BIOGRAPHICAL SKETCH

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NAME	POSITION TITLE
Eibl, Guido, Erwin Michael	**Professor**
eRA COMMONS USER NAME (credential, e.g., agency login) **Geibl2**	

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

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	MM/YY	FIELD OF STUDY
University of Regensburg, Germany		1990-1992	Medicine
Technical University of Munich, Germany	Dr. med.	1992-1996	Medicine
Freie University of Berlin, Germany		1996-1999	Surgical residency
David Geffen School of Medicine at UCLA		2000-2002	Research fellowship

A. Personal Statement

I have the expertise, training, and motivation necessary to successfully carry out and assist with the proposed animal studies outlined in your proposal. I am currently Professor in the Department of Surgery at the David Geffen School of Medicine at UCLA with no clinical duties and Director of Surgical Research in the Division of General Surgery. My research interest of the past 15 years has been pancreatic cancer, in particular inflammatory processes in pancreatic cancer development and progression. I am the Director of the Hirshberg Laboratory for Translational Pancreatic Cancer Research at UCLA. My research has been funded by the NIH since 2004 continuously and published in over 70 peer-reviewed articles. I successfully procured two R01 awards in the area of pancreatic cancer as the Principal Investigator and served as the Animal Model Core Director of a NCCAM-funded UCLA Center for Excellence in Pancreatic Diseases. In addition, I am presently the Principal Investigator of a NCI-funded Program Project Grant studying diet-induced promotion of pancreatic cancer. I have tremendous expertise in pancreatic cancer animal models, in particular transgenic and xenograft models for prevention and experimental therapeutics studies.

1) H.Funahashi, M.Satake, D.Dawson, N.-A.Huynh, H.A.Reber, O.J.Hines, **G.Eibl**. Delayed progression of pancreatic intraepithelial neoplasia in a conditional $Kras^{G12D}$ mouse model by a selective COX-2 inhibitor. Cancer Res 2007;67(15):7068-7071
2) K.Gao, H.Zhou, L.Zhang, J.W.Lee, Q.Zhou, S.Hu, J.Farrell, **G.Eibl**, D.T.Wong. Induction of systemic disease-specific salivary biomarker profiles in mouse models of melanoma and non-small cell lung cancer, PLoS ONE 2009 Jun 11;4(6):e5875 (PMCID: PMC2691577)
3) C.Lau, Y.Kim, D.Chia, N.Spielmann, **G.Eibl**, D.Elashoff, F.Wei, Y.-L.Lin, A.Moro, T.Grogan, S.Chiang, E.Feinstein, C.Schafer, J.Farrell, D.T.W.Wong. Role of pancreatic cancer-derived exosomes in salivary biomarker development. J Biol Chem 2013;288(37):26888-97 (PMCID: PMC3772238)
4) D.W.Dawson, K.Hertzer, A.Moro, G.Donald, H.-H.Chang, V.L.Go, S.J.Pandol, A.Lugea, A.S.Gukovskaya, G.Li, O.J.Hines, E.Rozengurt, **G.Eibl**. High fat, high calorie diet promotes early pancreatic neoplasia in the conditional KrasG12D mouse model. Cancer Prev Res 2013;6:1064-1073 (PMCID: PMC3835151)

B. Positions and Honors

Positions and Employment

2003 - 2004 Assistant Researcher, Section of Gastrointestinal Surgery,
David Geffen School of Medicine at UCLA
2004 - 2009 Adjunct Assistant Professor, Division of General Surgery,
David Geffen School of Medicine at UCLA

2004 - 2014 Scientific Director, Hirshberg Laboratory for Translational Pancreatic Cancer Research, David Geffen School of Medicine at UCLA
2004 - present Member, Cancer Translational Therapeutics & Gene Therapy, UCLA's Jonsson Comprehensive Cancer Center
2005 - present Research Scientist, Department of Veterans Affairs, Greater Los Angeles Health Care System, West Los Angeles, California, USA
2009 – 2013 Associate Professor in Residence, Division of General Surgery, David Geffen School of Medicine at UCLA
2012 - present Director of Surgical Research, Division of General Surgery, David Geffen School of Medicine at UCLA
2013 - present Professor in Residence, Division of General Surgery, David Geffen School of Medicine at UCLA
2014 - present Director, Hirshberg Laboratory for Translational Pancreatic Cancer Research, David Geffen School of Medicine at UCLA

Other Experience and Honors

Editorial duties:

- Associate Editor, Pancreas (2012-present)
- Topic Editor "Risk Factors for Pancreatic Cancer: Underlying Mechanisms and Potential Targets", Frontiers of Gastrointestinal Sciences (2012-present)

Reviewer services (ad hoc) in journals (selected from over 30 peer-reviewed journals): PNAS, Cancer Research, Clinical Cancer Research, Molecular Cancer Research, Molecular Cancer Therapeutics, Oncogene, Neoplasia, Carcinogenesis, International Journal of Cancer, Cancer, PLoS One, FEBS, Gastroenterology, Gut, Pancreas

Reviewer services for grant applications (ad hoc):

- National Institutes of Health (Oncology Fellowship, Chemo/Dietary Prevention, Cell-mediated Clinical Oncology Studies Special Emphasis Panel, SPORE in Brain, Leukemia, Myeloma, Sarcoma, Esophageal, GI, HN, and Pancreatic Cancers)
- AAAS (American Association for the Advancement of Science) Research Competitiveness Program

Member of NIH study sections:

- Chemo/Dietary Prevention (July 1, 2010 – June 30, 2014)

Awards and Honors:

Travel Award: American Pancreatic Association (1999), Research Scholarship: German Research Foundation (2000-2001), Travel Award: Cayman Chemical Company (2004); Cancer Research Highlight (2005 & 2007)

Professional memberships

German Surgical Society, American Pancreatic Association, American Association for Cancer Research, Center for Ulcer Research and Education, Jonsson Comprehensive Cancer Center, The Longmire Surgical Society, Society of University Surgeons

C. Contributions to Science

1. My early publications focused on understanding the factors that contribute to the severity and mortality of acute necrotizing pancreatitis. It is unclear what predisposes patients to develop a severe form of this disease and treatment options are mostly limited to supportive therapy. Using a variety of rat and mouse models of acute pancreatitis my group investigated the importance of microcirculatory disturbances as the main factor for multi-organ dysfunction and failure during severe acute pancreatitis, the main cause of mortality. We published several papers that highlight the importance of microcirculatory dysfunction as an important cause of respiratory, liver, and intestinal failure, which leads to bacterial translocation and sepsis. Several clinical trials from other groups were initiated based on these findings targeting specifically microcirculatory dysfunction.

a) **G.Eibl**, H.G.Hotz, J.Faulhaber, M.Kirchengast, H.J.Buhr, T.Foitzik. Effect of endothelin and endothelin receptor blockade on capillary permeability in experimental pancreatitis. Gut 2000;46:390-394

b) **G.Eibl**, H.J.Buhr, T.Foitzik. Therapy of microcirculatory disorders in severe acute pancreatitis: What mediator should we block? Intensive Care Med 2002;28:139-146
c) **G.Eibl**, B.Forgacs, H.G.Hotz, H.J.Buhr, T.Foitzik. Endothelin A but not endothelin B receptor blockade reduces capillary permeability in severe experimental pancreatitis. Pancreas 2002;25:E15-20
d) T.Foitzik, **G.Eibl**, P.Schneider, F.A.Wenger, C.A.Jacobi, H.J.Buhr. Omega-3 fatty acid supplementation increases anti-inflammatory cytokines and attenuates systemic disease sequelae in experimental pancreatitis. JPEN J Parenter Enteral Nutr 2002;26:351-356

2. After relocating to UCLA in 2000 I started focusing on inflammatory pathways in pancreatic cancer using in vitro and animal models of the disease. I was particularly interested in the role of cyclooxygenases and eicosanoids during pancreatic cancer development and growth. There was great interest in the scientific community in deciphering the role of cyclooxygenases and eicosanoids in tumor biology. However, their role in pancreatic cancer was unknown. My group published several papers that demonstrated the importance of these enzymes and lipid mediators in a variety of cellular processes. In addition, we evaluated interventional strategies aimed at inhibiting cyclooxygenase pathways and prostaglandin effects. We published the first manuscript showing that the natural progression of pancreatic cancer precursor lesions to pancreatic cancer in the conditional KrasG12D mouse model can be attenuated by pharmaceutical intervention, e.g. non-steroidal anti-inflammatory drugs.

a) **G.Eibl**, Y.Takata, L.G.Boros, J.Liu, Y.Okada, H.A.Reber, O.J.Hines. Growth stimulation of COX-2 negative pancreatic cancer by a selective COX-2 inhibitor. Cancer Res 2005;65(3):982-990
b) H.Funahashi, M.Satake, D.Dawson, N.-A.Huynh, H.A.Reber, O.J.Hines, **G.Eibl**. Delayed progression of pancreatic intraepithelial neoplasia in a conditional $Kras^{G12D}$ mouse model by a selective COX-2 inhibitor. Cancer Res 2007;67(15):7068-7071
c) H.Takahashi, A.Li, D.W.Dawson, O.J.Hines, H.A.Reber, **G.Eibl**. Cyclooxygenase-2 confers growth advantage to syngeneic pancreatic cancer cells. Pancreas 2011;40(3):453-459 (PMCID: PMC3077942)
d) H.Pham, C.E.Rodriguez, G.W.Donald, K.M.Hertzer, X.S.Jung, H.-H.Chang, A.Moro, H.A.Reber, O.J. Hines, **G.Eibl**. MiR-143 Decreases COX-2 mRNA Stability and Expression in Pancreatic Cancer Cells. Biochem Biophys Res Commun 2013;439:6-11 (PMCID: PMC3789599)

3. There is a great interest in the potential role of natural products to alleviate several human ailments, including cancer. However, very little mechanistic data exist that demonstrate the efficacy of certain natural products to attenuate cancer growth. Supported by a program project grant my group investigated the mechanisms of several phytochemicals (polyphenols) in inhibiting pancreatic cancer growth using in vitro and animal models of the disease. We demonstrated that certain polyphenols potently inhibited the growth of pancreatic cancer cells by a variety of mechanisms, including induction of apoptotic cell death.

a) I.Ohno, **G.Eibl**, I.Odinokova, M.Edderkaoui, R.D.Damoiseaux, M.Yazbec, R.Abrol, W.A.Goddard,III, O.Yokosuka, S.J.Pandol, A.S.Gukovskaya. Rottlerin stimulates apoptosis in pancreatic cancer cells through interactions with proteins of the bcl-2 family. Am J Physiol Gastrointest Liver Physiol 2010;298:G63-G73 (PMCID: PMC2806098)
b) H.Takahashi, M.C.Chen, H.Pham, E.Angst, J.C.King, J.Park, E.Y.Brovman, H.Ishiguro, D.M.Harris, H.A.Reber, O.J.Hines, A.S.Gukovskaya, V.L.W.Go, **G.Eibl**. Baicalein, a Component of Scutellaria Baicalensis, Induces Apoptosis by MCL-1 Down-Regulation in Human Pancreatic Cancer Cells. Biochim Biophys Acta 2011;1813:1465-1474 (PMCID: PMC3123440)
c) J.C.King, Q.-Y.Lu, G.Li, A.Moro, H.Takahashi, M.Chen, V.L.W.Go, H.A.Reber, **G.Eibl**, O.J.Hines. Evidence for activation of mutated p53 by apigenin in human pancreatic cancer. Biochim Biophys Acta 2012;1823:593-604 (PMCID: PMC3277744)
d) H.Pham, M.Chen, H.Takahashi, J.King, H.A.Reber, O.J.Hines, S.Pandol, **G.Eibl**. Apigenin inhibits NNK-induced focal adhesion kinase activation in pancreatic cancer cells. Pancreas 2012;41(8):1306-15 (PMCID: PMC3479318)

4. Based on my interest in inflammatory pathways in pancreatic cancer I became interested in investigating the link between obesity and pancreatic cancer. Obesity is an enormous health problem and there is enormous interest in the scientific community to understand the mechanisms, by which obesity promotes certain human

diseases, including cancer. Using the conditional KrasG12D mouse model, we were the first to show that diet-induced obesity in this model accelerates pancreatic neoplasia, which was associated with a robust inflammation in the pancreas. As another potential mechanism, by which obesity can promote tumor development we are investigating the insulin signaling pathway as an intriguing potential target for cancer prevention. In that aspect, we are evaluating the efficacy of metformin, an anti-diabetic drug, in inhibiting pancreatic cancer cell growth and tumor development. These studies are funded by a program project grant.

a) K.Kisfalvi, A.Moro, J.Sinnett-Smith, **G.Eibl**, E.Rozengurt. Metformin inhibits the growth of human pancreatic cancer xenografts. Pancreas 2013;42(5):781-5 (PMCID: PMC3681894)
b) D.W.Dawson, K.Hertzer, A.Moro, G.Donald, H.-H.Chang, V.L.Go, S.J.Pandol, A.Lugea, A.S.Gukovskaya, G.Li, O.J.Hines, E.Rozengurt, **G.Eibl**. High fat, high calorie diet promotes early pancreatic neoplasia in the conditional KrasG12D mouse model. Cancer Prev Res 2013;6:1064-1073 (PMCID: PMC3835151)
c) M.Ming, J.Sinnett-Smith, J.Wang, H.P.Soares, S.H.Young, **G.Eibl**, E.Rozengurt. Dose-dependent AMPK-dependent and independent mechanisms of berberine and metformin inhibition of mTORC1, ERK, DNA synthesis and proliferation in pancreatic cancer cells. PLoS ONE 2014 Dec 10;9(12):e114573 (PMCID: PMC4262417)

Complete list of published work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/guido.eibl.1/bibliography/41145254/public/?sort=date&direction=ascending.

D. Research Support

Ongoing Research Support

P01 CA163200 Eibl (PI) 08/01/2012 - 07/31/2017
NIH/NCI
Targeting diet-induced promotion of Kras-initiated pancreatic adenocarcinoma
This Program Project is designed to explore the mechanisms of diet-induced pancreatic cancer promotion utilizing genetically engineered animal models of the disease. The Program involves four projects and two cores. The role of a typical Western Diet on inflammation, intracellular signaling, cell death mechanisms, and desmoplasia during pancreatic cancer promotion will be explored.

TBG-122370 Dawson (PI) 01/12/2012 – 12/31/2015
American Cancer Society
Regulation and therapeutic targeting of Wnt signaling in pancreatic cancer
The project is designed to investigate the role of Wnt signaling in pancreatic cancer growth utilizing genetic and pharmacological approaches in cell culture and xenograft animal models.
Role: Co-Investigator

Completed Research Support

R01 CA122042 Eibl (PI) 08/01/2007 – 05/31/2013
NIH/NCI
The role of n-3 polyunsaturated fatty acids in pancreatic cancer
This project is designed to explore the efficacy of n-3 polyunsaturated fatty acids in therapy and prevention of pancreatic cancer using xenograft and transgenic animal models of the disease.

R01 CA104027 Eibl (PI) 03/01/2004 – 02/29/2009
NIH/NCI
The role of COX-2 and PPAR-γ in pancreatic cancer
This project is designed to explore the role of COX-2 in pancreatic cancer invasion and angiogenesis as well as to characterize the interaction between COX-2 and the nuclear receptor PPAR-γ.

P01 AT003960 Go (PI) 09/30/2007 – 09/29/2014
NIH/NCCAM
UCLA Center for Excellence in Pancreatic Diseases
The overall goal of the Center is to evaluate the effects of phytonutrients, in particular polyphenolic compounds, on inflammatory and proliferative diseases of the pancreas, including diabetes, pancreatitis, and pancreatic cancer, using metabolomic methodology.
Role: Animal Core Director, Project 2 Co-Leader, Project 3 Co-I

R21 CA137292 Rozengurt (PI) 07/01/2009 – 06/30/2012
NIH/NCI
Targeting crosstalk between insulin and Gq signaling systems in pancreatic cancer
The project proposes to characterize the mechanism(s) and growth-promoting effects of the crosstalk between insulin receptor and GPCR signaling in human pancreatic cancer cell lines and to characterize the inhibitory effects of metformin on the crosstalk between insulin receptor and GPCR signaling in vitro and in vivo.
Role: Co-Investigator

R21 CA127803 Hines (PI) 07/01/2007 – 06/30/2010
NIH/NCI
The role of CXCR2 in pancreatic cancer
The overall goal is to determine the role of the chemokine receptor CXCR2 on pancreatic cancer cell growth and angiogenesis using mouse models and human samples.
Role: Co-Investigator