BIOGRAPHICAL SKETCH

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NAME: **Jianying Zhang**

eRA COMMONS USER NAME (credential, e.g., agency login): **jianyingzhang**

POSITION TITLE: **Professor (with tenure)**

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

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
Zhengzhou University Medical School, Zhengzhou, Henan, China.	M.D.	1979-1984	Medicine
Xi'an Jiaotong University Medical School, Xi'an, Shanxi, China.	M.P.H.	1984-1987	Epidemiology
Xia'men University, Xia'men, Fujian, China.	Ph.D.	1992-1995	Tumor Molecular Biology and Tumor Immunology
The Scripps Research Institute, La Jolla, California.	Postdoctoral Fellow	12/1995-12/2001	Cancer Autoimmunity

NOTE: The Biographical Sketch may not exceed five pages. Follow instructions below.

A. Personal Statement

I am currently a tenured full professor in the Department of Biological Sciences, and a principal investigator of NIH-Sponsored Border Biomedical Research Center (BBRC) at The University of Texas at EL Paso (UTEP). My research career goal is to become a world-leading scientist in the field of cancer biomarker and cancer immunodiagnosis. I have focused my research career on the identification, characterization, and evaluation of tumor-associated antigens as biomarkers in cancer detection, and I have expertise in all the molecular, histo-pathological, immunological, and proteomic approaches proposed in this application for the cancer biomarker research.

I joined Eng Tan's lab at the Scripps Research Institute (La Jolla, CA) at the end of 1995 for postdoctoral training on cancer autoimmunity research, and I left to take a faculty position in the Department of Biological Sciences at UTEP (University of Texas at El Paso) in December 2001. During this time, I have developed and completed several research projects. With serum antibodies from patients with hepatocellular carcinoma (HCC), I was able to immunoscreen a cDNA expression library and isolate a cDNA encoding a 62 kDa protein (p62), which was further identified as a tumor-associated antigen *[J. Exp. Med. 1999]*. p62 is an IGF-2 mRNA binding protein and belongs to a new class of TAAs. This was an exciting finding because IGF-2 is a growth factor and overexpression had been shown before to be involved in promoting malignancy. p62 is thought to play a role in protecting IGF-2 mRNA from degradation, therefore more of the growth factor was being produced in cancer cells. Autoantibodies to p62 are present in 15-20% of patients with HCC and in a slightly lower but also significant frequency in many other human tumors. This finding has opened a new field of studies for understanding cancer biology and for cancer diagnosis. In a subsequent study, I identified another cDNA encoding an important TAA p90 *[Oncogenes, 2002].* In the past 15 years, I have published over 80 papers on TAA-related research in peer-reviewed biomedical journals. In this field, I was well recognized by peers as one of the leaders. I was invited by several peer-reviewed Immunology journals to write reviews or comments in this TAA-related field *(Autoimmunity Reviews 2002, 2007, 2011, 2014; Immunological Reviews*

2008; Expert Rev. Mol. Diagn. 2010, 2015). I was also invited by *Journal of Immunology Research* as Lead Guest Editor to edit two special issues (2014, 2016) of the journal on "Cancer Immunodiagnosis and Cancer Immunotherapy".

The overall goal of this clinical research project is to develop early detection signatures for prostate and liver cancer by integrating multi-omics and contemporary bioinformatic techniques as platforms to identify targeted diagnostic approaches. The proposed studies will lead to a productive line of research that will foster my career development. I expect that we will start to produce peer-reviewed publications in year 2 of the project period. At the conclusion of the project, I expect at least 3-5 high quality publications which will be published. I will serve as the Core Lead of this clinical research project in this application, and will work with all co-investigators or collaborators in this proposed project, and commit the time necessary to fulfill the project goals as described, as well as supervise research associate fellows, and graduate research assistants in this proposed project.

Cited References:

1. Tan EM, **Zhang J.** (2008). Autoantibodies to tumor-associated antigens: reporters from the immune system. *Immunological Reviews* 222:328-340.
2. **Zhang JY,** Tan EM. (2010). Autoantibodies to tumor-associated antigens as diagnostic biomarkers in hepatocellular carcinoma and other solid tumors. *Expert Rev. Mol. Diagn.* 10(3):321-328.
3. Li P, Shi JX, Dai LP, Chai YR, Zhang HF, Kankonde M, Kankonde P, Yu BF, **Zhang JY.** Serum anti-MDM2 and anti-c-Myc autoantibodies as biomarkers in the early detection of lung cancer. Oncoimmunology. 2016 Apr 22;5(5):e1138200.
4. Dai L, Li J, Tsay JJ, Yie TA, Munger JS, Pass H, Rom WN, Tan EM, **Zhang JY.** Identification of autoantibodies to ECH1 and HNRNPA2B1 as potential biomarkers in the early detection of lung cancer. Oncoimmunology. 2017 Mar 31;6(5):e1310359.

B. Positions and Honors

POSITIONS and Employment

August, 1987 – November, 1995, Lecturer & Assistant Professor, Zhengzhou University Medical School (former Henan Medical University), Zhengzhou, Henan, China.
December, 1995 – December, 2001, Postdoctoral Research Fellow, W.K. Autoimmune Disease Center, Department of Molecular & Experimental Medicine, The Scripps Research Institute, La Jolla, California.
December, 2001 – August, 2008, Assistant Professor and Lab Head, Cancer Autoimmunity and Cancer Epidemiology Research Lab, Department of Biological Sciences, The University of Texas at El Paso (UTEP), El Paso, Texas.
September, 2008 --- July, 2013, Associate Professor (with tenure) and Lab Head, Cancer Autoimmunity and Cancer Epidemiology Research Lab, Department of Biological Sciences, The University of Texas at El Paso (UTEP), El Paso, Texas.
August, 2013 --- Present, Professor (with tenure) and Lab Head, Cancer Autoimmunity and Cancer Epidemiology Research Lab, Department of Biological Sciences, The University of Texas at El Paso (UTEP), El Paso, Texas.

Other Experience and Professional Memberships

1997 – Present, Member of International Epidemiology Association (IEA).
1999 – Present, Active Member of American Association for Cancer Research (AACR).
2002 – Present, Member of Sigma Xi, The Scientific Research Society.
2005 - Present, Member of International Society for Preventive Oncology (ISPO).
2011-Present, Committee Member, Autoantibody Network (AAN), Canada.
2013-Present, Member of Henry Kunkel Society (HKS).
Peer Reviewer for Grants:

- National Natural Science Foundation of China (NSFC) (2005 --);
- NIH Grants Reviewer (2009--);
- Florida Department of Health (2010--).
- Cancer Research UK (2015--);
- National Science Foundation of Italy (2015--);

Editorial Board Member:

- Liver Cancer Review Letters. (2009 - Present);
- International Journal of Cancer Sciences. (2008 - Present);

- The Open Autoimmunity Journal. (2008 - Present);
- Life Science Journal. (2005 - Present);
- Journal of Medical Laboratory Technology. (2004 - Present).
- Clinical and Developmental Immunology (Special Issue: Systemic Autoimmune Diseases, Published in 2013, Guest Editor)
- Journal of Immunology Research (Special Issue: Cancer Immunodiagnosis and Cancer Immunotherapy, Published in 2014, Lead Guest Editor)
- Journal of Immunology Research (Special Issue: Systemic Autoimmune Diseases, Published in 2015, Guest Editor)
- Journal of Immunology Research (Special Issue: Cancer Immunodiagnosis and Cancer Immunotherapy, Published in 2016, Lead Guest Editor)

AD HOC Peer Reviewer for Scientific Journals: *British Journal of Cancer; BMC Cancer; Clinical Cancer Research; Cancer Letters; Clinical Immunology; Cancer Detection and Prevention; Cancer Research; Cancer Investigation; Clinical and Investigative Medicine; Ethnicity and Diseases; Expert Review of proteomics; Gastroenterology; Journal of Medical Laboratory Technology; Journal of Proteome Research; Journal of Thoracic Oncology; Life Sciences; Life Science Journal; Nature Cancer Reviews; Oncotargets; Marine Biotechnology; Molecular and Cellular Proteomics; Tumori, etc.* ***(Note: at least for 50 Journals)***

C. Contribution to Science

My most significant contributions to science:

I. Discovery of two important oncogenes encoding tumor-associated antigens (p62/IMP2 and p90/CIP2A). With serum antibodies from patients with hepatocellular carcinoma (HCC), I was able to immunoscreen a cDNA expression library and isolate a cDNA encoding a 62 kDa and 90 kDa proteins (p62 and p90), and which were further identified as two important tumor-associated antigens *[J. Exp. Med. 189:1101-1110,1999; Oncogenes, 21,5006-5015,2002]*. p62 is an IGF-2 mRNA binding protein and belongs to a new class of TAAs. This was an exciting finding because IGF-2 is a growth factor and overexpression had been shown before to be involved in promoting malignancy. p62/IMP2 is thought to play a role in protecting IGF-2 mRNA from degradation, therefore more of the growth factor was being produced in cancer cells. Autoantibodies to p62 are present in 15-20% of patients with HCC and in a slightly lower but also significant frequency in many other human tumors. p90 is a tumor-associated antigen that has been found to interact with PP2A and to inhibit its phosphatase activity. This property allows p90/CIP2A to stabilize the c-myc oncoprotein and thus promote tumor development *(Cell 130:51-62, 2007).* These findings have opened a new field of studies for understanding cancer biology and for cancer diagnosis.

Cited References:

1. **Zhang JY,** Chan EKL, Peng XX, Tan EM. (1999). A noval RNA-binding protein is an autoantigen in human hepatocellular carcinoma. *Journal of Experimental Medicine* 189:1101-1110.
2. Soo Hoo L, **Zhang JY**, Chan EKL. (2002). Cloning and characterization of a novel 90kDa 'companion' auto-antigen of p62 overexpressed in cancer. *Oncogene*, 21:5006-5015.
3. **Zhang JY,** Wang X, Peng XX, Chan EKL. (2002). Autoimmune responses in Chinese hepatocellular carcinoma. *Journal of Clinical Immunology* 22:98-105.
4. **Zhang JY**, Chan EKL. (2002). Autoantibodies to IGF-II mRNA binding protein p62 and overexpression of p62 in human hepatocellular carcinoma. *Autoimmunity Reviews*, 1:146-153.

II. Autoantibodies to tumor-associated antigens (TAAs) as biomarkers in immunodiagnosis of liver cancer and other solid tumors. How to establish a methodology to identify the high-risk individuals for liver cancer remains to be investigated. The multi-factorial and multi-step nature in the molecular pathogenesis of human cancers must be taken into account in both the design and interpretation of studies to identify markers which will be useful for early detection of cancer. Our studies demonstrated that a mini-array of multiple tumor-associated antigens (TAAs) might enhance autoantibody detection for diagnosis of liver cancer, especially for the alpha fetoprotein (AFP)-negative cases. It also suggests that different types of cancer might require different panels of TAAs to achieve the sensitivity and specificity required to make immunodiagnosis a feasible adjunct to tumor diagnosis *(J Hepatol. 46:107-114, 2007; Cancer Lett. 289:32-39, 2010; Clinical Immunology, 152:127-139, 2014； Oncotarget 6：11575-11584，2015；OncoImmunology 2016).* Regarding the importance of the study, the *Journal of Hepatology* published an Editorial Comment saying that *"Zhang et al. addressed an important issue*

that highlights a promising way for the development of biomarkers of diseases, and especially cancers. This study deals with the concept of "cancer immunomics" which allows a global analysis of the auto-antibodies against antigens in a neoplasm…… ". (Paradis et al. J. Hepatol 46:9-11, 2007.)

Cited References:

1. **Zhang JY**, Casiano CA, Peng XX, Koziol JA, Chan EKL, and Tan EM. (2003).Enhancement of antibody detection in cancer using panel of recombinant tumor-associated antigens. *Cancer Epidemiology, Biomarkers & Prevention,* 12:136-143.
2. Koziol JA**, Zhang JY**, Casiano CA, Peng XX, Chan EKL, and Tan EM. (2003). Recursive partitioning for tumor classification using a panel of recombinant tumor-associated antigens. *Clinical Cancer Research*. 9(14):5120-5126.
3. **Zhang JY*,** Megliorino R, Peng XX, Tan EM, Chen Y, Chan EK. (2007). Antibody detection using tumor-associated antigen mini-array in diagnosing human hepatocellular carcinoma. *Journal of Hepatology, 46:107-114. (**See Editorial Comments**: Paradis V, Bedossa P. In the new area of noninvasive markers of hepatocellular carcinoma. Journal of Hepatology 2007;46:107-114).*
4. Chen Y, Zhou Y, Qiu S, Wang K, Liu S, Peng XX, Li J, Tan EM, **Zhang JY*.** (2010). Autoantibodies to tumor-associated antigens combined with abnormal alpha-fetoprotein enhance immunodiagnosis of hepatocellular carcinoma. *Cancer Lett.* 289:32-39.

III. Functional study of tumor-associated proteins p90/CIP2A and p62/IMP2 in lung and breast cancer. As described above, p62/IMP2 is an IGF-2 mRNA binding protein and belongs to a new class of TAAs. p62/IMP2 is thought to play a role in protecting IGF-2 mRNA from degradation, therefore more of the growth factor was being produced in cancer cells. Our recent study has found that p62/IMP2 can stimulates the cell migration and reduces cell adhesion in breast cancer *(Oncotarget 6:32656-68, 2015).* One important tumor suppressor gene, protein phosphatase 2A (PP2A), has been found to be inactivated in lung cancer, by methylation-induced gene silencing, mutation, or by endogeneous inhibitors. p90/CIP2A has been found to interact with PP2A and to inhibit its phosphatase activity. This property allows p90/CIP2A to stabilize the c-myc oncoprotein and thus promote tumor development *(Cell 130:51-62, 2007).* However, the function of p90/CIP2A in cancer still needs to be investigated. Our preliminary data suggests that p90/CIP2A is overexpressed in lung cancer, and that its expression level does not correlate with age, gender or histological stage. The down-regulation of p90/CIP2A by shRNA in lung cancer cell lines causes a decrease in cell proliferation, clonogenic expansion, and anchorage-dependent cell growth. Taken together, our in vitro studies show that p90/CIP2A is essential for tumor growth. Several publications relating to this project have been recently published *（Oncotarget 2015; Molecular Biosystems 2015; BMC Cancer 2015, etc).*

Cited References:

1. Li Y, Francia G, **Zhang JY***. (2015). P62/IMP2 plays a role in breast cancer progression. *Oncotorget,* 6(32):32656-68.
2. Peng B, Lei N, Chai Y, Chan EK, and **Zhang JY***. (2015). CIP2A regulates cancer metabolism and CREB phosphorylation in non-small cell lung cancer. *Molecular Biosystems* 11(1):105-14.
3. Peng B, Chai Y, Li Y, Liu X, **Zhang J***. (2015). CIP2A overexpression induces autoimmune response and enhances JUN signaling pathway in human lung cancer. *BMC Cancer*， 15（1）：895-02.
4. Dai L, Peng XX, Tan EM, **Zhang JY*.** (2016). Tumor-Associated Antigen CAPERα and Microvessel Density in Hepatocellular Carcinoma. Oncotarget. 2016 Mar 29;7(13):16985-95.

IV. Using -omics approaches (proteomics and immunomics) to identify novel tumor-associated antigens （TAAs）as biomarkers in immunodiagnosis of liver cancer and other solid tumors. In the case of liver cancer, especially hepatocellular carcinoma (HCC), antecedent liver cirrhosis and chronic hepatitis are common precursor conditions and during transition to malignancy some patients develop novel autoantibodies that were not present during the preceding chronic liver disease phase. The hypothesis is that transition to malignancy can be associated with autoantibody responses to certain cellular proteins that might have some role in tumorigenesis. It is proposed that the information that the cancer patient's immune system is conveying in the form of autoantibodies to TAAs should be utilized to a greater extent in identifying early signs of tumorigenesis.

Cited References:

1. Looi KS, Nakayasu ES, Diaz RA, Tan EM, Almeida IC, **Zhang JY*.** (2008). Using proteomic approach to identify tumor-associated antigens as markers in hepatocellular carcinoma. *Journal of Proteome Research 7:4004-4012.*
2. Peng B, Huang X, Nakayasu ES, Petersen JR, Qiu S, Almeida IC, **Zhang JY***. (2013). Identification and characterization of alpha-enolase as an autoantigen in human liver fibrosis. *Journal of Proteome Research,* 12:1789-1796.

3. Dai L, Ren P, Liu M, Imai H, Tan EM, **Zhang JY***. (2014). Using immunomic approach to enhance tumor-associated autoantibody detection in diagnosis of hepatocellular carcinoma. *Clinical Immunology,* 152:127-139.
4. Dai L, Li J, Xing M, Sanchez TW, Casiano CA, **Zhang JY*.** Using Serological Proteome Analysis to Identify Serum Anti-Nucleophosmin 1 Autoantibody as a Potential Biomarker in European-American and African-American Patients With Prostate Cancer. Prostate. 2016 Nov;76(15):1375-86.

V. Epidemiologic studies relating genetic, environmental, dietary and lifestyle factors to the etiology of liver cancer in Henan populations. We have done a case-control epidemiological study to investigate the risk factors in liver cancer in Henan Province, China. *(International Journal of Epidemiology 1998; American Journal of Tropical Medicine and Hygiene 1998).* With my expertise in epidemiology, my lab has been collaborating with investigators in US, Mexico, and China to do population-based epidemiological study combined with molecular biology and immunology techniques to explore the dynamic changes of etiological factors of liver cancer and other cancers. In the past 20 years, we have published over 20 papers in the peer-reviewed biomedical journals.

Cited References:

1. **Zhang JY*,** Dai M, Wang X. (1998). A case-control study of hepatitis virus infection as risk factors for hepatocarcinoma. *International Journal of Epidemiology* 27:574-578.
2. **Zhang JY***, Wang X, Han SG, Zhuang H. (1998). A case-control study of risk factors for hepatocellular carcinoma in Henan, China. *American Journal of Tropical Medicine and Hygiene* 59:947-951.
3. Wang P, Xia HH, **Zhang JY,** Dai LP, Xu XQ, Wang KJ. (2007). Association of interleukin-1 gene polymorphisms with gastric cancer: A meta-analysis. *International Journal of Cancer*, 120:552-562.
4. Dai L, Wang K, **Zhang J,** Lv Q, Wu X, Wang Y. (2009). XRCC1 gene polymorphisms and esophageal squamous cell carcinoma risk in Chinese population: A meta-analysis of case-control studies. *International Journal of Cancer*, 125(5):1102-9.

(***Note: ****Corresponding Author; Based on the Google Scholar, some of my previous publications have been cited over 4890 times; h-index was 38, and i10-index was 92, until October 2018.*
see *https://scholar.google.com/citations?hl=en&user=38NtdLEAAAAJ)*

Note: Please see the URL link for My Bibliography.
http://www.ncbi.nlm.nih.gov/myncbi/collections/mybibliography/ or
http://www.ncbi.nlm.nih.gov/sites/myncbi/1NAWI5FDEGiAM/bibliography/51002001/public/?sort=date&direction=ascending

D. Additional Information: Research Support and/or Scholastic Performance

ONGOING RESEARCH SUPPORTS:

1. **NIH RCMI Program (5G12RR008124):** Border Biomedical Research Center
   Role: Participating investigator (PI: Robert Kirken)
   Period: 04/01/14-03/31/19
   This program strives to enhance the capability for biomedical research relevant to the Border region. There is no any overlap with the proposed project.

Completed Research Support

1. **NIH/NCI Grant (SC1CA166016; RO1 Equivalent Grant):** Autoantibodies to tumor-associated antigens as diagnostic biomarkers in liver cancer. *(Note: This is a RO1 equivalent grant)*
   Role: Principal Investigator
   Period: August 2011 – July 2016
   The goal of this project is to to identify TAAs and ant-TAAs as serological markers in detection and diagnosis of liver cancer. Although there was some conceptual overlap given that both projects deal with the idea of TAAs and ant-TAAs systems as markers in diagnosis of liver cancer, the major goals of the two projects are different. This sub-project application focuses on the continued and expanded discovery of new anti-TAAs autoantibodies as biomarkers in liver cancer, especially in Hispanic Population.
2. **NIH Grant (P20MD006988)—Sub-Project:** Immunoseroproteomics Profiling in Prostate Cancer: Focus on Health Disparities
   Role: Co-PI (PI: Dr. Carlos A. Casiano, Loma Linda University, CA)
   Period: 07/01/12-01/30/17
   The goal of this project is to profile anti-TAA antibodies in sera from prostate cancer patients using immunoproteomics and customized TAA mini-arrays. There is no any overlap with the proposed project.