as Principal Investigator

Presbyterian Health Foundation Equipment Grant, “Bringing OU Research to New Dimensions with Multiplex Technologies” Role: PI, 2008, Total direct costs: \$50,000.

Presbyterian Health Foundation Research Equipment Repair Fund, Role: PI, 1992, \$5,000 for repair of an ultracentrifuge.

State-Wide Inter-Institutional Collaborative Grants

Oklahoma IDeA Network of Biomedical Research Excellence Collaborative grant, “Structure Activity Relationship Studies to Develop Improved Cancer Drugs” Role: Collaborator, PI: Dana Rundle, PhD at the University of Central Oklahoma, 2012-2013, Total direct costs: \$49,919.

Oklahoma INBRE (IDeA Network of Biomedical Research Excellence) NIH/NCRR (P20RR016478), “Probing the Interactions of SHetA2 and Hsp70 Mortalin: A new route for Flex-Het Anticancer Activity?” Role: Co-Investigator, PI: William Kelly, PhD at Southwest Oklahoma State University, 2012-2013, Total direct costs: \$50,000.

Oklahoma INBRE (IDeA Network of Biomedical Research Excellence), “Investigations of SHetA2 mediated Mitochondrial changes” Role: Collaborator, PI: William Kelly, PhD at Southwestern Oklahoma State University, 2007-2008, Subcontract to Dr. Benbrook: \$15,383.

University of Central Oklahoma Basic Research Grant to Faculty, “Effects of heteroarotinoids on PKC activation and apoptosis in ovarian carcinoma organotypic cultures” Role: Collaborator, PI: Dana Rundel, PhD, at the University of Central Oklahoma, 2007-2008, Total direct costs \$10,000.

Oklahoma INBRE (IDeA Network of Biomedical Research Excellence), “Investigations of SHetA2 mediated Mitochondrial changes”, Role: Collaborator, PI: William Kelly, PhD at Southwest Oklahoma State University, 2006, Total direct costs: \$50,000, Subcontract to Dr. Benbrook: \$15,383.

Oklahoma Center for the Advancement of Science and Technology (OCAST), “Does HPV16 E5 affect EGF Receptor Endocytosis and Signaling?” Role: Co-I, PI: Brian Ceresa, PhD, 2003-2005, Total direct costs: \$100,000

Oklahoma INBRE (IDeA Network of Biomedical Research Excellence), “Investigations of SHetA2 mediated Mitochondrial changes in Human Cancer Organotypic Cultures” Role: Collaborator, PI: Principal Investigator: William Kelly, PhD at Southwestern Oklahoma State University, 2005, Total direct costs: \$50,000, Subcontract to Dr. Benbrook: \$15,383.

Oklahoma Biomedical Research Infrastructure Network (BRIN) Collaborative Grant, “Is Retinoid Induced Cell Apoptosis Mediated by Superoxide Radical Anion Production?” Role: Collaborator, PI: William J. Kelly, PhD at Southwestern Oklahoma State University, 2004, Total direct costs: \$50,000, Subcontract to Dr. Benbrook: \$15,383.

INVESTIGATIONAL NEW DRUG (IND) APPLICATIONS

A Phase 0 Study of SHetA2 (NSC 72168) in Stage IB2-IVb Cervical Cancer (PIND #: 121262). Prepared by Doris M. Benbrook, PhD, PI: S. Scott McMeekin, MD (Clinical Trial), Co-I's: Doris M. Benbrook, PhD (Pharmacodynamics), Lucila Garcia-Contreras, PhD (Formulation), Sukyung Woo PhD (Pharmacokinetics)

ONGOING CLINICAL TRIALS AND TRANSLATIONAL RESEARCH

A randomized Phase III trial of maintenance chemotherapy comparing 12 monthly cycles of single agent paclitaxel or CT-2103 (IND#70177) versus no treatment until documented relapse in women with advanced ovarian, primary peritoneal or fallopian tube cancer who achieve a complete clinical response to primary platinum/taxane chemotherapy. Gynecologic Oncology Group (GOG) Protocol #0212, Study Chair: Larry J Copeland, Scientific Collaborator: Doris M. Benbrook, PhD

COMPLETED CLINICAL TRIALS WITH COMPLETED OR ONGOING TRANSLATIONAL RESEARCH

A Randomized Double-Blind Phase II Trial of Celecoxib, a Cox 2 Inhibitor, in the Treatment of Patients with Cervical Intraepithelial Neoplasia 3 (CIN3). GOG Protocol #0207, Study Chair: Janet Rader, MD, Translational Research Chair: Doris M. Benbrook, PhD

A Phase II evaluation of Brivanib (BMS582664), an oral, multitargeted growth factor tyrosine kinase inhibitor in the treatment of recurrent or persistent endometrial carcinoma. GOG Protocol #02291, Study Chair: Matthew Powell, MD, Scientific Collaborator: Doris M. Benbrook, PhD

A Randomized, Controlled Phase II Evaluation of Megestrol in Different Dose and Sequence in the Treatment of Endometrial Intraepithelial Neoplasia (EIN) From A Referred Cohort of Atypical Endometrial Hyperplasia (AEH) or EIN. GOG Protocol #0224, Study Chair: Michael Method, MD, Collaborating Scientist: Doris M. Benbrook, PhD

A Phase II Evaluation of Brivanib (BMS582664), an Oral, Multitargeted Growth Factor Tyrosine Kinase Inhibitor in the Treatment of Recurrent or Persistent Endometrial Carcinoma. GOG Protocol #0229I, Study Chair: Matthew Powell, MD, Scientific Collaborator: Doris M. Benbrook, PhD

A Randomized Phase III trial of maintenance chemotherapy comparing 12 monthly cycles of single agent paclitaxel or Xyotax (CT-2103) (IND#70177) versus no treatment until documented relapse in women with advanced ovarian or primary peritoneal cancer who achieve a complete clinical response to primary platinum/Taxane chemotherapy. GOG Protocol #0212, Study Chair: Maurie Markman, MD, Scientific Collaborator: Doris M. Benbrook, PhD

A Phase II Evaluation of Enzastaurin in the Treatment of Persistent or Recurrent Epithelial Ovarian or Primary Peritoneal Carcinoma. GOG Protocol #170J, Study Chair: Lydia Usha, MD, Scientific Collaborator: Doris M. Benbrook, PhD

A Phase II evaluation of thalidomide in the treatment of recurrent or persistent endometrial carcinoma. GOG Protocol #0229-B, Study Chair: Scott McMeekin, MD, Translational Research Chair: Doris M. Benbrook, PhD.

A Phase II evaluation of thalidomide in the treatment of recurrent or persistent carcinosarcoma of the uterus. GOG Protocol #0230-B, Study Chair: Scott McMeekin, MD, Translational Research Chair: Doris M. Benbrook, PhD.

A Phase II evaluation of thalidomide in the treatment of recurrent or persistent leiomyosarcoma of the uterus. GOG Protocol #0231-B, Study Chair: Scott McMeekin, MD, Translational Research Chair: Doris M. Benbrook, PhD.

Comparison of Glycoprotein Expression and T-Synthase Function in Primary versus Metastatic Tumors. GOG Protocol #0221, Study Chair: Michael Gold, MD. Study Co-Chairs: Doris M. Benbrook, PhD, Richard Cummings, PhD and William Rodgers, MD.

A randomized study of tamoxifen verses thalidomide in patients with biochemical-recurrence-only epithelial ovarian cancer, cancer of the fallopian tube, and primary peritoneal cancer after first line chemotherapy. GOG Protocol # 0198, Study Chair: Jean A. Hurteau, MD, Translational Research Chair: Doris M. Benbrook, PhD.

Phase II Trial of Gleevec (Imatinib Mesylate Formerly Known as STI571) in Patients with CD1q17(+) Gynecologic Malignancies. PI: D. Scott McMeekin, MD, Translational Research Scientist Doris M. Benbrook, PhD.

DATA SAFETY AND MONITORING BOARD: Chair, “Laser and TLR-Agonist Immunotherapy: A Novel Autologous Melanoma Vaccine Strategy” PI: Mark F. Naylor, MD, Co-I’s: Kent Teague, Ph.D and Wei Chen, PhD. The board met bi-annually 2005-2009.

PUBLICATIONS

1. Benbrook, D.M. and Miller, R.V. (1986) Effects of Norfloxacin on DNA metabolism in pseudomonas aeruginosa. *Antimicrobial Agents and Chemotherapy*, **29**: 1-6. PMID:3015000.
2. Benbrook, D. & Pfahl, M. (1987) A Novel Thyroid Hormone Receptor Encoded by a cDNA Clone from a Human Testis Library. *Science*, **238**: 788-791. PMID:3672126.
3. Pfahl, M. & Benbrook, D. (1987) Nucleotide Sequence of cDNA Encoding a Novel Thyroid Hormone Receptor. *Nucleic Acids Research*, **15**: 9613. PMID:3684612.
4. Benbrook, D., Lernhardt, E. & Pfahl, M. (1988) A New Retinoic Acid Receptor Identified from a Hepatocellular Carcinoma. *Nature*, **333**: 669-672. PMID:2836738.
5. Benbrook, D.M. & Jones, N.C. (1990) The Heterodimerization of Creb and Jun. *Oncogene*, **5**: 295-302. PMID:2138276.
6. Benbrook, D.M. & Jones, N.C. (1994) Different Binding Specificities and Transactivation of Variant CRE's by CREB complexes. *Nucleic Acids Research*, **22**: 1463-1469. PMID:8190638.
7. Apfel, R., Benbrook, D., Lernhardt, E., Ortiz, M.A., and Pfahl, M. (1994) A novel orphan receptor specific for a subset of thyroid hormone-response elements and its interaction with the retinoid/thyroid hormone receptor subfamily. *Molecular and Cellular Biology*, **14**: 7015-7035. PMID:7935418.
8. Benbrook, D., Rogers, R., Medlin, M., and Dunn, S.T. (1995) Immunohistochemical analysis of differentiation and proliferation in organotypic cultures of cervical tumor cell lines. *Tissue and Cell*, **27**(3): 269-274. PMID:7645007.
9. Benbrook, D. M., Shen-Gunther, J., Nuñez, E.R., Dynlacht, J.R. (1997) Differential retinoic acid radiosensitization of cervical carcinoma cell lines. *Clinical Cancer Research*, **3**: 939-945. PMID:9815769.
10. Johnson, G.A., Mannel, R.S., Khalifa, M., Walker, J.L., Wren, M., Min, K.-W., Benbrook, D.M. (1997) Epidermal growth factor receptor in vulvar malignancies and its relationship to metastasis and patient survival. *Gynecological Oncology*, **65**: 425-429. PMID:9190969.
11. Benbrook, D.M., Lu, S., Flanagan, C., Shen-Gunther, J., Angros, L.H., Lightfoot, S.A. (1997) Biological assay for activity and molecular mechanism of retinoids in cervical tumor cells. *Gynecological Oncology*, **66**: 114-121. PMID:9234931.
12. Miller, A.M., Sahl, W.J., Brown, S.A., Young, S.K., Quinlan, C.M., Patel, P.R., Benbrook, D.M., Naylor, M.F. (1997) The role of human papillomavirus in the development of pyogenic granulomas. *International Journal of Dermatology*, **38**: 101-105. PMID:9352408.
13. Benbrook, D.M., Madler, M.M., Spruce, L.W., Birckbichler, P., Nelson, E.C., Subramanian, S., Weerasekare, G.M., Gale, J.B., Patterson, Jr., M.K., Wang, B., Wang, W., Lu, S., Rowland, T.C., DiSilvestro, P., Berlin, K.D., Lindamood, C., Hill, D.L. (1997) Biologically active heteroarotinoids exhibit anticancer activity and decreased toxicity. *Journal of Medicinal Chemistry*, **40**: 3567-3583. PMID:9357524.
14. Madler, M.M., Klucik, J., Soell, P.S., Brown, C.W., Liu, S., Berlin, K.D., Benbrook, D.M., Birckbichler, P.J., Nelson, E.C. (1998) Lithium hypochlorite-chlorox as a novel oxidative mixture for methyl ketones and methyl carbinols. *Organic Preparations & Procedures International*, **30**: 230-234.

15. Benbrook, D.M., Subramanian, S., Gale, J.B., Liu, S., Brown, C.W., Boehm, M.F., Berlin, K.D. (1998) Synthesis and characterization of heteroarotinoids demonstrates structure-specificity relationships. *Journal of Medicinal Chemistry*, **41**: 3753-3757. PMID:9733501.
16. DiSilvestro, P.A., Stanley, S.A., and Benbrook, D.M. (1999) Ki-67 expression in a cervical carcinoma organotypic model correlates with growth and EGF-R expression. *Journal of the Lower Genital Tract Disease*, **3**: 1-5.
17. Waliszewski, P. Waliszewski, M., Gordon, N., Hurst, R.E., Benbrook, D.M., Dhar, A., Hemstreet, G.P. (1999) Retinoid signaling in immortalized and carcinoma-derived human uroepithelial cells. *Molecular and Cellular Endocrinology*, **148**: 55-65. PMID:10221771.
18. Liu, S. Berlin, K.D., Simms-Kelley, MD, Nelson, E.C., and Benbrook, D.M. (1999) Optimization and Synthesis of (*E*)-4-[2-(3,4-Dihydro-4,4-dimethyl-2*h*-1-benzopyran-6-yl)-1-propenyl]benzoic Acid-11-[¹⁴C]. *Journal of Labelled Compounds and Radiopharmaceuticals*, **42**: 789-796.
19. Dhar, A., Liu, S., Berlin, K.D., Madler, M.M., Ivey, R.T., Birckbichler, P.J., Lu, S., Zacheis, D., Brown, C.W., Klucik, J., Nelson, E.C., Benbrook, D.M. (1999) Synthesis and Structure-Activity Relationships of Nitrogen Heteroarotinoids. *Journal of Medicinal Chemistry*, **42**: 3602-3614. PMID:10479291.
20. Zacheis, D., Dhar, A., Lu, S., Madler, M.M., Klucik, J. Brown, C.w., Liu, S., Clement, F., Subramanian, S., Weerasekare, G.M., Berlin, K.D., Gold, M., Houck, J.R., Fountain, K.R., Benbrook, D.M. (1999) Heteroarotinoids inhibit the growth of head and neck cancer cell lines *in vitro* and *in vivo* through both RAR and RXR retinoic acid receptors. *Journal of Medicinal Chemistry*, **42**: 4434-4445. PMID:10543887.
21. Salsman, S., Lu, S., Benbrook, D.M. (1999) The mechanism of retinoid radiosensitization is independent of AP-1 repression in cervical carcinoma cells. *Gynecologic Oncology*, **73**: 253-256. PMID:10329043.
22. Simoni, D., Roberti, M., Invidiata, F.P., Rondanin, R., Baruchello, R., Malagutti, C., Mazzali, A., Rossi, M., Grimaudo, S., Dusonchet, L., Meli, M., Raimondi, M.V., Landino, M., D'Alessandro, N., Tolomeo, M., Dhar, A., Lu, S. Benbrook, D.M. (2001) Heterocycle-Containing Retinoids. Discovery of a Novel Isoxazole Arotinoid Possessing Potent Apoptotic Activity in Multidrug and Drug-Induced Apoptosis Resistant Cells. *Journal of Medicinal Chemistry*, **44**:2308-2318. PMID:11428925.
23. Guruswamy, S., Lightfoot, S., Gold, M., Hassan, R., K. Darrell Berlin, Ivey, T.R., Benbrook, D.M. (2001) Effects of Retinoids on the Cancer Phenotype and Apoptosis in Organotypic Cultures of Ovarian Carcinoma. *Journal of the National Cancer Institute*, **93**: 516-525. PMID:11287445.
24. Scribner, D., Benbrook, D.M. (2002) Retinoids Enhance Cisplatin-based Chemoradiation in Cervical Cancer Cells In Vitro. *Gynecologic Oncology*, **85**: 223-225. PMID:11925151.
25. Kamelle, S., Sienko, A., Benbrook, D.M. (2002) A Hormonally Responsive Model of Cycling Endometrium. *Fertility & Sterility*, **78** (3): 596-602. PMID: 12215339
26. Hassan, R., Lerner, M.R., Benbrook, D.M., Lightfoot, S.A., Brackett, D.J., Wang, Q.-C., Pastan, I. (2002) Anti-tumor activity of SS(dsFv)PE38 and SS1(dsFv)PE38, recombinant anti-mesothelin immunotoxins against human gynecologic cancers grown in organotypic culture in vitro. *Clinical Cancer Research*, **8**: 3520-3526. PMID: 12429643
27. Benbrook, D.M. (2003) An ELISA method for detection of human antibodies to an immunotoxin. *Journal of Pharmacological and Toxicological Methods*. **47**: 169-175. PMID:12628308.

28. Mic, F. A., Molotkov, A., Benbrook, D. M., and Duester, G. (2003) Retinoid activation of RAR but not RXR is sufficient for mouse embryonic development. *Proceedings of the National Academy of Sciences*. **100**: 7135-7140. PMID:12782789.
29. Chun, K.-H., Benbrook, D. M., Berlin, K. D., Hong, W. K., and Lotan, R. (2003) Induction of apoptosis in head and neck squamous cell carcinoma (HNSCC) cell lines by heteroarotinoids through a mitochondrial dependent pathway. *Cancer Research*, **63**: 3826-3832. PMID:12839980.
30. Liu, S., Brown, C.W., Berlin, K.D., Dhar, A., Guruswamy, S., Brown, D., Gardner, G.J., Birrer, M., J., Benbrook, D.M. (2004) Synthesis of flexible sulfur-containing heteroarotinoids that induce apoptosis and reactive oxygen species with discrimination between malignant and benign cells. *Journal of Medicinal Chemistry*, **47**: 999-1007. PMID:14761202.
31. Brown, C.S., Liu, S, Klucik, J., Brown, C.W., Berlin, K. D., Brennan, P.J., Devinder, K., Benbrook, D.M. (2004) Novel heteroarotinoids as potential antagonists of *Mycobacterium Bovis* BCG. *Journal of Medicinal Chemistry*, **47**: 1008-1017. PMID:14761203.
32. Tillmans, T.D., Kamelle, S.A., Guruswamy, S., Gould, N.S., Rutledge, T.L., Benbrook, D.M. (2005) Sensitization of Cervical Cancer Cell Lines to Low Dose Radiation by Retinoic Acid Does Not Require Functional p53. *Gynecologic Oncology*, **97**: 142-150. PMID:15790450.
33. Benbrook, D.M., Kamelle, S.A., Guruswamy, S.B., Lightfoot, S.A., Rugledge, T.L., Gould, N.S., Hananafon, B.N., Dunn, S.T., Berlin, K.D. (2005) Flexible Heteroarotinoids (Flex-Hets) exhibit improved therapeutic ratios as anti-cancer agents over retinoic acid receptor agonists. *Investigational New Drugs*, **23**: 417-428. PMID:16133793.
34. Subramanian, S., Smith, C.M., Tabatabai, T., Bryan, C.D., Buettner, B., Hale, S., Wakefield, C.A., Benbrook, D.M., Berlin, K.D. (2005) Synthesis of novel heteroarotinoids with receptor activation capabilities and TGase activity. Single crystal analysis of (E)-4-[(2,3-dihydro-2,2,4,4-tetramethyl-2H-1benzo[b]thiopyran-6-YL)-1-propenyl]-2-methylbenzoic acid. *Phosphorus, Sulfur, and Silicon and the Related Elements*, **180**:67-77.
35. Zhang Y. Hua Y. Benbrook D.M. Covey J.M. Dai G. Liu Z. Chan K.K. High performance liquid chromatographic analysis and preclinical pharmacokinetics of the heteroarotinoid antitumor agent, SHetA2. (2006) *Cancer Chemotherapy & Pharmacology*, **58**(5):561-9. PMID:16534614.
36. Chiu, P.-M., Feng, H.-C., Benbrook, D.M., Ngan, H.Y.S., Khoo, U.-S., Xue, W.-S., Tsao, S.W., Chan, K.-W., Cheung, A.N.Y. (2006) Effect of all-trans retinoic acid on tissue dynamics of choriocarcinoma cell lines: an organotypic model. *Journal of Clinical Pathology*, **59**:845-850. PMID:16461808.
37. Matsuzaki, S. Hayes, J.M., Benbrook, D.M., Jankowiak, R. (2006) Nonphotochemical hole-burning study of selectively stained normal and cancerous human ovarian tissues. *Journal of Physical Chemistry B*, **110**: 16124-16130. PMID:16898770.
38. Lu, Shennan, Benbrook, D.M. (2006) Role of AP-1 antagonism in growth inhibition of cervical cancer cell lines by retinoids. *American Journal of Pharmacology and Toxicology* **1**(4): 45-53.
39. Guruswamy, S., Benbrook, D.M. (2006) Retinoids chemosensitize ovarian cancer cell lines to cisplatin independent of nuclear receptors and p53. *American Journal of Pharmacology and Toxicology* **1**(4): 87-93.
40. Hyde, J., Benbrook, D.M. (2006) Sensitivities of uterine adenocarcinoma, mixed mullerian tumor (MMT) and sarcoma cell lines to chemotherapeutic agents and a Flex-Het drug. *American Journal of Pharmacology and Toxicology* **1** (4): 88-91. PMID:19890461

41. Liu, T., Hannafon, B., Gill, L., Kelly, W., Benbrook, D.M. (2007) Flex-Hets differentially induce apoptosis in cancer over normal cells by directly targeting mitochondria. *Molecular Cancer Therapeutics*, **6**: 1814-1822. PMID:17575110.
42. McMeekin, D.S., Sill, M.W., Darcy, K.M., Stearns-Kurosawa, D.J., Eaton, L., Yamada, J., Benbrook, D.M. (2007) A phase II trial of thalidomide in patients with persistent or recurrent endometrial cancer and correlation with angiogenesis biomarkers: A Gynecologic Oncology Group study. *Gynecologic Oncology*, **105**: 508-516. PMID:17306350.
43. McMeekin, D.S., Sill, M. W., Darcy, K.M., Stearns-Kurosawa, D.J., Webster, K., Waggoner, S., Benbrook, D.M. (2007) A phase II trial of thalidomide in patients with refractory leiomyosarcoma of the uterus and correlation with biomarkers of angiogenesis: A Gynecologic Oncology Group study. *Gynecologic Oncology*, **106**:596-603. PMID:17597196.
44. Le, T.C., Berlin, K.D., Benson, S.D., Eastman, M.A., Bell-Eunice, G., Nelson, A.C., Benbrook, D.M. (2007) Heteroarotinoids with anti-cancer activity against ovarian cancer cells. *Open Medicinal Chemistry Journal*, **1**: 11-23. PMID:19662136.
45. Le, T.C., Berlin, K.D., Benbrook, D.M. (2007) Modified heteroarotinoids as potential anticancer agents-improved syntheses of 2-nitrotetralin and 2-aminotetralin. *Journal of the Saudi Chem Society*, **11**: 351-360.
46. Benbrook, D.M., Lightfoot, S., Ranger-Moore, J., Liu, T., Berry, W., Dozmorov, I. (2008) Karyometric and Gene Expression Analysis in an Organotypic Model of Endometrial Carcinogenesis and Chemoprevention. *Gene Regulation and Systems Biology*, **2**: 21-42. PMID:19784388.
47. Lin, Y.-D, Chen, S., Yue, P., Zou, W., Benbrook, D.M., Liu, S., Le, T.C., Berlin, K.D., Khuri, F.R., Sun, S.-Y. (2008) CAAT/Enhancer Binding Protein Homologous Protein-Dependent Death Receptor 5 Induction Is a Major Component of SHetA2-Induced Apoptosis in Lung Cancer Cells. *Cancer Research*, **68** (13): 5335-5344. PMID:18593935.
48. Ju, T., Lanneau, G.S., Gautam, T., Wang, Y., Xia, B., Stowell, S.R., Willard, M.T., Wang, W., Xia, J.Y., Zuna, R.E., Laszik, Z., Benbrook, D.M., Hanigan, M.H., Cummings, R.D. (2008) Human tumor antigens Tn and sialyl Tn arise from mutations in Cosmc. *Cancer Research*, **68**(6):1636-46. PMID:18339842.
49. Lin, Y., Liu, X., Yue, P., Benbrook, D.M., Berlin, K.D., Khuri, F.R., Sun S.-Y. (2008) Involvement of c-FLIP and survivin down-regulation in flexible heteroarotinoid-induced apoptosis and enhancement of TRAIL-initiated apoptosis in lung cancer cells. *Molecular Cancer Therapeutics*, **7**: 3556-3565. PMID:19001438
50. Myers, T., Chenedza, S., Lightfoot, S., Pan, Y., Dedmond, D., Cole, L., Tang, Y., Benbrook, D.M. (2008) Flexible Heteroarotinoid (Flex-Het) SHetA2 inhibits angiogenesis *in vitro* and *in vivo*. *Investigational New Drugs*, **27**:304-318. PMID:18802666.
51. Liu, Z., Zhang, Y.Hua, Y.F., Covey, J.M., Benbrook, D.M., Chan, K.K.(2008) Metabolism of A Sulfur-containing Heteroarotinoid Antitumor Agent, SHetA2 using Liquid Chromatography/tandem Mass Spectrometry. *Rapid Communications in Mass Spectrometry*, **22**: 3371-3381. PMID:18837006.
52. Liu, T., Masamha, P., Chenedza, P., Berlin, K.D., Lightfoot, S, He, Feng, Benbrook, D. M. (2009) Development of Flexible Heteroarotinoids (Flex-Hets) for Kidney Cancer. *Molecular Cancer Therapeutics*, **8** (5):1227-1238. PMID:19417155.

53. Tuller, E.R., Brock, A.L., Yu, H., Lou, J.r., Benbrook, D.M., Ding, W.-Q. (2009) PPAR α signaling mediates the synergistic cytotoxicity of clioquinol and docosahexaenoic acid in human cancer cells. *Biochemical Pharmacology*, **77**: 1480-1486. PMID:19426685.
54. Masamha, C. P., Benbrook, D.M. (2009) Cyclin D1 degradation is sufficient to induce G1 cell cycle arrest despite constitutive expression of cyclin E2 in SHetA2-treated ovarian cancer cells. *Cancer Research*, **69**: 6565-6572. PMID:19638577.
55. Palwai, N.R., Zang, X.-P., Harrison, R.G. Benbrook, D.M. Pento, J.T. (2009) Selective Growth Inhibition of Cancer Cells by L-Methioninase-Containing Fusion Protein Targeted to the Urokinase Receptor. *Pharmacology*, **84**:271-275. PMID:19797936
56. Tuller, E.R., Beavers, C.T., Lou, J.R., Ihnat, M.A., Benbrook, D.M., Ding, W.-Q. (2009) Docosahexaenoic acid inhibits superoxide dismutase 1 gene transcription in human cancer cells: the involvement of PPAR α and HIF-2 α signaling. *Molecular Pharmacology*, **78**:588-595. PMID:19528198.
57. Moxley, K.M., Chenedza, S., Benbrook, D.M. (2009) Induction of death receptor ligand -mediated apoptosis in epithelial ovarian carcinoma: the search for sensitizing agents. *Gynecologic Oncology*, **115**: 438-442. PMID:19804900
58. Chenedza, S., Benbrook, D.M. (2010) NF-kappaB is involved in SHetA2 circumvention of TNF-alpha resistance, but not induction of intrinsic apoptosis. *Anti-Cancer Drugs*, **21**: 297-305. PMID:20032777
59. Zheng, J., Lou, J.R., Zhang, X.-X., Benbrook, D.M., Hanigan, M.H., Lind, S.E., Ding, W.Q. (2010) N-acetylcysteine interacts with copper to generate hydrogen peroxide and selectively induce cancer cell death. *Cancer Letters*, **298**(2):186-94, PMID: 20667650
60. Hurteau, J., Brady, M.F., Darcy, K.M., McGuire, W.P., Edmonds, P., Pearl, M.L. Ivanov, I., Tewari, K.S., Mannel, R.S., Zanotti, K., Benbrook, D.M. (2010) Randomized Phase III Trial of Tamoxifen versus Thalidomide in Women with Biochemical-Recurrent-Only Epithelial Ovarian, Fallopian Tube or Primary Peritoneal Carcinoma after a Complete Response to First-Line Platinum/Taxane Chemotherapy with an Evaluation of Serum Vascular Endothelial Growth Factor (VEGF): A Gynecologic Oncology Group Study. *Gynecologic Oncology*, **119**:444-450. PMID:20846715
61. Nammalwar, B., Bunce, R. A., Benbrook, D.M., Lu, T., Li, H.-F. , Chen, Y.-D., Berlin, K. D. (2011) Synthesis of N-[3,4-Dihydro-4-(acetoxymethyl)-2,2,4-trimethyl-2H-1-benzothiopyran-6-yl]-N'-(4-nitrophenyl)thiourea and N-[3,4-dihydro-4-(hydroxymethyl)-2,2,4-trimethyl-2H-1-benzothiopyran-6-yl]-N'-(4-nitrophenyl)thiourea, a Major Metabolite of N-(3,4-Dihydro-2,2,4,4-tetramethyl-2H-1-benzothiopyran-6-YL)-N'-(4-nitrophenyl)thiourea', *Phosphorus, Sulfur, and Silicon and the Related Elements*, **186**: 1,189-204.
62. Usha, L., Sill, M. W., Darcy, K. M., Benbrook, D. M., Hurteau, J. A., Michelin, D. P., Mannel, R. S., Hanjani, P., De Geest, K., Godwin, A. K. (2011) A Gynecologic Oncology Group phase II trial of the protein kinase C-beta inhibitor, enzastaurin and evaluation of markers with potential predictive and prognostic value in persistent or recurrent epithelial ovarian and primary peritoneal malignancies. *Gynecologic Oncology*, **121**:455-461. PMID:21414654
63. Zheng, J., Benbrook, D.M., Yu, H., Ding, W.-Q. (2011) Clioquinol suppresses cyclin D1 gene expression through transcriptional and post-transcriptional mechanisms. *Anticancer Research*, **31** (9): 2739-2747. PMID: 21868515

64. Jiang, H., Taggart, J.E., Zhang, X., Benbrook, D.M., Lind, S.E., Ding, W.-Q. (2011) Nitroxoline (8-hydroxy-5-nitroquinoline) is more a potent anti-cancer agent than clioquinol (5-chloro-7-iodo-8-quinoline). *Cancer Letters*, **312**:11–17. PMID: 21899946
65. Dozmorov, I. M., Jarvis, J., Saban, R., Benbrook, D. M., Wakeland, E., Aksentijevich, I., Ryan, J., Chiorazzi, N., Guthridge, J. M., Drewe, E., Tighe, P. J., Centola, M., and Lefkovits, I. (2011) Internal standard-based analysis of microarray data--analysis of functional associations between HVE-genes. *Nucleic Acids Research*, **39**: 7881-7899, 2011. PMID: 22498038.
66. Ramachandran I., Thavathiru E., Ramalingam S., Natarajan G., Mills W., Benbrook D., Zuna R., Lightfoot S., Reis A.M.C, Anant S. and Queimado L. (2012) Wnt inhibitory factor 1 induces apoptosis and inhibits cervical cancer growth, invasion and angiogenesis in vivo. *Oncogene*, <http://dx.doi.org/10.1038/onc.2011.455>. PMID: 22002305
67. Kabirov, K.K. Kapetanovic, I.M., Benbrook, D.M., Dinger, N., Mankovskaya, I., Zakharov, A., Detrisac, C., Pereira, M., Martín-Jiménez, T., Onua, E., Banerjee, A., van Breemen, R.B., Nikolić, D., Chen, L., Lyubimov, A.V. (2012) Oral toxicity and pharmacokinetic studies of SHetA2, a new chemopreventive agent, in rats and dogs. *Drug and Chemical Toxicology*, **36**(3): 284-95. PMID: 22947079
68. Doppalapudi, R. S., Riccio, E. S., Davis, Z., Menda, S., Wang, A., Du, N., Green, C., Kopelovich, L., Rao, C. V., Benbrook, D. M., and Kapetanovic, I. M. (2012) Genotoxicity of the cancer chemopreventive drug candidates CP-31398, SHetA2, and phospho-ibuprofen. *Mutation Research*, **746**: 78-88, 2012. PMID: 22498038
69. McMeekin, D.S., Sill, M.W., Darcy, K.M., Abulafia, O., Hanjani, P., Pearl, M.L., Rubin, S.C., Rose, P.G., Small L, Benbrook, D.M. (2012) A phase II trial of thalidomide in patients with refractory uterine carcinosarcoma and correlation with biomarkers of angiogenesis: A Gynecologic Oncology Group study. *Gynecologic Oncology*, **12**: 356-61. PMID:22796461
70. Moxley, K.M., Benbrook, D.M., Queimado, L., Zuna, R.E., Thompson, D., McCumber, M., Premkumar, P., Thavathiru, E., Hines, L., Moore, K.N. (2013) The role of single nucleotide polymorphisms of the ERCC1 and MMS19 genes in predicting platinum-sensitivity, progression-free and overall survival in advanced epithelial ovarian cancer. *Gynecologic Oncology*, **130**: 77-382. PMID:23632208
71. Naylor, M.F,Thompson, D.M, Lightfoot, S., Benbrook, D.M. (2013) Anti-Cancer Activities and Interaction of Imiquimod and Flex-Het, SHetA2. *Journal of Cancer Therapy*, **4**: 7-19.
72. Benbrook, D.M., Guruswamy, S., Wang, Y., Sun, Z., Mohammed, A., Zhang, Y., Li, Q., Rao,C.V. (2013) Chemoprevention of Colon and Small Intestinal Tumorigenesis in APC^{min/+} Mice by SHetA2 (NSC721689) without Toxicity. *Cancer Prevention Research*, **6**: 908-916. PMID:23852423
73. Benbrook, D.M., Nammalwar, B., Long, A., Matsumoto, A., Singh, A., Bunce, R.A., Berlin, K.D. (2014) SHetA2 interference with mortalin binding to p66shc and p53 identified using drug-conjugated magnetic microspheres. *Investigational New Drugs*. **32**:412–423. PMID: 24254390
74. Bishop, E., Thavathiru, E., Benbrook, D. (2014) Insulin exerts direct effects on carcinogenic transformation of human endometrial organotypic cultures. *Cancer Investigation*, **32**: 63–70. PMID: 24499106

75. Slaughter, K.M., Thai, T., Penarozza, S., Benbrook, D.M., Thavathiru, E., Ding, K., Nelson, T., McMeekin, D.M., Moore, K.N. (2014) Measurements of adiposity as clinical biomarkers for first-line bevacizumab-based chemotherapy in epithelial ovarian cancer. *Gynecologic Oncology*, **133**: 11-15. PMID:24680585
76. Powell, M., Sill MW, Goodfellow, P.J., Benbrook, D.M., Lankes, H.A., Leslie, K.K., Jeske, Y., Mannel, R.S., Spillman, M.A., Lee, P.S. (2014) A Phase II Trial of Brivanib in Recurrent or Persistent Endometrial Cancer: An NRG Oncology/Gynecologic Oncology Group Study. *Gynecologic Oncology* **135**:38-43. PMID: 25019571
77. Long, A., Masamha, P., Benbrook, D.M. (2014) Differential roles of autophagy in ovarian cancer and healthy cells in response to SHetA2 drug. *Cell Death and Disease*, pending revision review.

REVIEWS

1. Hurst,R.E., Waliszewski, P., Waliszewska, M., Bonner, R.B., Benbrook, D.M., Dhar, A., Hemstreet, G.P. (1999) Complexity, retinoid-responsive gene networks, and bladder carcinogenesis. *Advances in Experimental Medicine and Biology*. **462**: 449-67. PMID:10599447
2. Benbrook, D.M. (2002) Refining Retinoids with Heteroatoms, *Minireviews in Medicinal Chemistry*, **2**: 277-283. PMID:12370069. (Invited)
3. Benbrook, D.M., Wilkerson, J. C. (2003) Nature Reviews Cancer. *JAMA*. **289**(8):1049-1050.
4. Benbrook, D.M. Organotypic Cultures Represent Tumor Microenvironment for Drug Testing. (2006) *Drug Discovery Today, Disease Models*. **2**: 143-148. (Invited)
5. Benbrook DM. Promise and problems of translational research. *Gynecologic Oncology*. **103**(2 Suppl 1): S14-7, 2006 Nov. PMID:17027066. (Invited)
6. Benbrook, D.M., Masamha, C.P. (2011) The pro-survival function of Akt kinase can be overridden or altered to contribute to induction of apoptosis. *Current Cancer Drug Targets*, **11**: 586-599. PMID:21486222
7. Benbrook, D.M., Long, A. (2012) Integration of Autophagy, Proteasomal Degradation, Unfolded Protein Response and Apoptosis. *Experimental Oncology*, **34**: 286-297. PMID:23070014 (Invited).
8. Benbrook, D.M. (2014) Book Review: Biotechnology and Biopharmaceuticals: Transforming Proteins and Genes Into Drugs, 2nd Edition. *Clinical Infectious Diseases*. 2014 Oct 9. Epub 2014/10/11. Eng. PMID: 25301211. (Invited and Peer-Reviewed)

BOOK CHAPTERS

1. Pfahl, M., Payne, J., Benbrook, D. & Wu, K.C. (1988) Differential Activation of a Hormone-Responsive Element in Various Cell Lines. *Steroid Hormone Action*, pp. 161-168.
2. Benbrook, D.M., Tonetti, D.A. & Miller, R.V. (1989) DNA Gyrase of *Pseudomonas Aeruginosa*: Inhibition by Quinolones. *Proceedings International Telesymposium on Quinolones*, Fernandez, P.B. (Ed.) J.R. Prous Science Publishers, pp.171-186.
3. Alberts, D.A., Barakat, R.R., Daly, M., Method, M.W., Benbrook, D.M., et al. (2004) Prevention of Gynecologic Malignancies. In Gershensen, D.M., McGGuire, W.P., Gore, M., Quinn, M.A., Thomas, G. editors. *Gynecologic Cancer: Controversies in Management*. Elsevier, Churchill, Livingston, Philadelphia, PA.

4. Benbrook D, Chambon P, Rochette-Egly C, Asson-Batres M. (2014) History of Retinoic Acid Receptors. In: Asson-Batres MA, Rochette-Egly C, eds. *The Biochemistry of Retinoic Acid Receptors: Structure, Activation, and Function at the Molecular Level*. Vol 70: Springer Netherlands; pp. 1-20 (Invited) PMID: 24962878

ABSTRACTS AND MEETING PRESENTATIONS: More than 90 abstracts presented at national and international meetings (1983-present).

INVITED LECTURES, SELECTED FROM PAST 5 YEARS: More than 100 invited lectures since 1991.

89. ***“Progress Report on Development of SHetA2 for Chemoprevention”*** April 3, 2010, HOPE Ovarian Cancer Survivor Group, University of Oklahoma Health Sciences Center
90. ***“Development of Flex-Het Drugs for Prevention and Treatment of Cancer: From basic laboratory science to clinical trials”*** June 23, 2010, University of Cape Town, Cape Town, South Africa
91. ***“Development of a Flex-Het Drug and Biomarkers for a Chemoprevention Clinical Trial”*** December 21, 2010, International Cancer Research Symposium 2010: Defining & Translating Science Behind Disease. Rajiv Gandhi Centre for Biotechnology, Thiruvananthapuram, Kerala, India
92. ***“Before You Can Shoot, You Need to Know What the Target Is”*** February 9, 2011, Symposium on Drug Design and Molecular Pharmacology. University of Southern California
93. ***“Collaboration in Drug Discovery and Translation to Clinical Trials”*** May 17, 2011, The 14th annual Rall Symposium for Undergraduate Research, North Central College, Naperville, IL
94. ***“Development of a Cancer Prevention Pill”*** October 22, 2011, Ovarian Cancer Support Group, Bartlesville, OK
95. ***“Heat Shock Proteins and Stress Response Pathways in Cancer Drug Development”*** October 12, 2012, Department of Biochemistry, Oklahoma State University, Stillwater, OK
96. ***“Stress Response in Ovarian Cancer Resistance”*** September 29, 2012, MD Anderson Cancer Center and Stephenson Cancer Center Collaborative Retreat, MD Anderson Cancer Center, Houston, TX
97. ***“Leveraging Cell Stress Response Pathways in Drug Discovery”*** December 3, 2012, Tumor Microenvironment and Drug Discovery Conference, Stephenson Cancer Center
98. ***“Curing Cancer with Chemistry”*** March 7, 2013, Chemistry Club Meeting, University of Central Oklahoma, Edmond, OK,
99. ***“Cancer Prevention”*** March 16, 2013, Women’s Enrichment Fellowship Talk Show, Forward in Faith Ministries International, Farmers Branch, TX
100. ***“Development of a Cancer Drug: From Tubes to Tissues to Treatments”*** September 24, 2013 Department of Cell Biology and Biochemistry, Texas Tech University, Lubbock Texas
101. ***“How Cancer Cells Use ER Stress and Autophagy to Eat Stroma”*** February 9th-11th, 2014, 1st Annual Meeting of the International Ovarian Cancer Consortium: Tumor Microenvironment and Drug Discovery, Stephenson Cancer Center, OUHSC, Oklahoma City, OK
102. ***“Drug-Conjugated Nanoparticles Reveal Mechanism of SHetA2 Drug Activity”*** 17-19 April 2014, 2nd International BAU Drug Design Congress, Istanbul, Turkey
103. ***“Autophagy and Immunology in Ovarian Cancer”*** August 28, 2014. MD Anderson Cancer Center/Stephenson Cancer Center (MDACC/SCC) Collaboration
104. ***“Integration of autophagy and apoptosis in the tumor microenvironment and downstream of mortalin/client protein disruption”*** September 5, 2014, Eppley Seminar Series, University of Nebraska