Paul Yaswen, Ph.D.

P_Yaswen@lbl.gov 510.734.6880

SENIOR ONCOLOGY DISCOVERY SCIENTIST

Cell Biology, Signal Transduction, Assay Development, Target Validation

Genetic manipulation technologies, project management, biomarker and mechanism of action studies
In-depth knowledge of cancer-associated signaling pathways and/or models of cancer
Understanding of cancer genetics, with ability to effectively leverage bioinformatics tools
Demonstrated experience with in vitro functional assays and generation of cancer models

Key Accomplishments

Scientific:

- Over 25 years of experience in Cancer and Systems Biology with broad expertise in cell & molecular biology, signal transduction, and assay development.
- Extensive experience using cultured human epithelial cells to model processes involved in immortal and malignant transformation, to identify and characterize potential oncogenes and tumor suppressor genes, to analyze determinants of cell-cycle entry and exit, and to examine regulation of differentiation.

Management:

- Independently directed and mentored a group of 4-6 researchers at a time over the course of 20+ years, including ~ 30 Ph.D. scientists.
- Strong project management skills for internal research projects and external collaborations.
- Responsible for management of project budgets of $0.5-2 M, facility and space planning, recruitment and hiring of key personnel.

PROFESSIONAL EXPERIENCE

Principal Investigator, Dept. of Cancer & DNA Damage Responses; Staff Sci. II
Lawrence Berkeley National Lab 2008 - present

- Discovered a unique role of the Rb tumor suppressor in mediating p16-initiated growth arrest in human mammary epithelial cells.
- Determined how telomerase is regulated by the c-myc oncogene and the p16 tumor suppressor.
- Contributed to studies dealing with unique targetable susceptibilities exhibited by breast cancer cells that overexpress the c-myc or ZNF217 oncogenes.
- Contributed to studies of how normal and malignant mammary epithelia differ in their responses to extracellular matrices.
- Co-led a study that determined how the interaction of tumor suppressors E-cadherin and PTEN regulates morphogenesis and growth arrest in human mammary epithelial cells.
- Determined how ionizing radiation can promote the outgrowth of pre-malignant cells.

Principal Investigator, Dept. of Cancer & Systems Biology; Staff Scientist II 2003 – 2008

- Determined how the p53 tumor suppressor integrates inter- and intra-cellular signals to regulate cellular proliferation.
- Contributed to the molecular and biochemical characterization of the ZNF217 oncogene, including a study showing ZNF217 suppresses cell death associated with chemotherapy and telomere dysfunction.
- Co-led a study that found a gene expression signature in organized and growth arrested mammary acini that predicts good outcome in breast cancer.
- Found altered expression and localization of telomere-associated protein TRF2 in immortally transformed and tumor-derived human breast cells.

- Contributed to an analysis of genomic instability in breast cancer in which cultured human mammary epithelial cells were used to model the changes in genomic instability that occur in vivo during transitions from hyperplasia to ductal carcinoma in situ to infiltrating carcinoma.

Principal Investigator, Dept. of Cell & Molecular Biology; Staff Scientist II **1990 - 2003**
- Co-led a study of the roles of the p53 and p16 tumor suppressors in determining the irreversibility of cellular senescence.
- Studied the mechanisms by which telomerase repression is overcome during immortalization of human cells.
- Showed that oncogene-induced senescence can proceed in the absence of intact p53 and Rb pathways.
- Determined that telomerase expression can induce resistance to TGFβ growth inhibition in human mammary epithelial cells.
- Found that the ZNF217 gene amplified in breast cancers promotes immortalization of human mammary epithelial cells.
- Showed loss of expression of the putative tumor suppressor $p57^{KIP2}$ during chemically induced immortalization of cultured human mammary epithelial cells.

NRSA Fellow, Dept. of Cell & Molecular Biology
Dana-Farber Cancer Institute, Boston, MA **1988 – 1990**
- Used subtractive hybridization to identify a novel calmodulin-related gene that is downregulated during transformation of human mammary epithelial cells.

Education

Brown University, Providence, RI
Ph.D., Cell and Molecular Biology

Tufts University, Boston, MA
B.Sc., Biology

Other activities

Member - Berkeley Stem Cell Center	2006 - present
Member - Breast Oncology Program, UCSF Comprehensive Cancer Center	1998 - 2009
Preceptor - Biology of Aging Training Program, LBNL/Buck Institute	2003 - present
Ad hoc member - Mol. Oncology Study Section, NIH, Center for Scientific Review	2005 - 2009

SELECTED PUBLICATIONS

Lawson, DA, Bhakta, N, Kessenbrock, K, Prummel, K, Yu, Y, Takai, K, Zhou, A, Eyob, H, Yaswen, P, Welm, A, Goga, A, Werb, Z. Single-cell analysis reveals a distinct stem cell program in early human metastatic breast cancer cells. Nature *In press*, 2015.

Hines WC, Yaswen P, Bissell MJ. Modelling breast cancer requires identification and correction of a critical cell lineage-dependent transduction bias. Nat Commun. 6:6927, 2015.

Yaswen P, MacKenzie KL, Keith WN, Hentosh P, Rodier F, Zhu J, Firestone GL, Matheu A, Carnero A, Bilsland A, Sundin T, Honoki K, Fujii H, Georgakilas AG, Amedei A, Amin A, Helferich B, Boosani CS, Guha G, Ciriolo MR, Chen S, Mohammed SI, Azmi AS, Bhakta D, Halicka D, Niccolai E, Aquilano K, Ashraf SS, Nowsheen S, Yang X. Therapeutic targeting of replicative immortality. Semin Cancer Biol. pii: S1044-579X, 2015.

Yaswen P. Reinforcing targeted therapeutics with phenotypic stability factors. Cell Cycle. 13:3818-22, 2014.

Nguyen-Ngoca, K-V., Cheung, K.J., Brenot, A., Shamira, E.R., Gray, R.S., Hines, W.C., Yaswen, P., Werb, Z., and Ewald, A.J. The ECM microenvironment regulates collective migration and local dissemination in normal and malignant mammary epithelium. Proc. Nat. Acad. Sci. (USA) 109:E2595-604, 2012.

Littlepage, L.E., Adler, A.S., Kouros-Mehr, H., Huang, G., Chou, J., Krig, S.R., Griffith, O.L., Korkola, J.E., Qu, K., Lawson, D.A., Xue, Q., Sternlicht, M.D., Dijkgraaf, G.J., Yaswen, P., Rugo, H.S., Sweeney, C.A., Collins, C.C., Gray, J.W., Chang, H.Y., and Werb, Z. The transcription factor ZNF217 is a prognostic biomarker and therapeutic target during breast cancer progression. Cancer Discov. 2:638-51, 2012.

Horiuchi, D., Kusdra, L., Huskey, N.E., Chandriani, S., Lenburg, M.E., Gonzalez-Angulo, A.M., Creasman, K.J., Bazarov, A.V., Smyth, J.W., Davis, S.E., Yaswen, P., Mills, G.B., Esserman, L.J., Goga, A. MYC pathway activation in triple-negative breast cancer is synthetic lethal with CDK inhibition. J Exp Med. 209:679-96, 2012.

Bazarov, A.V, Lee, W.J., Bazarov, I., Bosire, M., Hines, W.C., Stankovich, B., Chicas, A., Lowe, S.W., and Yaswen, P. The specific role of pRb in p16INK4A mediated arrest of normal and malignant human breast cells. Cell Cycle 11:1008-1013, 2012.

Krig, S.R., Miller, J.K., Frietze, S., Beckett, L.A., Neve, R.M., Farnham. P.J., Yaswen, P.I., and Sweeney, C.A. ZNF217, a candidate breast cancer oncogene amplified at 20q13, regulates expression of the ErbB3 receptor tyrosine kinase in breast cancer cells. Oncogene 29:5500-10, 2010.

Bazarov, A.V., Hines, W.C., Lee, L., Bassett, E., Beliveau, A., Campeau, E., Mukhopadhyay, R., Lee, W.J., Melodyev, S., Zaslavsky, Y., Rodier, F., Benhattar, J., Ren, B., Campisi, J., and Yaswen, P. $P16^{INK4A}$ mediated suppression of telomerase in normal and malignant human breast cells. Aging Cell 9:736-46, 2010.

Mukhopadhyay, R., Costes, S., Bazarov, A., Hines, W.C., Barcellos-Hoff, M.H., and Yaswen, P. Promotion of variant human mammary epithelial cell outgrowth by ionizing radiation: an agent-based model supported by in vitro studies. Breast Cancer Res. 12:R11, 2010.

Bazarov, A., Hines, W.C., Mukhopadhyay, R., Beliveau, A., Melodyev, S., Zaslavsky, Y., and Yaswen, P. Telomerase activation by c-Myc in human mammary epithelial cells requires additional genomic changes. Cell Cycle 8: 3373-3378, 2009.

Fournier, M.V., Fata, J., Martin, K., Yaswen, P., and Bissell, M.J. Interaction of E-cadherin and PTEN regulates morphogenesis and growth arrest in human mammary epithelial cells. Cancer Res. 69:4545-52, 2009.

Beliveau, A., Bassett, E., Lo, A.T., Garbe, J., Rubio, M.A., Bissell, M.J., Campisi, J., and Yaswen, P. p53-dependent integration of telomere and growth factor deprivation signals. Proc. Nat. Acad. Sci. (USA), 104:4431-6, 2007.

Krig, S.R., Jin, V.X., Bieda, M.C., O'geen, H., Yaswen, P., Green, R., and Farnham, P.J. Identification of genes directly regulated by the oncogene ZNF217 using ChIP-chip assays. J. Biol. Chem. 282:9703-12, 2007.

Fournier, M., Martin, K.J., Xhaja, K., Bosch, I., Yaswen, P., and Bissell, M.J., Gene expression signature in organized and growth arrested mammary acini predicts good outcome in breast cancer. Cancer Res. 66:7095-102, 2006.

Huang, G., Krig, S., Kowbel, D., Xu, H., Hyun, B., Volik, S., Feuerstein, B., Mills, G.B., Stokoe, D., Yaswen, P., and Collins, C. ZNF217 suppresses cell death associated with chemotherapy and telomere dysfunction. Hum Mol Genet. 14:3219-25, 2005.

Nijjar, T., Bassett, E., Garbe, J., Takenaka,Y., Stampfer, M.R., Gilley, D., Yaswen, P. Accumulation and altered localization of telomere-associated protein TRF2 in immortally transformed and tumor-derived human breast cells. Oncogene 24:3369-3376, 2005.

Chin, K., Ortiz de Solorzano, C., Knowles, D., Jones, A., Chou, W., Garcia Rodriguez, E., Kuo, W-L. Ljung, B-M., Chew, K., Garbe, J., Myambo, K., Krig, S., Stampfer, M., Yaswen, P., Gray, J.W., and Lockett, S.J. In situ analyses of genome instability in breast cancer. Nature Gen. 36: 984-988, 2004.

Beauséjour, C.M., Krtolica, A., Galimi, F., Narita, M., Lowe, S.W., Yaswen, P. and Campisi, J. Reversibility of human cellular senescence: Roles of the p53 and p16 pathways. EMBO J. 22: 4212-4222, 2003.

Stampfer, M.R., Garbe, J., Nijjar, T., Wigington, D., Swisshelm, K., and Yaswen, P. Loss of p53 function accelerates acquisition of telomerase activity in indefinite lifespan human mammary epithelial cell lines. Oncogene, 22: 5238-5251, 2003.

Olsen, C.L., Gardie, B., Yaswen, P., and Stampfer, M.R. Raf-1-induced growth arrest in human mammary epithelial cells is p16-independent and is overcome in immortal cells during conversion. Oncogene 21, 6328–6339, 2002.

Stampfer, M.R., Garbe, J., Levine, G., Lichtsteiner, S., Vasserot, A.P., and Yaswen, P. hTERT expression can induce resistance to TGFβ growth inhibition in $p16^{INK4A}$(-) human mammary epithelial cells. Proc. Nat. Acad. Sci. (USA), 98: 4498-4503, 2001.

Nonet, G.H., Stampfer, M.R., Chin, K., Gray, J.W., Collins, C.C., and Yaswen, P. The *ZNF217* Gene amplified in breast cancers promotes immortalization of human mammary epithelial cells. Cancer Res. 61: 1250-1254, 2001.

Nijjar, T., Wigington, D., Garbe, J., Waha, A., Stampfer, M.R., and Yaswen, P. $p57^{KIP2}$ expression and loss of heterozygosity during immortal conversion of cultured human mammary epithelial cells. Cancer Res. 59:5112-5118, 1999.

Garbe, J., Wong, M., Wigington, D., Yaswen, P., and Stampfer, M.R. Viral oncogenes accelerate conversion to immortality of cultured human mammary epithelial cells. Oncogene 18:

2169-2180, 1999.

Collins, C., Rommens, J.M., Kowbel, D., Godfrey, T., Tanner, M.,Hwang, S., Polikoff, D., Nonet, G., Cochran, J., Myambo, K., Jay, K.E., Froula, J., Cloutier, T., Kuo, W-L., Yaswen, P., Dairkee, S., Giovanola, J., Hutchinson, G.B., Isola, J., Kallioniemi, O-P., Palazzolo, M., Martin, C., Erickson, C., Pinkel, D., Albertson, D., Li, W-B., and Gray, J.W. Positional cloning of ZNF217 and NABC1: Genes amplified at 20q13.2 and overexpressed in breast carcinoma. Proc. Natl. Acad. Sci. USA 95:8703-8708, 1998.

Close, M.J., Howlett, A.R., Roskelley, C.D., Desprez, P.Y., Bailey, N., Rowning, B., Teng, C.T., Stampfer, M.R., and Yaswen, P. Lactoferrin expression in mammary epithelial cells is mediated by changes in cell shape and actin cytoskeleton. J. Cell Science 110:2861-2871, 1997.

Stampfer, M.R., Bodnar, A., Garbe, J., Wong, M., Pan, A., Villeponteau, B., and Yaswen, P. Gradual phenotypic conversion associated with immortalization of cultured human mammary epithelial cells. Mol. Biol. Cell 8:2391-2405, 1997.

Yaswen, P., Smoll, A., Peehl, D., Trask, D.K., Sager, R., and Stampfer, M.R. Downregulation of a novel calmodulin-related gene during transformation of human mammary epithelial cells. Proc. Natl. Acad. Sci. USA 87: 7360-7364, 1990.

Yaswen, P., Hayner, N.T., and Fausto, N. Isolation of oval cells by centrifugal elutriation and comparison with other cell types purified from normal and preneoplastic livers. Cancer Res. 44: 324-331, 1984.