

**BIOGRAPHICAL SKETCH**

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NAME Daniel L. Gustafson	POSITION TITLE Associate Professor		
eRA COMMONS USER NAME GUSTAFSON.DANIEL	Department of Clinical Sciences		
EDUCATION/TRAINING <i>(Begin with baccalaureate or other initial professional education, such as nursing, and include postdoctoral training.)</i>			
INSTITUTION AND LOCATION	DEGREE <i>(if applicable)</i>	YEAR(s)	FIELD OF STUDY
Santa Clara University, Santa Clara, CA	B.S.	1987	Biology
University of Nevada, Reno, NV	Ph.D.	1992	Pharmacology/Physiology
Colorado State University, Ft. Collins, CO & University of Colorado Health Sciences Center, Denver, CO	PostDoc	1993-1996	Radiation Biology and Pharmacology

**A. POSITIONS AND HONORS****Research and Professional Experience:**

1988-1992	Graduate Research Assistant, Cell and Molecular Pharmacology and Physiology Program, University of Nevada, Reno, NV.
1992-1993	Postdoctoral Fellow, Department of Nutrition, University of Nevada, Reno, NV.
1993-1996	Postdoctoral Trainee, Department of Radiological Health Sciences, Colorado State University, Fort Collins, CO and School of Pharmacy, University of Colorado Health Sciences Center, Denver, CO.
1996-1999	Assistant Professor, Department of Environmental Health, Faculty, Cell and Molecular Biology Graduate Program, Colorado State University, Fort Collins, CO.
1999-2006	Assistant Professor, Department of Pharmaceutical Sciences, University of Colorado Health Sciences Center, Denver, CO.
1999-Present	Director, Pharmacology Core, University of Colorado Cancer Center, University of Colorado Health Sciences Center, Denver, CO.
2006-2007	Associate Professor, Department of Pharmaceutical Sciences, University of Colorado Health Sciences Center, Denver, CO.
2007-Present	Associate Professor, Department of Clinical Sciences, Colorado State University, Fort Collins, CO.
2008-Present	Director of Research, Animal Cancer Center, Colorado State University, Fort Collins, Co.

**Honors and Awards:**

1987	Nominated Sigma Xi, Santa Clara University Chapter
1992	George Bierkamper Award for outstanding graduate student in the Cell and Molecular Pharmacology and Physiology Program, University of Nevada School of Medicine
1994-1996	NRSA Postdoctoral Fellowship (NCI), Mitomycin C Sensitivity in CHO Cell Mutants and Hybrids, Sponsors: C.A. Waldren and D. Ross
1998-2003	Howard Temin Award (NCI), Predictive Models for Combination Cancer Chemotherapy

**B. SELECTED PEER-REVIEWED PUBLICATIONS****Recent and Representative Publications: (SELECTED FROM A TOTAL OF 60)**

- Gustafson, DL** and Pritsos, CA. Bioactivation of mitomycin C by xanthine dehydrogenase from EMT6 mouse mammary carcinoma tumors. J Natl Cancer Inst 1992; 84:1180-1185. PMID 1635086
- Pritsos, CA, Sokoloff, M and **Gustafson, DL**. PZ-51 (Ebselen) *in vivo* protection against Adriamycin-induced mouse cardiac and hepatic lipid peroxidation and toxicity. Biochem Pharmacol 1992;44:839-841. PMID 1510734
- Gustafson, DL** and Pritsos, CA. Enhancement of xanthine dehydrogenase mediated metabolism of

- mitomycin C by dicumarol. *Cancer Res* 1992;52:6936-6939. PMID 1281039
4. **Gustafson, DL** and Pritsos, C.A. Kinetics and mechanism of mitomycin C bioactivation by xanthine dehydrogenase under aerobic and hypoxic conditions. *Cancer Res* 1993; 53:5470-5474. PMID 8221687
  5. **Gustafson, DL**, Beall, HD, Bolton, EM, Ross, D and Waldren, CA Expression of human NADPH:quinone oxidoreductase (DT-diaphorase) in chinese hamster ovary cells: effect on the toxicity of antitumor quinones. *Mol Pharmacol* 1996;50:728-735. PMID 8863816
  6. Cross, JV, Deak, JC, Rich, EA, Qian, Y, Lewis, M, Parrott, LA, Mochida, K, **Gustafson, D**, Vande Pol, S, and Templeton, DJ. Quinone reductase inhibitors block SAPK/JNK and NFKB pathways and potentiate apoptosis. *J Biol Chem* 1999; 274:31150-31154. PMID 10531305
  7. **Gustafson, DL**, Franz, HR, Ueno, AM, Smith, CJ, Doolittle, DJ and Waldren, CA. Vanillin (3-methoxy-4-hydroxybenzaldehyde) inhibits mutation induced by hydrogen peroxide, N-methyl-N-nitrosoguanidine (MNNG) and mitomycin C but not <sup>137</sup>Cs-γ-radiation at the CD59 locus in human-hamster hybrid A<sub>L</sub> cells. *Mutagenesis* 2000;15:207-213. PMID 10792012
  8. **Gustafson,DL** and Long,ME. Alterations in P-glycoprotein expression in mouse tissues by doxorubicin: implications for pharmacokinetics in multiple dosing regimens. *Chem-Biol Int* 2001; 138:43-57. PMID 11640914
  9. **Gustafson, DL**, Rastatter, JC, Colombo, T, and Long, ME. (2002). Doxorubicin pharmacokinetics: macromolecule binding, metabolism, and excretion in the context of a physiologic model. *J Pharmac Sci* 2002;91:1488-1501. PMID 12115848
  10. **Gustafson, DL**, Siegel, D, Rastatter, JC, Merz, AL, Parpal, JC, Kepa, JK, Ross, D, and Long, ME. (2003). Kinetics of NAD(P)H:quinone oxidoreductase inhibition by mitomycin C in vitro and in vivo. *J Pharmacol Exp Therap* 2003;305:1079-1086. PMID 12649308
  11. Ou, YC, Conolly, RB, Thomas, R., **Gustafson, DL**, Long, ME, Dobrev, ID, Chubb, LS, Xu, Y, Lapidot, SA, Andersen, ME, and Yang, RSH. Stochastic simulation of hepatic preneoplastic foci development for four chlorobenzene congeners in a medium-term bioassay. *Toxicol Sci* 2003;73:301-314. PMID 12700395
  12. **Gustafson, DL**, Long, ME, Zirrolli, JA, Duncan, MW, Holden, SN, Pierson, AS and Eckhardt, SG. (2003). Analysis of docetaxel pharmacokinetics in humans with the inclusion of later sampling time points afforded by the use of a sensitive tandem LCMS assay. *Cancer Chemother Pharmacol* 2003;52:159-166. PMID 12759775
  13. Siegel, D, **Gustafson, DL**, Dehn, DL, Han, JY, Boonchong, P, Berliner, LJ and Ross, D. NAD(P)H:quinone oxidoreductase 1 (NQO1): role as a superoxide scavenger. *Mol Pharmacol* 2004;65:1238-1247. PMID 15102952
  14. Witta, SE, **Gustafson, DL**, Pierson, AS, Menter, A, Holden, SN, Basche, M, Persky, M, O'Bryant, CL, Baron,A, Long, ME, Gibbs, A, Kelly, K, Bunn, PA, Jr, Chan, DC, Pallansch, P and Eckhardt, SG. A phase I and pharmacokinetic study of exisulind and docetaxel in patients with advanced solid tumors. *Clin Cancer Res* 2004;10:7229-7237. PMID 15534096
  15. **Gustafson, DL** Merz, AL, and Long, ME. Pharmacokinetics of combined doxorubicin and paclitaxel in mice. *Cancer Lett* 2005;220:161-169. PMID 15766591
  16. **Gustafson, DL**, Long, ME, Bradshaw, EL, Merz, AL and Kerzic, PJ. P450 induction alters paclitaxel pharmacokinetics and tissue distribution with multiple dosing. *Cancer Chemother Pharmacol* 2005;56:248-254. PMID 15856231
  17. Zirrolli, JA, Bradshaw, EL, Long, ME and **Gustafson, DL**. Rapid and Sensitive LC/MS/MS analysis of the novel tyrosine kinase inhibitor ZD6474 in mouse plasma and tissues. *J Pharmaceut Biomed Anal* 2005;39:705-711. PMID 15935603
  18. Thienelt,CD, Bunn, PA Jr, Hanna, N, Rosenberg,A, Needle, MN, Long, ME, **Gustafson, DL**, and Kelly, K A multicenter phase I/II study of cetuximab in combination with paclitaxel and carboplatin in untreated patients with stage IV non-small cell lung cancer (NSCLC). *J Clin Oncol* 200523:8786-8793. PMID 16246975
  19. Selting, KA, Ogilvie,GK, **Gustafson, DL**, Long, ME, Lana, SE, Walton, JA, Hansen, RA, Turner, AS, Laible, I and Fettman, MJ. Evaluation of the effects of dietary n-3 fatty acid supplementation on the pharmacokinetics of doxorubicin in dogs with lymphoma. *Am J Vet Res* 2006;67:145-151. PMID 16426224
  20. Frederick,B, **Gustafson, D**, Bianco, C, Ciardiello, F, Dimery I and Raben, D. ZD6474, an inhibitor of VEGFR and EGFR tyrosine kinase activity in combination with radiotherapy. *Int J Radiation Oncology Biol Phys* 2006;64:33-37. PMID 16377413

21. **Gustafson, DL**, Bradshaw-Pierce, EL, Merz, AL, and Zirrolli, JA. Tissue distribution and metabolism of ZD6474 in tumor bearing nude mice following oral dosing. *J Pharmacol Exp Ther* 2006;318:872-880. PMID 16644900
22. Basche, M, **Gustafson, DL**, Holden, SN, O'Bryant, CL, Gore, L, Witta, S, Schultz, MK, Morrow, M, Grolnic, S, Conrad, D, Levin, A, Creese, BR, Kangas, M, Roberts, K, Nguyen, T, Davis, K, Addison, RS, Moore, J, and Eckhardt, SG. A phase I and pharmacokinetic study of PI-88 in patients with advanced solid tumors. *Clin Cancer Res* 2006;12:5471-5480. PMID 17000682
23. Guo, W, Reigan, P, Siegel, D, Zirrolli, J, **Gustafson, D** and Ross, D. The bioreduction of a series of benzoquinone ansamycins by NAD(P)H:quinone oxidoreductase 1 (NQO1) to more potent heat shock protein 90 (HSP90) inhibitors, the hydroquinone ansamycins. *Mol Pharmacol* 2006 70:1194-1203. PMID 16825487
24. Helfrich, BA, Raben, D, Varella-Garcia, M, **Gustafson, D**, Chan, DC, Bemis, L, Coldren, C, Barón, A, Zeng, C, Franklin, WA, Hirsh, FR, Gazdar, A, Minna, J and Bunn, PAJr. Antitumor activity of the epidermal growth factor receptor (EGFR) tyrosine kinase inhibitor gefitinib (ZD1839, Iressa) in non-small cell lung cancer cell lines correlates with gene copy number and EGFR mutations but not EGFR protein levels. *Clin Cancer Res* 2006;12:7117-7125. PMID 17145836
25. Flaig, TW, **Gustafson, DL**, Su, L-J, Zirrolli, J, Harrison, G, Pierson, AS, Agarwal, R and Glode, LM. A phase I and pharmacokinetic study of silybinin phytosome in prostate cancer patients. *Invest New Drugs* 2007;25:139-146. PMID 17077998
26. Lana, S, U'ren, L, Plaza, S, Elmslie, R, **Gustafson, D** and Dow, S. (2007). Comparison of continuous low-dose oral chemotherapy with conventional doxorubicin chemotherapy for adjuvant therapy of hemangiosarcoma in dogs. *J Vet Intern Med* 2007;21:764-769. PMID 17708397
27. Bradshaw-Pierce, EL, Eckhardt, SG and **Gustafson, DL**. A physiologically-based pharmacokinetic model of docetaxel disposition: from mouse to man. *Clin Cancer Res* 2007; 13:2768-2776. PMID 17473210
28. Hariharan, S, **Gustafson, D**, Holden, S, McConkey, D, Davis, D, Morrow, M, Basche, M, Gore, L, Zang, C, O'Bryant, CL, Baron, A, Galleman, D, Colevas, D and Eckhardt, SG. Assessment of the biological and pharmacological effects of the  $\alpha_v\beta_3$  and  $\alpha_v\beta_5$  integrin receptor antagonist, cilengitide (EMD 121974), in patients with advanced solid tumors. *Ann Oncol* 2007;18:1400-1407. PMID 17693653
28. Zhang, Y, Bradshaw-Pierce, EL, DeLille, A, **Gustafson, DL**, and Anchordoquy, TJ. In vivo comparative study of Lipid/DNA complexes with different in vitro serum stability: effects on biodistribution and tumor accumulation. *J Pharm Sci* 2007;97:237-250. PMID 17721944
29. Troiani, T, Serkova, NJ, **Gustafson, DL**, Henthorn, TK, Lockerbie, O, Merz, A, Long, M, Morrow, M, Ciardiello, F, and Eckhardt, SG. Investigation of two dosing schedules of vandetanib (ZD6474), an inhibitor of vascular endothelial growth factor receptor and epidermal growth factor receptor signaling, in combination with irinotecan in a human colon cancer xenograft model. *Clin Cancer Res* 2007;13:6450-6458. PMID 17975157
30. **Gustafson, DL**, Frederick, B, Merz, AL and Raben, D. Dose scheduling of the dual VEGFR and EGFR tyrosine kinase inhibitor vandetanib (ZD6474, Zactima®) in combination with radiotherapy in EGFR-positive and EGFR-null human head and neck tumor xenografts. *Cancer Chemother Pharmacol* 2008; 61:179-188. Epub, 3/29/2007. PMID 17393165
31. Chow, LQM, **Gustafson, D**, O'Bryant, C, Gore, L, Basche, M, Holden, S, Morrow, M, Grolnic, S, Creese, B, Roberts, K, Davis, K, Addison, R and Eckhardt, SG. A phase I and pharmacological and biological study of PI-88 and docetaxel in patients with advanced malignancies. *Cancer Chemother Pharmacol* 2008 (In Press). PMID 18320191
32. Bradshaw-Pierce, EL, Steinhauer, CA, Raben, D and **Gustafson, DL**. Pharmacokinetic-directed dosing of vandetanib and docetaxel in a mouse model of human squamous cell carcinoma. *Mol Cancer Therap* 2008; (In Press).

### **C. RESEARCH SUPPORT**

#### **Research Projects Ongoing or Completed During the Last 3 Years:**

**Project Title:** Pharmacology Core, University of Colorado Cancer Center Support Grant.

**Active Dates:** 02/01/06 – 01/31/11

Principal Investigator/Program Director (Last, First, Middle):

Funding Agency: NCI – 2 P30 CA46934

Level of Participation: Core Director (PI: Bunn)

This is part of the University of Colorado Comprehensive Cancer Center Core Support Grant and is for the support of cancer pharmacology research across the UCCC. The Pharmacology Core received an Outstanding/Excellent review in the 2005 competitive renewal site visit.

**Project Title:** Dual Compartmental Targeting of Cancer

Active Dates: 01/01/05 – 12/31/08

Funding Agency: NCI – 5 RO1 CA101988

Level of Participation: Principal Investigator

Combination therapies containing molecularly targeted agents and conventional cytotoxic chemotherapy are becoming common in cancer therapy. Therefore, studies that address how to optimize the efficacy of these combinations based on drug dosing, sequencing and scheduling are an important component of therapeutic development. To this end, we propose to study ZD6474, a mixed VEGFR and EGFR inhibitor, in combination with docetaxel and CPT-11 in breast and colon cancer models, respectively.

**Project Title:** MEK Inhibition and Drug Combinations in Melanoma Treatment

Active Dates: 01/01/05 -

Funding Agency: Start Up Funds

Level of Participation: Principal Investigator

This project involves the use of human melanoma models to study MEK inhibitors and how to optimize clinical use with cytotoxic therapies. The project focuses on the timing of MEK inhibitor treatment with other therapies and how to optimize efficacy with regards to dose and scheduling.

**Project Title:** Pharmacology Core Fee for Service

Active Dates: 02/01/06 –

Funding Agency: Fee For Service

Level of Participation: Director

This is a fee for service core laboratory operated within my laboratory that provides analytical support to pharmacology and toxicology studies.

**Project Title:** Cancer Supercluster

Active Dates: 08/01/07 – 7/31/12

Funding Agency: President's Office, Colorado State University (\$450,000 annual)

Level of Participation: Co-Director, Cancer Biology Program

This program, developed and sponsored by the President's office and the Colorado State University Research Foundation is intended to foster collaboration and entrepreneurship amongst individual's doing cancer related research at the University. It is a multi-disciplinary, across colleges program that encompasses clinical sciences, basic sciences and engineering.