BIOGRAPHICAL SKETCH
Training Partner.

NAME: Kreeger, Pamela Kay

eRA COMMONS USER NAME: kreeger

POSITION TITLE: Associate Professor Biomedical Engineering, Cell and Regenerative Biology

EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Valparaiso University, Valparaiso, IN	B.S.	05/2000	Chemistry
Northwestern University, Evanston, IL	Ph.D.	06/2005	Chemical Engineering
Massachusetts Institute of Technology, Cambridge, MA	Postdoctoral	07/2005 – 12/2008	Biological Engineering

A. Personal Statement

My research focuses on how interactions between cellular and microenvironmental components influence phenotypic decisions in ovarian cancer and other diseases. We utilize two engineering approaches to carry out our research: 1) the development of controlled *in vitro* models where inputs such as ECM, soluble factors, or protein expression can be independently regulated and 2) computational modeling to analyze multivariate data to determine which inputs can be used to control the system. Ultimately, the results of these studies will influence the development of molecular- and materials-based therapies.

1. PK Kreeger. “Using partial least squares regression to analyze cellular response data.” *Science Signaling*. 6, p. tr7, 2013. PMCID: Policy Exempt – not resulting from NIH funding
2. MJ Carroll, LE Stopfer, PK Kreeger. "A simplified culture system to examine soluble factor interactions between mammalian cells." *Chemical Communications*. 50, p5279-5281. 2014. PMCID: PMC3999236
3. CS Kim, IP Mitchell, A Desotell, PK Kreeger, KS Masters. “Immobilized EGF stimulates persistent, directed keratinocyte migration via activation of PLCγ1.” *FASEBJ.* 30, p 2580-2590. 2016. PMCID: PMC4904288
4. Carroll MJ, Kapur A, Felder M, Patankar MS, Kreeger PK. “M2 macrophages induce ovarian cancer cell proliferation via a heparin binding epidermal growth factor/matrix metalloproteinase 9 intercellular feedback loop.” *Oncotarget.* 7, p 86608-86620. 2016. PMCID in progress

B. Positions and Honors

Positions

2009 - 2016	Assistant Professor, Dept. of Biomedical Engineering, UW-Madison
2009 -	Member, Carbone Cancer Center, UW-Madison
2009 -	Trainer, Cellular and Molecular Biology Program, Computation and Informatics in Biology and Medicine, Genomic Sciences Training Program, UW-Madison
2012 -	Trainer, Molecular and Cellular Pharmacology Program, UW-Madison
2014 -	Member, McPherson Eye Research Institute, UW-Madison
2015 -	Affiliate, Dept. of Cell and Regenerative Biology, UW School of Medicine and Public Health
2016 - present	Associate Professor, Dept. of Biomedical Engineering, UW-Madison
2016 - present	Associate Professor, Dept. of Cell and Regenerative Biology, UW School of Medicine and Public Health

Other Experience and Professional Memberships

2003 -	Member, Biomedical Engineering Society
2009 -	Member, American Society of Engineering Education
2010, 2014	NSF GRFP Panel
2012	NIH Microphysiological Systems Special Emphasis Panel
2013 - 2015	INSERM: Systems Biology Applied to the Cancer Research Panel
2015, 2016	NIH MABS *ad hoc*
2016	NCI U01 Questions in Cancer Systems Biology Special Emphasis Panel
2017	NCI PQ8 Special Emphasis Panel

Awards and Honors

2000	Valparaiso University *Summa Cum Laude*
2000 – 2001	Northwestern University Cabell Fellow
2001 – 2004	National Defense Science and Engineering Graduate Fellowship
2001	National Science Foundation Fellowship (declined)
2002	Metz Scholarship in Reproductive Biology
2004 – 2005	Northwestern University Fellow
2006	Anna Fuller Fund Fellow in Molecular Oncology
2008	American Cancer Society Postdoctoral Fellow
2010	NSF CAREER Award
2013	American Cancer Society Research Scholar
2013	James G. Woodburn Award for Excellence in Teaching
2014	*Chemical Communications* Emerging Investigator
2014	*Cellular and Molecular Bioengineering* Young Innovator
2014	NIH New Innovator
2017	Vilas Associate

C. Contribution to Science

1. During my doctoral thesis, I developed a novel 3D *in vitro* system for ovarian follicle culture that maintained the physical interactions between the oocyte and the supporting somatic cells of the follicle. I utilized this system to study the impact of soluble factors and the ECM on mouse follicle and oocyte development. The paper reporting the successful fertilization and birth from oocytes from follicles cultured in this system (item 3 below) was chosen by *Nature Medicine* as one of the 10 most significant publications in reproductive biology of the decade (during 2001-2010). This system has since been translated to study human follicle growth, with the ultimate goal of providing a method to mature follicles from cancer patients that cryopreserve their ovary prior to initiating treatment.

1. PK Kreeger, TK Woodruff, and LD Shea. "Murine granulosa cell morphology and function are regulated by a synthetic Arg-Gly-Asp matrix." *Molecular and Cellular Endocrinology*. 205, p 1-10, 2003.
2. PK Kreeger, JW Deck, TK Woodruff, and LD Shea. "The *in vitro* regulation of ovarian follicle development using alginate-extracellular matrix gels." *Biomaterials*. 27, p 714-723, 2006. PMCID:PMC2648392
3. PK Kreeger, NN Fernandes, TK Woodruff, and LD Shea. "Regulation of mouse follicle development by follicle stimulating hormone in a three-dimensional *in vitro* culture system is dependent on follicle stage and dose." *Biology of Reproduction*. 73, p 942-950, 2005. PMCID:PMC2662519
4. M Xu, PK Kreeger, LD Shea, and TK Woodruff. "Tissue engineered follicles produce live, fertile offspring." *Tissue Engineering*. 12, p 2739-2746, 2006. PMCID: PMC2648391

2. A core focus of my post-doctoral research and independent lab has been the development of data-driven systems biology models to understand cellular decisions. In particular, I have utilized partial least squares regression (PLSR) models to analyze how cells integrate multiple stimuli to make phenotypic decisions. PLSR is a multivariate regression technique that analyzes the relationship between independent and dependent variables based on the covariation between the two data sets. These studies have resulted in insights into how

cellular networks respond to different genetic mutations and how changes in the levels of proteins in the cell network impact behavior.

1. PK Kreeger, R Mandhana, SK Alford, KM Haigis, DA Lauffenburger. “RAS mutations impact TNF-induced apoptosis responses of colon carcinoma cells via ERK-modulatory negative and positive feedback circuits along with non-ERK pathway effects.” *Cancer Research*. 69, p 8191-8199, 2009. PMCID:PMC2927135
2. RD Prasasya, KZ Vang, PK Kreeger. “A multivariate model of ErbB network composition predicts ovarian cancer cell response to canertinib.” *Biotechnology and Bioengineering*. 109, p. 213-224, 2012. PMCID:PMC3786202
3. R Liu, KZ Vang, PK Kreeger, SH Gellman, KS Masters. “Experimental and computational analysis of cellular interactions with nylon-3-bearing substrates.” *Journal of Biomedical Materials Research: Part A*. 100, p2750-2759. 2012. PMCID:PMC3429641
4. L Wickert, S Pomerenke, I Mitchell, KS Masters, PK Kreeger. Keratinocyte response to EGF is dependent upon stiffness cues. *Sci Reports*. 6: 20139, 2016. PMCID: PMC4735862

3. A second focus of my lab has been the development of mass-action models to analyze network behavior in a variety of systems. These mechanistic models provide a unique method to analyze different hypotheses *in silico*. For example, with this modeling approach I examined different mechanisms regulating follicle dynamics and determined that the dynamics of this system are inconsistent with a proposed stem cell mechanism. Additionally, analysis of these models can identify which component of a complex network controls system behavior, as shown in our recent publications modeling the IGF and ERα networks.

1. RD Prasasya, D Tian, PK Kreeger. Analysis of cancer signaling networks by systems biology to develop therapies. *Seminars in Cancer Biology*. 21, p. 200-206, 2011. PMCID: Policy Exempt – not resulting from NIH funding
2. D Tian, PK Kreeger. Analysis of the quantitative balance between insulin-like growth factor (IGF)-1 ligand, receptor, and binding protein levels to predict cell sensitivity and therapeutic efficacy. *BMC Systems Biology.* 8: 98, 2014. PMCID: PMC4236724
3. D Tian, P Rajbhandari, K Bjorkland, NM Solodin, ET Alarid, PK Kreeger. A kinetic model identifies phosphorylated estrogen receptor-α (ERα) as a critical regulator of ERα dynamics in breast cancer. *FASEBJ.* 29, p 2022-2031, 2015. PMCID: PMC4415015
4. D Tian, I Mitchell, PK Kreeger. Quantitative analysis of the impact of insulin-like growth factor 2 receptor and IGF binding proteins on IGF1R phosphorylation. *BMC Systems Biology.* 10:15, 2016. PMCID: PMC4746774

Complete List of Published Work in MyBibliography:
http://www.ncbi.nlm.nih.gov/sites/myncbi/pamela.kreeger.1/bibliograpahy/43013971/public/?sort=date&direction=ascending

D. Research Support

Active

NIH 1DP2CA195766-01 09/30/14-08/31/19
Analysis of how quantitative cellular network variation impacts tumor progression
Role: PI
The goal of this study is examine how changes in protein levels (rather than mutations) impact tumor progression in ovarian cancer. We will develop biomimetic environments to analyze this question in both early and late stage disease and utilize computational modeling tools to identify new therapeutic strategies.

NIH 1R21CA202040-01 12/01/15-11/30/17
Impact of soluble and physical stimuli on tumor angiogenesis and drug sensitivity
Role: PI

The goal of this study is to determine how parameters in the tumor microenvironment influence sensitivity to anti-angiogenic therapies in breast cancer.

NSF CBET-1401584 08/01/14-07/31/17
Promotion of tissue engineering angiogenesis via analysis of cellular decision-making processes in response to mechanical and biomolecular cues
Role: PI (co-PI: KS Masters)
The goal of this study is to use both experimental and computational methods to identify tissue engineering scaffold design parameters that optimally support angiogenesis and develop novel strategies for improving angiogenesis in scaffold environments that are intrinsically less supportive of angiogenesis.

American Cancer Society RSG-13-026-01-CSM 01/01/13-12/31/16 (in NCE)
Macrophage-tumor cell interactions in ovarian cancer
Role: PI
The goal of this study is to analyze the interactions between ovarian cancer tumor cells and primary macrophages in a novel microfluidic culture system.

NIH R21 EY026222 08/01/16-09/30/18
Identification of novel therapeutic targets for age-related macular degeneration via a combined tissue engineering and systems biology approach
Role: co-I (PI: KS Masters)
The goal of this study is to test the hypothesis that physical changes that occur in age-related macular degeneration (AMD) influence neo-angiogenesis and utilize this information to 1) help determine biomarkers of environments that are sensitive to anti-VEGF therapy and 2) identify new therapeutic strategies that may complement anti-VEGF therapy.

Completed Support

NSF CAREER CBET-0951613 03/01/10-02/28/16 (NCE)
Quantitative analysis of endocrine disrupting chemicals
Role: PI

NIH R01-GM099031 09/01/11-08/31/16 (NCE)
Combinatorial analysis of migration stimuli for enhanced wound healing
Role: co-I (PI: KS Masters)