BIOGRAPHICAL SKETCH

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NAME: Christopher C. Benz, M.D.

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

POSITION TITLE: Professor & Program Director

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
University of California, Los Angeles	B.S.	1968	Biochemistry
University of Michigan, Ann Arbor	M.D.	1972	Medicine
VGH/CCabc & UBC, Vancouver, B.C., Canada	Residency	1972-1978	Int.Med., Heme-Onc
Yale Univ. School of Med., New Haven, CT	Subspecialty	1978-1979	Oncology

A. Personal Statement

For over 30 years Benz lab translational research efforts in Oncology have focused on identifying molecular strategies to improve breast cancer diagnostics and therapeutics. Professor Benz, holding faculty appointments at both the Buck Institute (for lab research) and UCSF (for clinical activities) has published nearly 300 peer-reviewed studies and has served on multiple national and international review and oversight committees including the National Cancer Institute's DTP/DCTD Biological Resources Branch Oversight Committee, the American Association of Cancer Research's Task Force on Cancer and Aging, and the national Steering Committee for the NCI/NHGRI-funded The Cancer Genome Atlas (TCGA) program. Dr. Benz provides weekly care for breast cancer patients at the UCSF Carol Franc Buck Breast Care Center, and he remains active in the I-SPY2 clinical trial network and also in the statewide UC Athena program. He has successfully invented, licensed and introduced into the clinic and a worldwide phase 2 trial (Hermione) a new cancer therapeutic (chemotherapy-containing HER2-targeted immunoliposome (licensed as MM-302). For the past decade he has co-led (with Profs. David Haussler and Josh Stuart at UCSC) the Buck Institute-UC Santa Cruz Genome Data Analysis Center for both the national TCGA and GDAN networks; in this capacity, he has been co-senior author on multiple high impact pan-cancer studies including one (Cell 2014) distinguished for being among the top 10 clinical research achievements noted in 2015 (ClinicalResearchForum.org). Over the past 3 decades, Professor Benz has trained/mentored 25 postdocs, 12 doctoral (PhD) and 8 masters (MS) students, and hosted several senior sabbatical scientists in his lab; former Benz lab trainees currently occupy distinguished career positions in academia and industry, both in the US and abroad.

B. Positions and Honors

1979-1980 Postdoctoral Associate, Oncology-Pharmacology, Yale University School of Medicine
1981-1982 Instructor, Department of Medicine, Yale University School of Medicine
1982-1983 Assistant Professor of Medicine, Yale University School of Medicine
1983-1988 Assistant Professor of Medicine (in residence), University of California, San Francisco
1984-1987 Director, U.C.S.F. Hormone Receptor Laboratory
1988-1994 Associate Professor of Medicine, U.C.S.F.
1994- Professor of Medicine in Residence, U.C.S.F. (Adjunct Professor, 9/2000-present)
1994-1995 Acting Director, U.C.S.F. Cancer Research Institute
1995- Member, Joint UCSF-UCB Graduate Group in Bioengineering
1997-1998 Visiting Scientist/Professor of Mol. Medicine, Univ. Basel & Friedrich Miescher Inst., Basel CH
2000- Director; Cancer & Developmental Therapeutics Program; Buck Institute for Research on Aging
2015- Elizabeth MA Stevens Distinguished Buck Institute Professorship

C. Contribution to Science

1. Reclassifying breast cancer and other malignancies based on multi-platform molecular data and cancer-driving pathways to better personalize therapy. In partnership with UCSC computer scientists and bioinformaticians and co-directing one of the TCGA's 7 GDAC centers between 2012-2016, Benz and colleagues analyzed over 10,000 different cases from 33 different cancer types to produce a comprehensive genomic and pathway atlas that has now reclassified all human malignancies based on their molecular characteristics rather than their sites of origin and microscopic features. The ongoing NCI/CCG GDAN network is now applying these same approaches to tumor and patient samples from completed and outcome annotated clinical trials. Outside these national consortium networks, and working alongside UCSF breast cancer investigators and clinicians, Benz has helped establish several international collaborations (UK, Sweden) and co-directs the molecular characterization of 30 year old tumor archives annotated with full clinical follow-up data enabling: i) the identification and validation of prognostic multi-gene signatures and pathways (e.g. our Integrated Cytokine Score) driving the outcome of the ~20% of breast cancers known as "triple-negative" that lack any form of targeted therapeutics; and ii) the predictive identification of newly diagnosed breast tumors whose molecular and biological characteristics are so indolent as to not pose any significant recurrence risk and therefore not require adjunctive systemic therapy.

- Yau C, Esserman L, Moore DH, Waldman F, Sninsky J, and Benz CC. A multigene predictor of metastatic outcome in early stage receptor-negative and triple-negative breast cancer. Breast Cancer Research 12:R85, 2010. *PMCID: PMC3096978*
- Yau C, Sninsky J, Kwok S, Wang A, Degnim A, Ingle JN, Gillett C, Tutt A, Waldman F, Moore D, Esserman L, Benz CC. An optimized five-gene multi-platform predictor of hormone receptor negative and triple negative breast cancer metastatic risk. Breast Cancer Res 15: R103, 2013. *PMCID: PMC3978448*
- Cancer Genome Atlas Network (Benz CC, writing committee). Comprehensive molecular portraits of human breast tumors. Nature 490: 61-70, 2012. *PMCID: PMC3465532*
- Hoadley KA et al. (Benz CC, senior co-author with Cancer Genome Atlas Research Network). Multiplatform analysis of 12 cancer types reveals molecular classification within and across tissues of origin. Cell 158: 929-944, 2014 *PMCID: PMC4152462*
- Hoadley KA, Yau C, Hinoue T, Wolf DM, Lazar AJ, Drill E, Shen R, Taylor AM, Cherniak AD, Thorsson V, Akbani R, Bowlby R, Wong CK, Wiznerowicz M, Sanchez-Vega F, Robertson AG, Schneider BG, Lawrence MS, Noushmehr H, Malta TM, Cancer Genome Atlas Research Network, Stuart JM, Benz CC, Laird PW. Cell-of-origin patterns dominate the molecular classification of 10,000 tumors from 33 types of cancer. Cell 173: 291-304, 2018 *PMCID: PMC5957518*

2. Developing novel and more effective targeted treatments against breast cancers overexpressing either estrogen receptors (ER, wildtype or mutant) or the ERBB2/HER2 growth factor receptor. Nearly 80% of all breast cancers overexpress ER and/or HER2, and with metastatic progression mutations in these receptor systems contribute largely to their acquired clinical resistance to current receptor-targeted therapeutics. The Benz lab has pioneered the use of mass spectrometry to characterize novel post-translational modifications (PTMs) affecting receptor systems and contributing to their cancer-driving mechanisms. These novel findings include: i) ER (hinge domain) phosphorylation, leading to our commercial development of a new anti-pER monoclonal and a new clinical indication for CDK2 inhbitors; and ii) acetylation of translation controlling proteins that control the stability of HER2 transcripts, leading to potentially new therapeutics and new clinical indications for approved HDAC-1 inhibiting drugs.

- Scott GK, Marx C, Berger CE, Saunders LR, Verdin E, Schäfer S, Jung M, and Benz, CC. Destabilization of ERBB2 transcripts by targeting 3' UTR mRNA associated HuR and histone deacetylase-6 (HDAC6). Mol Cancer Res. 6: 1250-1258, 2008. *PMCID: PMC2583372*
- Marx C, Held JM, Gibson BW, and Benz CC. ErbB2 trafficking and degradation associated with K48 and K63 polyubiquitination. Cancer Research 70: 3709-3717, 2010. *PMCID: PMC2862137*
- Held JM, Britton DJ, Scott GK, Lee EL, Schilling B, Baldwin MA, Gibson BW and Benz CC. Ligand binding promotes CDK-dependent phosphorylation of ER alpha on hinge serine 294 but inhibits ligand-independent phosphorylation of serine 305. Mol. Cancer Res. 10: 1120-1132, 2012. *PMCID: PMC3950940*
- Wilson-Edell KA, Kehasse A, Scott GK, Yau C, Rothschild DE, Schilling B, Gabriel BS, Yevtushenko MA, Hanson IM, Held JM, Gibson BW, and Benz CC. RPL24: a potential therapeutic target whose depletion or acetylation inhibits polysome assembly and cancer cell growth. Oncotarget 5: 5165-5176, 2014 *PMCID: PMC4148130*

- Scott GK, Chu D, Kaur R, Malato J, Rothschild DE, Frazier K, Eppenberger-Castori S, Hann B, Park BL, Benz CC: ERpS294 is a biomarker of ligand or mutational ER activation and a breast cancer target for CDK2 inhibition. Oncotarget 8: 83432-83445, 2016 *PMCID: PMC5663526*

3. Designing a new breast cancer prevention approach based on community-based findings from a high-risk population. While the increasing worldwide incidence of ER+ breast cancer has been linked to aging, it is also most pronounced in selected geographic and ethnic populations, including Caucasian women over age 40 who live in Marin County, which is among the world's highest breast cancer incidence populations. Following our 2002 Buck-sponsored scientific symposium addressing this local issue organized by Benz, he partnered with Marin County (MCDHHS) epidemiologists to initiate the Marin Women's Study (MWS) in 2006, that has since enrolled and surveyed >14,000 Marin women (at the time of their screening mammogram) and collected >8,000 saliva samples, cryobanked and processed into DNA and solute fractions. Along with county epidemiologists, Benz and colleagues reported several key findings from this high incidence population, the most recent being the novel observation that women who experience hypertension during pregnancy (~8% of all pregnant women), and who carry a specific polymorphic (SNP) variant of the IGF1R gene, are strongly protected from developing breast cancer decades later, a conclusion subsequently validated in the statewide California Teacher's Study. Based on their biological hypotheses explaining this epidemiologic observations, Benz and colleagues have now initiated a new breast cancer prevention project, introduced their two risk protecting parameters into the statewide ATHENA WISDOM trial, are now participating in larger international study cohorts (ALSPAC, UKBiobank), and are evaluating normal breast biopsy samples from donors around the USA (Komen Tissue Bank) to prove their mechanistic hypothesis and generate additional biological rationale to launch a new breast cancer prevention trial.

- Jupe ER, Dalessandri KM, Mulvihill JJ, Miike R, Knowlton NS, Pugh TW, Zhao LP, DeFreese DC, Manjeshwar S, Gramling BA, Wiencke JK, Benz C. A steroid metabolizing gene variant in a polyfactorial model improves risk prediction in a high incidence breast cancer population. BBA Clinical 2: 94-102, 2014 *PMCID: PMC4633888*.
- Mockus M, Prebil LA, Ereman R, Dollbaum C, Powell M, Yau C, Benz CC. First pregnancy characteristics, postmenopausal breast density, and salivary sex hormone levels in a population at high risk for breast cancer. BBA Clinical 3: 189-195, 2015 *PMCID: PMC4547694.*
- Prebil LA, Ereman RR, Powell MJ, Kerlikowske K, Shepherd JA, Hurlbert MS, Benz CC. First pregnancy events and future breast density: modification by age at first pregnancy and specific VEGF and IGF1R gene variants. Cancer Causes and Control 25: 859-868, 2014 *PMCID: PMC4048469.*
- Powell MJ, Von Behren J, Neuhausen S, Reynolds P, Benz CC. Functional IGF1R variant predicts breast cancer risk in women with preeclampsia in California Teachers Study. Cancer Causes and Control. 28: 1027-1032, 2017 *PMCID: PMC5613056.*

Complete List of ~300 publications in My NCBI Bibliography: http://goo.gl/7xM2Da

D. RESEARCH SUPPORT

Ongoing Research Support

U24 CA210990 (UCSC PI: Stuart; Buck PI: Benz) 9/1/2016 – 8/31/2021
NIH award to UCSC and Buck Institute
UCSC-Buck Specialized Genomic Data Analysis Center for the Genomic Data Analysis Network
To provide integrated pathway and network analyses analysis of multi-platform "omic" datasets for federally funded clinical trials for which tumor and patient samples are coupled to clinical outcomes (treatment responses and survival).

U01 CA187945 (UCSF PI: Esserman; MDACC PI: Berry) 09/18/2014 – 08/31/2019
Subcontract from UCSF to Buck awarded by National Cancer Institute/NIH
Modeling the impact of targeted therapy based on breast cancer subtypes.
International collaboration to extend existing CISNET modeling for breast cancer treatment outcomes to demonstrate the likelihood of further improving clinical outcomes by better matching subtype-specific treatments, using longitudinal data from Sweden (Stockholm Breast Cancer Registry).

U01 CA196406 (UCSF PI: Esserman) 09/16/2015 – 08/31/2020
Subcontract from UCSF to Buck awarded by National Cancer Institute/NIH
"Molecular and Cellular Characterization of Screen-Detected Lesions (MCL) Consortium."

Elucidate the molecular and contextual basis of IDLE ultralow risk lesions and tumor immune microenvironment of high risk in situ and invasive breast cancers within a consortium of 7 nationally awarded centers task with generally characterizing and comparing the molecular and cellular nature of screen-detected prostate, lung, pancreas and breast cancers.

Recently Completed Research Support

R01 CA071468-15A1 (Benz) 08/23/1996 – 02/28/2016
National Cancer Institute/NIH
Mass spectrometry to decode PTM patterns and enhance the biomarker utility of ER
Employing multiple reaction monitoring (MRM) mass spectrometry (MS) to quantitate ligand-dependent and ligand-independent induction of ER posttranslational modifications (PTMs) with particular emphasis on ER hinge domain phosphorylation patterns.

U24 CA143858 (UCSC PI: Haussler; Buck PI: Benz) 10/01/2009 – 08/31/2015
NIH award to UCSC and Buck Institute
Standardization of input and output data types and integration of datasets
To develop advanced analysis and visualization tools for integrative analysis of datasets for the NCI/NHGRI-funded The Cancer Genome Atlas (TCGA) program.

CBCRP Translational Research Award (UCSF PI: Esserman; Buck Co-PI: Benz) 08/01/2012– 07/31/2015
Subcontract from UCSF to Buck awarded by California Breast Cancer Research Program
Predicting early and late recurrence to improve care.
Multi-institutional effort to compare candidate gene signatures and develop a personalized breast cancer predictor score for recurrence risk.

1R21CA155679-01A1 (Benz) 07/01/2011-06/30/2014
National Cancer Institute/NIH
Polyribosome targets mediating mRNA decay for cancer prediction and therapy
This R21 project aims to identify and characterize novel targets and biomarkers involved in a previously unrecognized cellular mechanism promoting the rapid decay of oncogenic transcripts.

P50 CA58207 (Gray)/Proj-3 (Park/Benz/Marks) 09/01/1990 – 11/30/2013
NIH/NCI Bay Area Breast SPORE Competing Renewal (Proj 1) (Buck subcontract)
Proj-3: Nanoparticle-based chemotherapy against aggressive breast cancer subtypes.
This component uses an interdisciplinary approach combining different methodologies to examine the impact of mRNA translation on lifespan and metabolism utilizing three different model systems, flies, worms, and mammalian cells.

U24 CA0126477 (Fisher/UCSF PI; Gibson/Buck PI) 10/01/2006 – 08/31/2013
National Cancer Institute
Targeted and global proteomic strategies for early breast cancer detection. This collaborative network critically assessed mass spectrometry and proteomic approaches and technologies aimed at identifying and detecting peptides and tumor biomarkers in cancer patient blood samples.