
BIOGRAPHICAL SKETCH

NAME Joseph R. Testa, Ph.D., FACMG	POSITION TITLE Senior Member; Carol & Kenneth E. Weg Chair in Human Genetics; Co-Leader, Cancer Biology Program; Co-Leader, Personalized Kidney Cancer Therapy Keystone Program Chair, Mesothelioma Working Group
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EDUCATION/TRAINING

INSTITUTION AND LOCATION	DEGREE	YEAR(s)	FIELD OF STUDY
Fordham University, New York, NY	Ph.D.	1976	Biological Sciences
University of Chicago, Chicago, IL	Research Associate	1976-1980	Cancer Cytogenetics (with Janet Rowley)

RESEARCH POSITIONS

1975-1976	Associate in Research, Department of Therapeutic Radiology, Yale University
1976-1979	Research Associate, Department of Medicine, University of Chicago
1978-1980	Assistant Director, Cytogenetics Laboratory (Medicine), University of Chicago
1979-1980	Research Associate (Assistant Professor), Department of Medicine, University of Chicago
1980-1982	Chief, Cytogenetics Unit, NCI-Baltimore Cancer Research Program, NIH
1980-1983	Assistant Professor, Department of Medicine, University of Maryland
1982-1989	Associate Professor, Department of Pathology/Program of Oncology, University of Maryland
1987-1988	Visiting Scientist, BRI, NCI-Frederick Cancer Research Facility (with George Vande Woude)
1989-1992	Member and Director, Section of Molecular Cytogenetics, Fox Chase Cancer Center
1992-present	Senior Member, Fox Chase Cancer Center (FCCC)
1993-present	Adjunct Professor, Dept. Path. & Lab. Medicine, University of Penn. School of Medicine
1999-present	Director, Human Genetics Program: Carol & Ken E. Weg Chair in Human Genetics, FCCC
2007-present	Director, Genomics Facility, FCCC
2008-present	Scientific Leader, Personalized Kidney Cancer Therapy Keystone Program, FCCC
2008-present	Co-Leader, Cancer Biology, FCCC
2008-present	Chair, Mesothelioma Working Group, Thoracic Oncology Program, FCCC

HONORS

B.S. *cum laude* (1969); *Phi Beta Kappa*, Fordham University (1977); Leukemia Society of America Special Fellow Award (1982-1984); Leukemia Society of America Scholar Award (1984-1990); Stohlman Memorial Scholar Award (1987); Irving Selikoff Award for Cancer Research (1999); Member, NCI Board of Scientific Counselors, Basic Sciences (2006-2011); Landon Foundation-AACR Innovator Award for International Collaboration in Cancer Research (team award) (2008); ACS Scientific Research Award, Southeast PA Region (2009)

EDITORIAL BOARDS

Cancer Genetics & Cytogenetics (1987-present); *Genes, Chromosomes & Cancer* (1989-present); *Leukemia Research* (1996-present); *Cytogenetic & Genome Research* (2000-2007); *Cancer Research* (Associate Editor) (2006-present); *Oncogene* (2008-present); *Genes and Cancer* (2009-present)

BOARD CERTIFICATION:

1987 Diplomat (Clinical Cytogenetics), American Board of Medical Genetics

SELECTED PEER-REVIEWED PUBLICATIONS (from a total of 330 original articles, reviews, and chapters)

- Testa, J.R., Mintz, U., Rowley, J.D., Vardiman, J.W., Golomb, H.M. Evolution of karyotypes in acute nonlymphocytic leukemia. *Cancer Res.* 39: 3619-3627, 1979.
- Testa, J.R., Hogge, D.E., Misawa, S., Zandparsa, N. Chromosome 16 rearrangements in acute myelomonocytic leukemia with abnormal eosinophils. *N. Engl. J. Med.* 310: 468, 1984.
- Staal, S.P., Huebner, K., Croce, C.M., Parsa, N.Z., Testa, J.R. The *AKT1* proto-oncogene maps to human chromosome 14, band q32. *Genomics* 2: 96-98, 1988.
- Bellacosa, A., Testa, J.R., Staal, S.P., Tsichlis, P.N. A retroviral oncogene, *akt*, encoding a serine-threonine kinase containing an SH2-like region. *Science* 254: 274-277, 1991.
- Cheng, J.Q., Godwin, A.K., Bellacosa, A., Taguchi, T., Franke, T.F., Hamilton, T.C., Tsichlis, P.N., Testa, J.R. *AKT2*, a putative oncogene encoding a member of a novel subfamily of serine-threonine protein kinases, is amplified in human ovarian carcinomas. *Proc. Natl. Acad. Sci. (USA)* 89: 9267-9271, 1992.
- Bellacosa, A., Franke, T.F., Gonzalez-Portal, M.E., Datta, K., Taguchi, T., Gardner, J., Cheng, J.Q., Testa, J.R., Tsichlis, P.N. Structure, expression and chromosomal mapping of *c-akt*: relationship to *v-akt* and its implications. *Oncogene* 8: 745-754, 1993.
- Testa, J.R., Getts, L.A., Salazar, H., Liu, Z., Handel, L., Godwin, A.K., Hamilton, T.C. Spontaneous transformation of rat ovarian surface epithelial cells results in well to poorly differentiated tumors with a parallel range of cytogenetic complexity. *Cancer Res.* 54: 2778-2784, 1994.
- Testa, J.R., Siegfried, J.M., Liu, Z., Hunt, J.D., Feder, M.M., Litwin, S., Zhou, J.-Y., Taguchi, T., Keller, S.M. Cytogenetic analysis of 63 non-small cell lung carcinomas: recurrent chromosome alterations amid frequent and widespread genomic upheaval. *Genes Chromosomes Cancer* 11: 178-194, 1994.
- Altomare, D.A., Guo, K., Cheng, J.Q., Sonoda, G., Walsh, K., Testa, J.R. Cloning, chromosomal localization and expression analysis of the mouse *Akt2* oncogene. *Oncogene* 11: 1055-1060, 1995.
- Bianchi, A.B., Mitsunaga, S., Cheng, J.Q., Klein, W.M., Jhanwar, S.C., Seizinger, B., Kley, N., Klein-Szanto, A.J.P., Testa, J.R. High frequency of inactivating mutations in the neurofibromatosis type 2 gene (*NF2*) in primary malignant mesotheliomas. *Proc. Natl. Acad. Sci. (USA)* 92: 10854-10858, 1995.
- Cheng, J.Q., Ruggeri, B., Klein, W.M., Sonoda, G., Altomare, D.A., Watson, D.K., Testa, J.R. Amplification of *AKT2* in human pancreatic cancer cells and inhibition of *AKT2* expression and tumorigenicity by antisense RNA. *Proc. Natl. Acad. Sci. (USA)* 93: 3636-3641, 1996.
- Cheng, J.Q., Altomare, D.A., Klein, M.A., Lee, W.-C., Kruh, G.D., Lissy, N.A., Testa, J.R. Transforming activity and mitosis-related expression of the *AKT2* oncogene: evidence suggesting a link between cell cycle regulation and oncogenesis. *Oncogene* 14: 2793-2801, 1997.
- Altomare, D.A., Lyons, G.E., Mitsuuchi, Y., Cheng, J.Q., Testa, J.R. *Akt2* mRNA is highly expressed in embryonic brown fat and the *AKT2* kinase is activated by insulin. *Oncogene* 16: 2407-2411, 1998.
- Mitsuuchi, Y., Johnson, S.W., Moonblatt, S., Testa, J.R. Translocation and activation of *AKT2* in response to stimulation by insulin. *J. Cell. Biochem.* 70: 433-441, 1998.
- Riccio, A., Aaltonen, L.A., Godwin, A.K., Loukola, A., Percesepe, A., Salovaara, R., Masciullo, V., Genuardi, M., Paravatou-Petsotas, M., Bassi, D.E., Ruggeri, B.A., Klein-Szanto, A.J.P., Testa, J.R., Neri, G., Bellacosa, A. The DNA repair gene *MBD4* (*MED1*) is mutated in human carcinomas with microsatellite instability. *Nat. Genet.* 23: 266-268, 1999.
- Apostolou, S., De Rienzo, A., Murthy, S.S., Jhanwar, S.C., Testa, J.R. Absence of *BCL10* mutations in human malignant mesothelioma. *Cell* 97: 684-686, 1999.
- Xiao, G.-H., Jeffers, M., Bellacosa, A., Mitsuuchi, Y., Vande Woude, G.F., Testa, J.R. Anti-apoptotic signaling by hepatocyte growth factor/Met via the phosphatidylinositol 3-kinase/Akt and mitogen-activated protein kinase pathways. *Proc. Natl. Acad. Sci. (USA)* 98: 247-252, 2001.
- Tanno, S., Tanno, S., Mitsuuchi, Y., Altomare, D.A., Xiao, G.-H., Testa, J.R. *AKT* activation up-regulates insulin-like growth factor-I receptor expression and promotes invasiveness of human pancreatic cancer cells. *Cancer Res.* 61: 589-593, 2001.

- Altomare, D.A., Tanno, S., De Rienzo, A., Klein-Szanto, A.J., Tanno, S., Skele, K.L., Hoffman, J.P., Testa, J.R. Frequent activation of AKT2 kinase in human pancreatic carcinomas. *J. Cell. Biochem.* 87:470-476, 2002.
- Xiao, G.-H., Beeser, A., Chernoff, J., Testa, J.R. p21-activated kinase links Rac/Cdc42 signaling to merlin. *J. Biol. Chem.* 277: 883-886, 2002.
- Wang, H.Q., Altomare, D.A., Skele, K.S., Di Cristofano, A., Kuhajda, F.P., Testa, J.R. Positive feedback regulation between AKT activation and fatty acid synthase expression in ovarian carcinoma cells. *Oncogene* 24: 3574-3582, 2005.
- Xiao, G.H., Gallagher, R., Shetler, J., Skele, K., Altomare, D., Pestell, R.G., Jhanwar, S., Testa, J.R. The *NF2* tumor suppressor gene product, merlin, inhibits cell proliferation and cell cycle progression by repressing cyclin D1 expression. *Mol. Cell. Biol.* 25: 2384-2394, 2005.
- Altomare, D.A., You, H., Xiao, G.-H., Ramos-Nino, M.E., Skele, K.L., De Rienzo, A., Jhanwar, S.C., Mossman, B.T., Kane, A.B. and Testa, J.R. Human and mouse mesotheliomas exhibit elevated AKT/PKB activity, which can be targeted pharmacologically to inhibit tumor cell growth. *Oncogene* 24(40) 6080-9, 2005.
- Altomare, D.A., Testa, J.R. Perturbations of the AKT signaling pathway in human cancer. *Oncogene* 24: 7455-7464, 2005.
- Lin, D.C.C., Quevedo, C., Brewer, N.E., Grimes, M.L., Testa, J.R., Miller, F.D., Kaplan, D.R. APPL1 associates with TrkA and GIPC1, and is required for NGF-mediated signal transduction. *Mol. Cell. Biol.* 26: 8928-8941, 2006.
- Poulikakos, P.I., Xiao, G.H., Gallagher, R., Jablonski, S., Jhanwar, S.C., Testa, J.R. Re-expression of the tumor suppressor *NF2*/merlin inhibits invasiveness in mesothelioma cells and negatively regulates FAK. *Oncogene* 25: 5960-5968, 2006.
- Mabuchi, S., Altomare, D.A., Connolly, D.C., Klein-Szanto, A., Litwin, S., Hoelzle, M.K., Hensley, H.H., Hamilton, T.C., Testa, J.R. RAD001 (Everolimus) delays tumor onset and progression in a transgenic mouse model of ovarian cancer. *Cancer Res. (Priority Report)* 67: 2408-2413, 2007.
- Lee, H., Kim, D., Dan, H.C., Wu, E.L., Nicosia, S.V., Golemis, E.A., Liu, W., Coppola, D., Brem, S.S., Testa, J.R., Cheng, J.Q. Identification and characterization of putative tumor suppressor NGB, a GTP-binding protein that interacts with the neurofibromatosis 2 protein. *Mol. Cell. Biol.* 27: 2103-2119, 2007.
- Mabuchi, S., Altomare, D.A., Cheung, M., Zhang, L., Poulikakos, P.I., Hensley, H.H., Schilder, R.J., Ozols, R.F., Testa, J.R. RAD001 inhibits human ovarian cancer cell proliferation, enhances cisplatin-induced apoptosis, and prolongs survival in an ovarian cancer model. *Clin. Cancer Res.* 13: 4261-4270, 2007.
- Tan, Y., Timakhov, R.A., Rao, M., Altomare, D.A., Xu, J., Liu, Z., Gao, Q., Jhanwar, S.C., Di Cristofano, A., Wiest, D.L., Knepper, J.E., Testa, J.R. A novel recurrent chromosomal inversion implicates the homeobox gene *Dlx5* in T-Cell lymphomas from Lck-Akt2 transgenic mice. *Cancer Res.* 68: 1296-1302, 2008.
- Tarn, C. Rink, L., Merkel, E., Flieder, D., Pathak, H., Koumbi, D., Testa, J.R., Eisenberg, B., von Mehren, M., Godwin, A.K. Insulin-like growth factor 1 receptor is a potential therapeutic target for gastrointestinal stromal tumors. *Proc. Natl. Acad. Sci. USA* 105: 8387-8392, 2008.
- Carbone, M., Pannuti, A., Zhang, L., Testa, J.R., Bocchetta, M. A novel mechanism of late gene silencing drives SV40 transformation of human mesothelial cells. *Cancer Res.* 68: 9488-9496 2008. PMID: PMC2666620.
- Altomare, D.A., Menges, C.W., Pei, J., Zhang, L., Skele-Stump, K.L., Carbone, M., Kane, A.B., Testa, J.R. Activated $TNF\alpha/NF\kappa B$ signaling via down regulation of Fas-associated factor 1 in asbestos-induced mesotheliomas from *Arf* knockout mice. *Proc. Natl. Acad. Sci. USA* 106: 3420-3425, 2009. PMID: PMC2644256.
- Pei, J, Feder, MM, Al-Saleem, T, Liu, Z, Liu, A, Hudes, GR, Uzzo, RG, Testa, JR. Combined classical cytogenetics and microarray-based genomic copy number analysis reveal frequent 3;5 rearrangements in clear cell renal cell carcinoma. *Genes Chromosomes Cancer.* 2010; 49:610-19.
- Menges, CW, Chen, Y, Mossman, BT, Chernoff, J, Yeung, AT, Testa, JR. A phosphotyrosine proteomic screen identifies multiple tyrosine kinase signaling pathways aberrantly activated in malignant mesothelioma. *Genes Cancer.* 2010; 1:493-505.
- Mabuchi, S, Kawase, C, Altomare, DA, Morishige, K, Hayashi, M, Sawada, K, Ito, K, Terai, Y, Nishio, Y, Klein-Szanto, AJ, Burger, RA, Ohmichi, M, Testa, JR, Kimura, T. Vascular endothelial growth factor is a

promising therapeutic target for the treatment of clear cell carcinoma of the ovary. *Mol Cancer Ther.* 2010; 9:2411-22.

Feng, H., Stachura, D.L., White, R.M., Gutierrez, A., Zhang, L., Sanda, T., Jette, C.A., Testa, J.R., Neubergh, D.S., Langenau, D.M., Kutok, J.L., Zon, L.I., Traver, D., Fleming, M.D., Kanki, J.P., Look, A.T. T-cell lymphoblastic lymphoma cells express high levels of both BCL2 and ICAM1 leading to a blockade of tumor cell intravasation. *Cancer Cell* (in press)

CURRENT RESEARCH SUPPORT

Principal Investigator/ Project Director:

- 09/01/06-08/31/11 Role of Tumor Suppressors and AKT in Mesothelioma
NCI, DHHS; PHS Grant PO1 CA114047
P01 Project 3: Mesothelioma Pathogenesis
- 12/01/08-11/30/13 Basis for Lymphomagenesis in Akt2 Transgenic Mice
NCI, DHHS; PHS Grant RO1 CA77429
- 01/01/09-12/31/10 Combinatorial Targeting of Tyrosine Kinases that are Aberrantly Activated in
Malignant Mesothelioma
Mesothelioma Applied Research Foundation
- 09/15/10-09/14/13 Role of the Inflammasome in Asbestos-Induced Mesothelioma Formation
DOD, PRCRP Idea Award, CA093492

Co-Investigator/Participant:

- 01/01/08-12/31/10 AKT Function in Ovarian Tumor Cell Invasiveness and *In Vivo* Pathogenesis
(Mentor to Dr. D. Altomare)
Liz Tilberis Scholar Award, Ovarian Cancer Research Fund
- 03/01/09-02/28/11 AKT Function in Pancreatic Tumor Cell Invasiveness and *In Vivo* Pathogenesis
NCI, DHHS; PHS Grant R21 CA129302
(pending; percentile 10.8)
- 04/01/10-03/31/15 The Role of p21-Activated Kinases in Malignant Mesothelioma NCI, DHHS
(Co-P.I., with Jon Chernoff, M.D., Ph.D.)