BIOGRAPHICAL SKETCH

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NAME: **Robert D. Arnold, Ph.D. "Rusty"**

eRA COMMONS USER NAME (credential, e.g., agency login): **RDARNOLD**

POSITION TITLE: **Associate Professor**, **Director of Specialized Pharmaceutical Experimental Center for Translational Research and Analysis** (***SPECTRA***)

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Plattsburgh State, SUNY, Plattsburgh, NY	B.Sc.	05/1999	Biochemistry (honors)
University at Buffalo, SUNY, Amherst, NY	Ph.D.	02/2004	Pharmaceutical Sciences
University at Buffalo & Roswell Park Cancer Institute, Buffalo, NY	Post-Doc	08/2005	Cancer Therapeutics, Non-Invasive Imaging & Nanomedicine

A. Personal Statement

I am an industrial (Wyeth-Ayerst Research) and academically (University at Buffalo and Roswell Park Cancer Institute) trained pharmaceutical scientist with >20 years expertise in nanomedicine and experimental therapeutics, specifically developing novel lipid-nanoparticles as drug carriers and diagnostic agents for the treatment of cancers, *in vitro* and *in vivo* evaluation and pharmacokinetic-pharmacodynamic analysis and modeling of existing and novel therapeutics. My NIH funded research (R01) is related to development of targeted nanomedicines that exploit differences in tumor pathophysiology to aid in detection and treatment of primary and metastatic disease and improving methods to more accurately evaluate cancer biology (previous R43 and R44 w/CDRFC). My research group utilizes a variety of *in vitro* and *in vivo* models of human cancers (breast, prostate, brain and pancreatic) applies non-compartmental and computational approaches to the analysis of systemic kinetics and tissue distribution studies, including studies to examine the effect of drug efficacy and toxicity. My laboratory has all the resources to conduct *in vitro* and *in vivo* tumor growth, pharmacokinetic (***PK***) and pharmacodynamic (***PD***) - efficacy/toxicity studies in small animals (mouse, rat and dogs) and software to support analysis, modeling and simulation of PK/PD data. As MPI, PI and CO-I I have received both NIH, private and state/local funding in excess of $6.8 million since 2005 and have published 28 papers since 2013 and have 5 research papers under review. I serve as the director of the Auburn University ***S***pecialized ***P***harmaceutical and ***E***xperimental ***C***enter for ***T***ranslational ***R***esearch and ***A***nalysis (***SPECTRA***) and have provided consultation or PK/PD services for over 17 different investigators and 50 different projects, including NIH, NSF, DOD, academic and industry. Further, I hold a DEA license (Registration Number AA9588142) for acquisition and use of controlled (Schedules 2, 2N, 3, 3N, 4 and 5) substances.

B. Positions and Honors

Academic and Professional Appointments:

1994-1997 ***Assistant to Associate Scientist***, Liquid & Parenteral Formulations, Pharmaceutical Sciences R&D, Wyeth-Ayerst Research, Rouses Point, NY

1997-2003 ***Graduate Research Assistant***, Department of Pharmaceutical Sciences, University at Buffalo, Amherst, NY

2004-2005 ***Postdoctoral Fellow***, Departments of Pharmaceutical Sciences, University at Buffalo, & Cancer Biology, Preclinical Imaging Facility, Roswell Park Cancer Institute, Buffalo, NY

2005-2012 ***Assistant Professor***, Department of Pharmaceutical & Biomedical Sciences, College of Pharmacy, University of Georgia, Athens, GA * recommended for promotion 5/2012

2012-present ***Associate Professor***, Department of Drug Discovery & Development, School of Pharmacy, Auburn University, Auburn, AL *tenure awarded 2015 *awarded Full (8/2018)

2012-present ***Adjunct Professor,*** Department of Small Animal Surgery and Medicine, School of Veterinary Medicine, University of Georgia, Athens, GA. *with graduate faculty standing

2013-present ***Director,*** Auburn University ***S***pecialized ***P***harmaceutical & ***E***xperimental ***C***enter for ***T***ranslational ***R***esearch & ***A***nalysis "***SPECTRA***"

2015-present ***Adjunct Associate Professor****, Department of Pathobiology, School of Veterinary Medicine, Auburn University, Auburn AL.*

Other Experience and Select Professional Memberships

2011-present ***Reviewer*** – NIH, Special Emphasis Panel/Scientific Review Group, Innovative Research in Cancer Nanotechnology, ZRG1 IMST-L (55), 3/18, Washington, DC, NIH, 2018/05 , Developmental Therapeutics (DT) Study Section, 2/18, San Diego, CANIH, National Institute of General Medical Sciences (NIGMS) Special Emphasis Panel, 2018/01 ZGM1 RCB-4 (SC), 11/2017, Bethesda, MD**,** NIH IRG Oncology-2, Translational Clinical, Developmental Therapeutics (DT) Study Section, 10/2016, Alexandria, VA., NIH, Bioengineering Research Partnerships (BRPs): ZRG-1 BST-A 55 S, 4/16, NIH, IRG Oncology-2, Translational Clinical, Developmental Therapeutics (DT) Study Section, 2/2015, Arlington, VA –ad hoc member, NINDS NSD-B Study Section, 2/2015 Alexandria, VA, -ad hoc member (phone), NIH/NCI Special Emphasis Panel/Scientific Review Group, ZCA1 SRLB-U(C1)B, Topic 327, Drug Reformulation, 3/14, DC; NIH, Study Section, Nanotechnology (NANO), 5/13 and 9/12, Special Emphasis Panel/Scientific Review Group ZRG1 ETTN-P -(50) R PAR-11-304, Development of Appropriate Pediatric Formulation and Drug Delivery Systems, 3/12, CA and NIH, Special Emphasis Panel/Scientific Review Group ZRG1 ETTN-P -(11) B, Drug Discovery for Aging, Neuropsychiatric and Neurologic Disorders, 3/12, CA**,** NIH, Special Emphasis Panel/Scientific Review Group ZRG1 ETTN-C (11) B-Neuropharmacology & Imaging, 6/09, 8/09, 11/09, 3/10

2009 ***Reviewer*** – Achievement Rewards for College Scientists Foundation Fellowships, 2009

2008-present ***Reviewer*** – American Association of Colleges of Pharmacy - New Investigator Grant Program, Biology Section

2005-present ***Journal Referee****,* Cancer Chemotherapy & Pharmacology, Clinical Cancer Research, Cancer Research, Acta Biomaterialia, Journal of Pharmacology & Experimental Therapeutics, The AAPS Journal, AAPS Pharm. Sci. Tech., Journal of Pharmaceutical and Biomedical Analysis, Biomedical Chromatography, and American Journal of Pharmaceutical Education, and Medicinal Research Reviews

2012-present ***Member*****,** Auburn University Research Initiative in Cancer, Auburn Al.

2009-present ***Member*****,** Interdisciplinary Toxicology Program, University of Georgia, GA

2011-present ***Member***, Nanoscale Science & Engineering Center, University of Georgia, Athens, GA

1997-present ***Member****,* American Association of Pharmaceutical Scientists (AAPS)

2002-present ***Member****,* American Association of Cancer Researchers (AACR)

2010-present ***Member****,* American Society of Pharmacology and Experimental Therapeutics (ASPET)

Honors, Awards, Fellowships (last 5 years)

2015-16 AACP Academic Leadership Fellows Program

2014 President's Outstanding Collaborative Units Award, New Interdisciplinary Area – Pharmaceutical Engineering, Auburn University

2013 Faculty Research Excellence Award, Harrisons School of Pharmacy, Auburn University

2011 *Teacher of the Year, University of Georgia, College of Pharmacy*

2009 *Induction in Rho Chi Society – Academic Honors Society of Pharmacy*

2007-12 *Georgia Cancer Coalition - Distinguished Research Cancer Scholar*

C. Contributions to Science

1. **Contribution to Sciences Relevant to Measurement of Prostate Cancer Growth and Tumor Imaging:** The overall goal of my research program has been focused on exploiting differences in the pathophysiology of disease states, specifically cancers, with the development and optimization nano-particulate based strategies to improve detection and treatment of disease. Early in my career I demonstrated that repetitive administration of pegylated, long-circulating liposomes containing doxorubicin resulted in enhanced permeability of brain tumors to subsequent treatments. This work laid foundation for developing concomitant therapies that exploit this "window" of opportunity and provided mechanistic insights into biodistribution of liposomes and other nanoparticles. Over the last 8 years I have secured R21 (MPI) and current R01 (PI)

focusing on gaining insights into strategies that alter the rate and extent of drug release and particulate uptake in breast and prostate cancers. My laboratory has also collaborated on development and use of hyperthermia based magnetic nanoparticles, novel imaging tehcniques and use of 3D tumor micro mimetic systems. Overall my laboratory is conducting research that is critical to understanding the biology related to biodistribution, uptake and activity of nanomedicines.

a. Zhu, G., Mock, J., Aljuffali, I., *Cummings, B.S*. and **Arnold**, **R**.**D**., Secretory phospholipase A_2 responsive liposomes, *Journal of Pharmaceutical Sciences*, (2011) 100(8) 3146-3158, doi: 10.1002/jps.22530, Epub 3/11

b. Zhao, Q., Luning, W., Cheng, R., Mao, L., **Arnold**, **R**.**D**., Howerth, E. Chen, G. and Platt, S., Magnetic nanoparticle-based hyperthermia for head & neck cancer in mouse models, *Theranostics*, (2012); 2(1) 86-94. doi:10.7150/thno.3854

c. Chaudhuri, T.R., **Arnold**, **R**.**D**., Yang, J., Turowski, S., Qu, Y., Spernyak, J., Mazurchuk, R., Mager, D.E. and Straubinger, R.M., Mechanisms of Tumor Vascular Priming by a Nanoparticulate Doxorubicin Formulation, *Pharmaceutical Research,* (2012); 29(12):3312-24, doi: 10.1007/s11095-012-0823-4

d. Mock, J., Costyn, L.J., Wilding, S.L., **Arnold**, **R**.**D**. and *Cummings, B.S*., Evidence for distinct mechanisms of uptake and antitumor activity of secretory phospholipase A_2 responsive liposome in prostate cancer, *Integrative Biology*, (2013), 5: 172-182, doi: 10.1039/C2IB20108

e. Quach, N.D., **Arnold**, **R**.**D**. and Cummings, B.S., Secretory Phospholipase A_2 Enzymes as Pharmacological Targets for Treatment of Disease, *Biochemical Pharmacology*, (2014) 90: 338-348, doi: 10.1016/j.bcp.2014.05.022

f. Quach, N., Mock, J.N., Scholpa, N.E., Eggert, M., **Arnold**, **R**.**D**. and *Cummings, B.S*., Role of the phospholipase A_2 receptor in liposomal drug delivery in prostate cancer cells, *Molecular Pharmaceutics* (2014), 11(10) 3443-3451 doi: 10.1021/mp500174p

g. Pati, S., Nie, B., **Arnold**, **R**.**D**. and Cummings, B.S., Extraction, chromatographic and mass spectrometric methods for lipid analysis, (Invited Review), *Biochemical Chromatography,* (2016) 30(5) 695-709, doi: 10.1002/bmc.3683, epub 12/15

h. Chaudhari, A.A., Jasper, S.L., Dosunmu, E., Miller, M.E., **Arnold**, **R**.**D**., Singh, S.R. and Pillai, S.R., Novel pegylated silver coated carbon nanotubes kill Salmonella but they are non-toxic to eukaryotic cells, *Journal of Nanobiotechnology* (2015) 13(1) 1-17 doi:10.1186/s12951-015-0085-5

i. Brannen A., Eggert M., Smith, M., Nahrendorf, M., **Arnold**, **R**.**D**. and Panizzi, P. Multi-Angle In Vivo Bioluminescence Imaging Using the Mouse Imaging Spinner (MiSpinner) Shows Potential For Accurate Monitoring of Tumor Development, *Scientific Reports* (2018) 8(3321), doi:10.1038/s41598-018-21668-4

j. Pradhan, S., Smith, A.M., Garson, C.J., Hassani, I., Seeto, W., Pant, K., Arnold**,** R**.**D., Prabhakarpandian, B. and Lipke, E.A., A microvascularized tumor-mimetic platform for assessing anti-cancer drug efficacy, *Scientific Reports* (2018), 8(317) 1-15, doi:10.1038/s41598-018-21075-9

2. **Contribution to Sciences Relevant to Experimental Therapeutics & Dose Optimization:** In pursuing this research, pharmacokinetic (PK) and pharmacodynamic (PD) principles are used as tools for the selection of novel therapeutic agents, design of rational passively and actively targeted drug delivery systems. My laboratory utilizes a variety of computational approaches to establish exposure-response relationships, develop PK/PD models and conduct simulations to evaluate potential dosing schedules and or develop novel hypothesis. This work is iterative in nature and has permitted the evaluation of the disposition of complex nanomedicines and their drug release kinetics. Utilizing my expertise in PK/PD analysis we used population and mechanistic computational modeling to examine factors that control distribution of Tocosol™, a nano-emulsion containing paclitaxel in humans and correlated exposure to antitumor activity and toxicity. These approaches have also been applied to a variety of collaborators examining the effects of antagonists to drug efflux proteins, drug-drug interactions and in collaboration with veterinarians who are working to translate FDA approved drugs for humans to various companion and exotic (zoo and wildlife) animals.

a. **Arnold**, **R.D**., Mager, D.E., Slack, J.E. and Straubinger, R.M., Effect of repetitive administration of Doxorubicin-containing liposomes on plasma pharmacokinetics and drug biodistribution in a rat brain tumor model. *Clinical Cancer Research*, (2005) 11(24):8856-8865, doi:10.1158/1078-0432

b. O'Conner, R., O'Leary, M.O., Ballot, R., Collins, C., Kinsella, P., Mager, D.M., **Arnold**, **R**.**D**., O'Driscoll, L.O., Larkin, A.M., Kennedy, S., Fennelly, D., Clynes, M. and Crown, J.*,* A Phase 1 clinical and pharmacokinetic study of the multidrug resistance protein-1 (MRP-1) inhibitor sulindac, in combination with epirubicin in patients with advanced cancer. *Cancer Chemotherapy and Pharmacology*, (2007) 59(1):79-87, doi:10.1007/s00280-006-0240-7

c. Bulitta, J.B., Zhao, P., **Arnold**, **R**.**D**., Kessler, D.R., Daifuku, R., Pratt, J., Luciano, G., Hanauske, A.R., Gelderblom, H., Awada, A. and Jusko, W.J., Mechanistic population pharmacokinetics of total and unbound paclitaxel for a new nanodroplet formulation vs. Taxol in cancer patients, *Cancer Chemotherapy and Pharmacology*, (2009) 63:1035-1048, doi:10.1007/s00280-008-0827-2

d. Bulitta, J.B., Zhao, P., **Arnold**, **R**.**D**., Kessler, D.R., Daifuku, R., Pratt J., Luciano, G., Hanauske, A.R., Gelderblom, H., Awada, A. and Jusko, W.J., Multiple-pool lifespan models for neutropenia to characterize the population pharmacodynamics of unbound paclitaxel from two formulations in cancer patients, *Cancer Chemotherapy and Pharmacology*, (2009) 63:1049-1063, doi: 10.1007/s00280-008-0828-1

e. Zhang, S., Sagawa, K., **Arnold**, **R**.**D**., Tseng, E., Xiaougdong, W. and Morris, M.E., Interactions between the flavonoid Biochanin A and P-glycoprotein substrates in rats: *in vitro* and *in vivo*, *Journal of Pharmaceutical Sciences,* (2010) 99(1): 430-41. doi: 10.1002/jps.21827

f. Aljuffali, I., Mock, J., Costyn, L.J., Cummings, B.S., Nagy, T. and **Arnold**, **R**.**D**., Enhanced antitumor activity of low-dose continuous administration schedules of Topotecan in prostate cancer, *Cancer Biology and Therapy,* (2011) 12(5) 407-420, doi:10.4161/cbt.12.5.15950

g. Burton, A.J., Giguère, S., Berghaus, L.J., Coulson, G.B., Hondalus, M.K. and **Arnold**, **R**.**D**., Efficacy liposomal gentamicin against *Rhodococcus equi* in a mouse infection model and co-localization with *R. equi* in equine alveolar macrophages, *Vet Microbiol* (2015) 176(3) 292-300 doi: 10.1016/j.vetmic.2015.01.015

h. Mouli, S., Nanaykkara, G., Fu, R., AlAsmari, A., Haitham, E., Berlin, A., Lohani, M., Nie, B., Navazis, N.A., Smith, F., **Arnold**, **R**.**D**., Beyers, R., Denney, T., Dhanasekaran, M., Quindry, J., Zhong, J. and Amin, R., B.S., The role of frataxin in doxorubicin mediated cardiac hypertrophy, *American Journal Physiological, Heart and Circulatory Physiology* (2015) 309:H844-H859, doi:10.1152/ajpheart.00182.2015

i. Kang, JY., Eggert, M., Mouli, S., Aljuffali, I., Fu, X., Nie, B., Sheil, A., Waddey, K., Oldham, C.D., May, S.W., Amin, R. and **Arnold**, **R**.**D**., Pharmacokinetics, antitumor and cardioprotective effects of liposome-encapsulated phenylaminoethyl selenide in human prostate cancer rodent models, *Pharmaceutical Research* (2015), 32(3) 852-862 doi: 10.1007/s11095-014-1501-5

j. Huang, J., Milton, A., **Arnold**, **R**.**D**., Smith, F., Panizzi, J.R. and Panizzi, P. Methods for measuring myeloperoxidase activity toward assessing inhibitor efficacy in living systems, *Journal of Leukocyte Biology,* (2016) 99(4) 541-548, doi: 10.1189/jlb.3RU0615-256R

D. Research Support

Ongoing Extramural Research Support:

R44 BBA N44CO67006-79 (Phipps) 9/15/16-09/14/18
NIH, SBIR – Phase II RFP No. PHS2014-1, Topic 328
Validation of 3D Human Tissue Culture Systems that Mimic the Tumor Microenvironment. The objective of this application is to validate the use of a novel hydrogel-microfluidic device that better simulates *in vivo* human tumor microenvironment. Dr. Arnold will oversee *in vivo* drug screening and cytotoxicity studies.
Role: Co-PI (w/Lipke, subcontract for CDFR Corporation)

1R01 1EB016100-01 (Arnold) 1/01/13-12/31/17
NIH/NIBIB, PAR-11-148,
Secretory phospholipases (sPLA$_2$) & their receptors for delivering nanoliposomes. The primary objective of this application is to determine the roles of secreted phospholipase A$_2$ (sPLA$_2$) and PLA$_2$ receptor (PLA2R) on the

disposition, intracellular uptake and antitumor activity of lipid based nanoparticles. Dr. Arnold is responsible for overall management and publication of findings from this project. Specifically, his group will prepare and determine the effect of peptide-targeted formulations and determining their activity in cell based and nude mouse model of human prostate primary and metastatic cancer.
Role: PI

1R15AG048643-01 (Amin/Suppiramaniam) 9/01/16-10/31/19
NIH, PA13-313
Novel central PPAR gamma signaling improves cognition in Alzheimer's disease. The goal of this application is to elucidate the mechanisms underlying a novel PPAR gamma agonist for treatment of Alzheimer's disease. Dr. Arnold will assist with study design, quantification and pharmacokinetic analysis of compound 9, beta amyloid and other analytes.
Role: Co-I

Past Extramural Research Support:

R43 HHSN261201400037C (Phipps) 10/01/14-09/30/15
NIH, SBIR – Phase I RFP No. PHS2014-1, Topic 328
3D Tissue Culture System for Tumor Microenvironment. The objective of this application is to advance the development of a novel hydrogel-microfluidic device to better simulate tumor microenvironment. Dr. Arnold oversaw drug screening and cytotoxicity studies.
Role: Co-PI (w/Lipke, subcontract from CDFR Corporation)

(Giguère) 04/01/12-03/31/14
Grayson-Jockey Club Research Foundation, Inc.,
Liposomal gentamicin for the treatment of R. equi. The overall goal of this grant is to determine the efficacy of novel gentamicin liposomes *in vitro* and *in vivo* activity against *R. equi,* a gram-positive, facultative intracellular bacterium that is a common cause of pneumonia in young foals. Dr. Arnold was responsible for assisting in the development and characterization of gentamicin liposomes, evaluation of their *in vitro* and *in vivo* release kinetics, plasma pharmacokinetics, and pharmacologic activity in mice and foals.
Role: Co-I

(Epstein/Brainard) 08/01/11-08/01/13
Abbott Animal Healthcare
Assessment of the effects of two formulations of hydroxyethylstarch on cardiovascular parameters and platelet function in normal horses. The objective of this grant is to determine the effect of a novel formulation of hydroxyethylstarch (HES) on coagulation in horses. Dr. Arnold was responsible for quantification and pharmacokinetic/pharmacodynamic analysis of HES.
Role: Co-I

1R21 EB008153, (**Arnold**/Cummings) 06/01/09-05/31/12*
NIH/NIBIB, PAR-08-053
$sPLA_2$ Selective degradation of nanoparticles. The primary objective of this grant is to determine the effect of secretory phospholipase A_2 on the degradation of lipid based nanoparticles. Dr. Arnold was responsible for evaluating the effect of $sPLA_2$ on lipids based formulations and determining the activity of novel $sPLA_2$ targeted nanoparticles in cell based and a murine model of human prostate primary and metastatic cancer.
Role: MPI (Multiple-PI), *1 year no cost extension