

### BIOGRAPHICAL SKETCH

Provide the following information for the Senior/key personnel and other significant contributors in the order listed on Form Page 2. Follow this format for each person. **DO NOT EXCEED FOUR PAGES.**

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|--|---|
| NAME<br><b>Jean J. Latimer, Ph.D.</b>                                      | POSITION TITLE<br>Associate Professor, Department of<br>Pharmaceutical Sciences, College of<br>Pharmacy, Nova Southeastern University |
| eRA COMMONS USER NAME (credential, e.g., agency login)<br><b>LATIMER_J</b> |   |

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<br>(if applicable)   | MM/YY | FIELD OF STUDY                    |
|--|-----------------------------|-------|-----------------------------------|
| Cornell University, Ithaca, NY   | B.A.                        | 1982  | Cell Biology                      |
| SUNY at Buffalo, Roswell Park Cancer<br>Institute Division, Buffalo, NY                            | Ph.D.                       | 1989  | Molecular and Cellular<br>Biology |
| Laboratory of Radiobiology and<br>Environmental Health, University of<br>California, San Francisco | Post-Doctoral<br>Fellowship | 1993  | Developmental<br>Biology          |

#### A. Personal Statement

I have a background in performing functional assays of DNA repair based on my postdoctoral training at the Department of Energy funded Laboratory of Radiobiology at UCSF under Dr. James Cleaver. I have extended this work into the molecular analysis of individual gene expression of the Nucleotide Excision Repair pathway using the model systems established in my own laboratory at the University of Pittsburgh Medical Center. Together with Dr. Stephen Grant I have also performed functional analyses of DNA repair and somatic mutation on some rare human DNA repair disorders (shown in the list of publications below).

My laboratory has developed a number of important *in vitro* models related to the human breast and breast cancer. My background in developmental biology and murine embryonic stem cells has allowed my laboratory to establish a tissue engineering system that involves multiple autologous cell types from the non-diseased breast. We have established 48/48 reduction mammaplasty extended explants, 12 of which are from African American patients. This system culminates in an organotypic breast epithelial/myoepithelial ductal system *in vitro*, after one month, over a field of stromal fibroblasts. We have also created 56 tumor cell lines about half of which have matching adjacent isogenic counterparts. We have published reduction mammaplasty culture work previously in *Experimental Cell Research*, *Cell and Tissue Research*, *Stem Cells* and *PNAS*.

#### B. Positions and Honors

- 1993-2011 **Assistant Professor**, Departments of Obstetrics, Gynecology and Reproductive Sciences and Human Genetics, University of Pittsburgh, Pittsburgh, PA
- 1993-2011 **Investigator**, Magee-Womens Research Institute, Magee-Womens Hospital, Pittsburgh, PA
- 1994-2011 **Member**, Molecular and Cellular Carcinogenesis Program, University of Pittsburgh Cancer Institute, Pittsburgh, PA
- 1999-2011 **Member**, Molecular Genetics and Biochemistry Graduate Faculty, Interdisciplinary Biomedical Graduate Program, University of Pittsburgh, Pittsburgh, PA
- 2004-2011 **Member**, Center for Environmental Oncology, University of Pittsburgh Cancer

- Institute, Pittsburgh, PA
- 2006-2011 **Member**, Cellular and Molecular Pathology Graduate Faculty, Interdisciplinary Biomedical Graduate Program, University of Pittsburgh, Pittsburgh, PA
- 2006-2011 **Member**, Cancer Stem Cells Program, University of Pittsburgh Cancer Institute, Pittsburgh, PA
- 2011-present **Associate Professor**, Department of Pharmaceutical Sciences, Nova Southeastern University, Fort Lauderdale, FL
- 2011-present **Director**, Cancer Research Laboratory, College of Pharmacy, Nova Southeastern University, Fort Lauderdale, FL

### Federal Advisory Committees

- 1999-2001 Institute of Medicine/National Cancer Policy Board Committee to Study Technologies for the Early Detection of Breast Cancer
- 2001, 2006-2007 Army Prostate Cancer CDMRP: Clinical and Experimental Therapeutics
- 2001 NASA: Cellular Biotechnology and Tissue Engineering
- 2001, 2007-2008 Army Breast Cancer CDMRP: Cell Biology
- 2003 NASA: Radiation Biology
- 2003 Army Breast Cancer CDMRP: Concept Awards
- 2004-2005 Army Breast Cancer CDMRP: Molecular Biology and Genetics
- 2004-2007 Army Breast Cancer CDMRP: Clinical and Experimental Therapeutics
- 2006-2007, 2012-2013 Army Breast Cancer CDMRP: Era of Hope Scholar Review Panel
- 2009 NIH/NCI: RC1 Challenge Grant Program Basic and Translational Oncology SEP
- 2009 Army Breast Cancer CDMRP: Pathobiology
- 2010 Army Prostate Cancer CDMRP: Cellular and Molecular Biology
- 2013-2015 Army Breast Cancer CDMRP: Postdoctoral Awards
- 2015-16 Chair, American Institute of Biological Sciences Breast Cancer Review Panel

### Patents

- 2000 Epithelial Cell Cultures Useful For *in Vitro* Testing. U.S. Patent #6,074,874
- 2002 Methods Related to Primary HMEC. U.S. Patent #6,383,805

### **C. Selected Peer-Reviewed Publications (of 39)**

#### Most relevant to the molecular etiology of breast cancer

1. Wend, P., Runke, S., Wend, K., Anchondo, B., Yesayan, M., Jordan, M., Hardie, N., Lodenkemper, C., Ulasov, I., Lesniak, M.S., Wolsky, R., Bentolila, L.A., Grant, S.G., Elashoof, D., Lehr, S., **Latimer, J.J.**, Bose, S., Sattar, H., Krum, S.A., and Miranda-Carboni, G.A. (2013) WNT10B/ $\beta$ -catenin signaling induces HMGA2 and proliferation in metastatic triple-negative breast cancer. *EMBO Mol. Med.* **5**: 1–16 (published online 1-11-13).
2. Visus, C., Ito, D., Dhir, R., Szczepanski M.J., Chang, Y. J., **Latimer, J.J.**, Grant, S.G., and DeLeo, A.B. (2011) Identification of hydroxysteroid (17 $\beta$ ) dehydrogenase type 12 (HSD17B12) as a CD8+ T-cell-defined human tumor antigen of human carcinomas. *Cancer Immunol. Immunother.* **60**: 919–929 (published online 3-16-11).
3. **Latimer, J.J.**, Johnson, J.M., Kelly, C.M., Miles, T.D., Beaudry-Rodgers, K.A., Lalanne, N.A., Vogel, V.G., Kanbour-Shakir, A., Kelley, J.L., Johnson, R.R., and Grant, S.G. (2010) Nucleotide excision repair deficiency is intrinsic in sporadic stage I breast cancer. *Proc. Natl. Acad. Sci. USA* **107**: 21725–21730 (published online 11-30-10).
4. California Breast Cancer Research Program (2010) **Pathways to Breast Cancer: A Case**

**Study for Innovation in Chemical Safety Evaluation** (Schwarzman, M., and Jansses, S., eds.), University of California, Berkeley, 36 pages.

- Grant, S.G., Melan, M.A., **Latimer, J.J.**, and Witt-Enderby, P.A. (2009) Melatonin and cancer: a review of clinical studies, cellular mechanisms and future perspectives. *Expert Rev. Mol. Med.* **11**: E5.

Most relevant to genotoxicity and carcinogenesis

- Latimer, J.J.**, Majekwana, V.J., Pbón-Padín, Y.R., Pimpley, M.R., and Grant, S.G. Regulation and dysregulation of mammalian nucleotide excision repair. (2015) *Photochem. Photobiol. Photochemistry and Photobiology* (published online 11-13-14) doi: 10.1111/php.123.
- Latimer, J.J.**, and Kelly, C.M. (2014) Unscheduled DNA synthesis: the clinical and functional assay for global genomic DNA nucleotide excision repair. *Meth. Mol. Biol.* **1105**: 511–532.
- Sajithlal, G.S., Rothermund, K., Zhang, F., Dabbs, D.J., **Latimer, J.J.**, Grant, S.G., and Prochownik, E.V. (2010) Permanently blocked stem cells derived from breast cancer cell lines. *Stem Cells* **28**: 1008–1018.
- Latimer, J.J.**, Johnson, J.M., Miles, T.D., Dimsdale, J.M., Edwards, R.P., Kelley, J.L., and Grant, S.G. (2008) Cell-type-specific level of DNA nucleotide excision repair in primary human mammary and ovarian epithelial cell cultures. *Cell Tissue Res.* **333**: 461-467.
- Grant, S.G., Das, R., Cerceo, C.M., Rubinstein, W.S., and **Latimer, J.J.** (2007) Elevated levels of somatic mutation in a manifesting *BRCA1* mutation carrier. *Pathol. Oncol. Res.* **13**: 276-283.
- Donovan, M., Miles, T.D., **Latimer, J.J.**, Grant, S., Talbott, E., Sasco, A.J., and Davis, D.L. (2006) Association between biomarkers of environmental exposure and increased risk of breast cancer. *Nature Rev. Cancer* **6**: c1.
- Rubinstein, W.S., **Latimer, J.J.**, Sumkin, J.H., Huerbin, M.B., Grant, S.G., and Vogel, V.G. (2006) Prospective screening study of 0.5 Tesla dedicated magnetic resonance imaging for the detection of breast cancer in young, high risk women. *BMC Women's Health* **6**: 10.
- Latimer, J.J.**, Rubinstein, W.S., Johnson, J.M., Kanbour-Shakir, A., Vogel, V.G., and Grant, S.G. (2005) Haploinsufficiency for *BRCA1* is associated with normal levels of DNA nucleotide excision repair in breast tissue and blood lymphocytes. *BMC Med. Genet.* **6**: 26.
- Latimer, J.J.**, Nazir, T., Flowers, L.C., Forlenza, M.J., Beaudry-Rodgers, Kelly, C.M., Conte, J.A., Shestak, K., Kanbour-Shakir, A., and Grant, S.G. (2003) Unique tissue-specific level of DNA nucleotide excision repair in primary human mammary epithelial cultures. *Exptl. Cell Res.* **291**: 111–121.
- Institute of Medicine (2001) **Mammography and Beyond: Developing Technologies for the Early Detection of Breast Cancer** (Nass, S.J., Henderson, I.C., and Lashoff, J.C., eds.), National Academy Press, Washington, D.C., 288 pages.

**D. Research Support (Last Three Years)**

Ongoing research support

“Persistently Elevated Somatic Mutation as a Biomarker for Clinically Relevant Exposures in Gulf War Illness”

(Grant, S.G., PI, Latimer Co-I \$581,848)

Congressionally Directed Medical Research Program

7/1/16-6/31/19

The major aim of this grant is to evaluate somatic mutation and DNA repair capacity in GWI patients and controls and correlate these data with disease severity.

“Can DNA Repair Capacity in Breast Cancer Stem Cells Predict Recurrence?”

(Latimer, J.J., PI; \$15,000)

President's Faculty Research & Development Grant

6/1/16-5/31/17

Nova Southeastern University

*The major aim of this study is to isolate and quantify cancer stem cells from 5 recurrent stage II and III cell lines using flow cytometry and compare the cancer stem cell percentage and Nucleotide Excision Repair Capacity with 5 non recurrent stage I and II cell lines. All cell lines will be from chemotherapy naive patients and Dr. Latimer's collection of breast cancer cell lines (N=55).*

“Somatic mutation and DNA repair in Gulf War Illness”

(Latimer co- PI; \$15,000)

President's Faculty Research & Development Grant

6/1/16-5/31/17

Nova Southeastern University

*The major aim of this grant is to evaluate somatic mutation and DNA repair capacity in GWI patients and controls and correlate these data with disease severity.*

“Novel Transformation Assay to Identify Florida Environmental Breast Carcinogens”

(Latimer, J.J., PI; \$10,000)

President's Faculty Research & Development Grant

6/1/13-5/31/15

Nova Southeastern University

*The major aim of this pilot study is to evaluate the potency and proportion of stem cells in non diseased breast cell lines from women of Caucasian and African American ancestry.*

“Detailed Molecular Profiling of Sporadic Stage I Breast Cancer”

(Grant, S.G., PI; \$10,000)

President's Faculty Research & Development Grant

6/1/13-5/31/15

Nova Southeastern University

*The major aim of this pilot study is to determine whether specific miRNAs negatively regulate the expression of key Nucleotide Excision Repair genes in early stage breast cancer cell lines.*

“The Role of DNA Repair, Genomic Instability and Stem Cells in Leukemia Relapse”

(Latimer, J.J., PI; \$30,000)

Children's Leukemia Research Association, Inc.

7/31/12-7/30/16

*The major aim of this grant is to render leukemia cell lines resistant to chemotherapeutic drugs and then study the changes in functional DNA repair and DNA repair gene expression.*

“Human Breast Tissue Engineering Model for Environmental Chemical Assessment”

(Latimer, J.J., PI; \$100,000)

Florida Breast Cancer Foundation

10/1/12-9/30/14

*The major aim of this grant is to use two of Dr. Latimer's novel breast cell lines to quantify the impact of four major endocrine disruptors present in consumer products on organotypic ductal differentiation and related gene expression.*

Completed Research Support (Last 3 Years)

“Stem cells and DNA repair in childhood leukemias” (Latimer, J.J., PI; \$250,000)

Children's Leukemia Research Association, Inc. 6/1/11—5/31/13

“Novel drugs targeting breast cancer stem cells” (Prochownik, E.V., PI; \$200,000)

Hillman Fund, UPMC 9/1/10—8/31/12

“PARP inhibitor treatment of triple negative breast cancer” (Pulhalla, S., PI; \$100,000)

The Shapira Foundation 9/1/10—8/31/12

“Red blood cell content of inorganic and organic compounds in children with autism and controls”

(Kingston, H.S., PI; \$700,000) 6/1/10—5/30/12

The Teresa and H. John Heinz III Foundation/The Richard King Mellon Foundation

“Impact of environmental xenoestrogens on African American breast cancer” (Latimer, J.J., PI; \$150,000)

Program Director/Principal Investigator (Last, First, Middle): Latimer, Jean J.

The Pittsburgh Foundation 10/1/09—9/30/11