Cover Letter

Dear Hiring Manager,

I'm Jianxun (Greg) Wang, encompassing a comprehensive expertise spanning genetics, cell biology, immunology, pharmacology, and toxicology. With a Research Fellow at MGH, Harvard Medical School, and Beth Israel Deaconess Medical Center, my skills encompass a wide array of biomedical techniques in vitro and in vivo, I've made significant contributions to numerous peer-reviewed articles in esteemed journals. I think I fit the translational medicine job regarding biomarkers.

Biomarkers, with their spatial-temporal patterns across the whole body, can be organ and cell-type specified. Understanding their production and clearance requires knowledge of whole-body physiology and pathology, encompassing vital organs such as the heart, kidney, liver, and immune and gut systems etc. My educational background in pharmacology and toxicology equips me with a solid understanding of pharmacodynamics, pharmacokinetics, and drug distribution throughout the body, clearance via liver and kidney, akin to biomarker behaviors.

I have strong experience in establishing and handling various disease models in vivo. The disease models I have initiated and completed include transaortic constriction (TAC)-induced cardiac hypertrophy and heart failure, type1 and type2 diabetes, lupus autoimmunity (MRL/lpr), and RYGB-induced body weight loss. I also created multiple transgenic/gene knockout mice lines, to answer specific scientific issues regarding these disease models. I acquired direct hands-on experience on these organs and cells, such as heart, kidney, intestine, immune system including spleen, T cells, etc. and this experience provides me insights into organ-specific physiological and pathological characteristics, also provide me capability to judge and design experiment to test the biomarkers .

Technically, I have a set of simple and reliable protein methods that could effectively identify appropriate protein targets for disease treatment from in vivo disease models. The targets can be validated in vitro and in vivo, based on physiology, pathology, and disease models.

I succeeded in finding a compound called shp2 inhibitor, which has been patented, for treating autoimmune lupus disease, published in the JCI paper('Inhibition of SHP2 ameliorates the pathogenesis of systemic lupus erythematosus'. J Clin Invest, 2016 Jun 1;126(6):2077-92). The paper requires a set of complex procedures such as animal colony maintenance, drug dose screening, blood collection, tissue processing and data analysis to get published. I am proficient in this set of complex procedures to get the targets validated in vitro and in vivo.

This set of protein techniques can quickly lock on key targets for production of the biomarkers. I can design a specific panel to figure out the signaling pathways using the limited in vivo samples, and identify the important targets from the limited in vivo samples, according to the signaling transduction pathway.

In addition to my biomedical background, I have recently completed specialized training in data science and bioinformatics at the Network Technology Academy Institute in the USA. Proficient in R, Python, Linux, and SQL, I have applied these skills in genetic heterogeneity assays in cancer samples and RNA-seq analysis using Next-Generation Sequencing (NGS). Detailed project information, including scripts and results, is available on my GitHub profile: https://github.com/GregWang1

My expertise extends to data cleaning, transformation, and a spectrum of statistical analyses, including machine learning algorithm to conduct multivariate assays on larger datasets for screening biomarkers /targets across various disease models. For example, Random Forest pick up the important features/biomarkers, and Bayesian inference continues update of features and biomarkers, even with limited sample sizes, monitoring the correct direction of the experiment design and progress.

I am enthusiastic about the opportunity to contribute my expertise to your team and discuss how I can add significant value to your organization. Thank you for considering my application. I look forward to further discussing how I can positively impact your team.

Best regards,

Jianxun Wang(Greg)

Please see papers showcasing hands-on experiences on vital organs:

1. Autoimmune lupus: T cells/cytokines

(**Wang J**, et al. Inhibition of SHP2 ameliorates the pathogenesis of systemic lupus erythematosus. J Clin Invest. 2016 May 16.)

2. Diabetes on heart failure

(**Wang J**, et al. Cardiac metallothionein induction plays the major role in the prevention of diabetic cardiomyopathy by zinc supplementation. Circulation. 2006 Jan 31;113(4):544-54.)

3. Creation of Surgical TAC model and creation of OGG1 transgenic mouse model on heart

 (**Wang J**, et al. Cardiac overexpression of 8-oxoguanine DNA glycosylase 1 protects mitochondrial DNA and reduces cardiac fibrosis following transaortic constriction. Am J Physiol Heart Circ Physiol. 2011 Nov;301(5):H2073-80.)

4. Metabolites on cardiac fibrosis

(**Wang J**, et al. Reduced cardiac fructose 2,6 bisphosphate increases hypertrophy and decreases glycolysis following aortic constriction. PLOS ONE. 2013;8(1))

5. Drug on signaling pathways in heart.

(**Wang J**, et al. In vivo efficacy of the AKT inhibitor ARQ 092 in Noonan Syndrome with multiple lentigines-associated hypertrophic cardiomyopathy. PLoS One. 2017; 12(6))

6. Intestine crypts

(He S, …**Wang J**, et al. Stiffness Restricts the Stemness of the Intestinal Stem Cells and Skews Their Differentiation Toward Goblet Cells. Gastroenterology. 2023 Jun;164(7):1137-1151.)

CURRICULUM VITAE

Name: Jianxun Wang

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Education:

08/2023	Data Science & Bioinformatics	Network Technology Academy Institute, USA
06/2011 Ph.D.	Pharmacology & Toxicology	University of Louisville, USA
06/2007 M.S.	Pharmacology & Toxicology	University of Louisville, USA
06/1994 M.S.	Genetics	Sun Yat-sen University, China
06/1991 B.S.	Cell Biology	Lanzhou University, China

Research Fellow:

11/2018-03/2022   Research Fellow, MGH, Department of Surgery, Center for Engineering in Medicine at Harvard Medical School

07/2011-09/2018   Research Fellow, Cardiovascular, Beth Israel Deaconess Medical Center (BIDMC) at Harvard Medical School

Skills and Techniques

1. Data Science:

Python, Linux, R, SQL and Bioinformatics

2. Biomedical:

Designing primers; PCR; RT-PCR and Cloning;

Extraction of Protein; RNA; nuclei DNA and mitochondrial DNA;

Gene array; siRNA; RPA; EMSA; Immunoprecipitation;

Western blot; Northern blot and Southern blot;

Cryostat sections; In situ hybridization and Immunohistochemistry/immunofluorescence;
Metabolites assay in tissues: lactate; pyruvate; glycogen; ATP; phosphocreatine; Fru-2,6-P2; pyridine nucleotides (NADH; NADPH; NAD; NADP);6-keto-PGF1α; PGE2; nitrite and nitrate

Multicolor Flow cytometry; Isolation and culture of immune cells from mouse and human; ELISA

Echocardiography

TAC surgery (Trans-aortic-constriction for induction of cardiac hypertrophy and heart failure);

RYGB surgery (Roux-en-Y gastric bypass for weight loss)

In vivo mouse handling:

Injection of drugs with iv, ip or sc;

Collecting peripheral blood for immune cell assay with flow cytometry and serum cytokine assay by ELISA;

Collecting urine for assaying kidney dysfunction;

Isolation & Assay of immune cells infiltrating in kidney and heart;

Monitoring heart functions with echocardiography for drug toxicity;

Surgery of trans-aortic-constriction for induction of heart failure to test drug protection;

Roux-en-Y gastric bypass for weight loss;

Pathological study of kidney and heart with H&E, immunohistochemistry and immunofluorescence.

Report of Technological and Other Scientific Innovations

Patents:

SHP2 INHIBITORS AND METHODS OF TREATING AUTOIMMUNE AND/OR GLOMERULONEPHRITIS-ASSOCIATED DISEASES USING SHP2 INHIBITORS (2014)

Pub. No.: WO/2015/003094
International , Application No.: PCT/US2014/045318
Publication Date: 08.01.2015
International Filing Date: 02.07.2014

Report of Scholarship

Original Peer Reviewed Articles:

1. **Wang J**, Wang Q, Ye F. Genetic instability in cancer tissues analyzed by random amplified polymorphic DNA PCR. _Chin Med J (Engl)._ 2002 Mar;115(3):430-2

2. Wang Y, Guo Y, Zhang SX, Wu WJ, **Wang J**, Bao W, Bolli R. Ischemic preconditioning upregulates inducible nitric oxide synthase in cardiac myocyte. _J Mol Cell Cardiol_. 2002 Jan;34(1):5-15.

3. Wang Y, Kodani E, **Wang J**, Zhang SX, Takano H, Tang XL, Bolli R. Cardioprotection during the final stage of the late phase of ischemic preconditioning is mediated by neuronal NO synthase in concert with cyclooxygenase-2. _Circ Res._ 2004 Jul 9;95(1):84-91.

4. Cai L, **Wang J**, Li Y, Sun X, Wang L, Zhou Z, Kang YJ. Inhibition of superoxide generation and associated nitrosative damage is involved in metallothionein prevention of diabetic cardiomyopathy. _Diabetes._ 2005 Jun;54(6):1829-37.

5. Song Y, **Wang J***, Li Y, Du Y, Arteel GE, Saari JT, Kang YJ, Cai L. Cardiac metallothionein synthesis in streptozotocin-induced diabetic mice, and its protection against diabetes-induced cardiac injury. _Am J Pathol._ 2005 Jul;167(1):17-26. **(*, Co-first author)**

6. **Wang J**, Song Y, Elsherif L, Song Z, Zhou G, Prabhu SD, Saari JT, Cai L. Cardiac metallothionein induction plays the major role in the prevention of diabetic cardiomyopathy by zinc supplementation. _Circulation_. 2006 Jan 31;113(4):544-54. Epub 2006 Jan 23.

7. Wang Q, Donthi RV, **Wang J**, Lange AJ, Watson LJ, Jones SP, Epstein PN. Cardiac phosphatasedeficient 6-phosphofructo-2-kinase/fructose-2,6-bisphosphatase increases glycolysis, hypertrophy, and myocyte resistance to hypoxia. _Am J Physiol Heart Circ Physiol_. 2008 Jun;294(6):H2889-97

8. **Wang J**, Wang Q, Watson LJ, Jones SP, Epstein PN. Cardiac overexpression of 8-oxoguanine DNA glycosylase 1 protects mitochondrial DNA and reduces cardiac fibrosis following transaortic constriction. _Am J Physiol Heart Circ Physiol_. 2011 Nov;301(5):H2073-80.

9. **Wang J**, Xu J, Wang Q, Brainard RE, Watson LJ, Jones SP, Epstein PN. Reduced cardiac fructose 2,6 bisphosphate increases hypertrophy and decreases glycolysis following aortic constriction. _PLOS ONE_. 2013;8(1)

10. Lauriol J, Keith K, Jaffré F, Couvillon A, Saci A, Goonasekera SA, McCarthy JR, Kessinger CW, **Wang J**, Ke Q, Kang PM, Molkentin JD, Carpenter C, Kontaridis MI. RhoA signaling in cardiomyocytes protects against stress-induced heart failure but facilitates cardiac fibrosis. _Sci Signal_. 2014 Oct 21;7(348)

11. **Wang J**, Mizui M, Zeng LF, Bronson R, Finnell M, Terhorst C, Kyttaris VC, Tsokos GC, Zhang ZY, Kontaridis MI. Inhibition of SHP2 ameliorates the pathogenesis of systemic lupus erythematosus. _J Clin Invest._ 2016 May 16.

   Nat Rev Rheumatol. 2016 Jul;12(7):376. 10.1038/nrrheum.2016.94. Epub 2016 Jun 3
   Systemic lupus erythematosus: SHP2 inhibition ameliorates disease in lupus-prone mice.
   Shipman L. PMID: 27256710 DOI: 10.1038/nrrheum.2016.94

   Nat Rev Drug Discov. 2016 Jun 30;15(7):456. doi: 10.1038/nrd.2016.128.
   Autoimmune disease: Reversing systemic lupus erythematosus.
   Crunkhorn S. PMID: 27357019 DOI:10.1038/nrd.2016.128.

12. **Wang J,** Chandrasekhar V, Abbadessa G, Yu Y, Schwartz B, Kontaridis MI. In vivo efficacy of the AKT inhibitor ARQ 092 in Noonan Syndrome with multiple lentigines-associated hypertrophic cardiomyopathy _PLoS One._ 2017; 12(6)

13, Gibb AA, Epstein PN, Uchida S, Zheng Y, McNally LA, Obal D, Katragadda K, Trainor PJ, Conklin DJ, Brittian KR, Tseng MT, **Wang J**, Jones SP, Bhatnagar A, Hill BG. Exercise-Induced Changes in Glucose Metabolism Promote Physiologic Cardiac Growth. _Circulation_. 2017 Aug 31.

14, Pannu PR, Chukwudi C, **Wang J**, Yang PJ, Esfahani FN, Saeidi N. Physical properties of food or bile redirection do not contribute to the intestinal adaptations after Roux-en-Y Gastric Bypass in rats. Obes Sci Pract. 2022 Dec 8;9(3):274-284

15, He S, Lei P, Kang W, Cheung P, Xu T, Mana M, Park CY, Wang H, Imada S, Russell JO, **Wang J**, Wang R, Zhou Z, Chetal K, Stas E, Mohad V, Bruun-Rasmussen P, Sadreyev RI, Hodin RA, Zhang Y, Breault DT, Camargo FD, Yilmaz ÖH, Fredberg JJ, Saeidi N. Stiffness Restricts the Stemness of the Intestinal Stem Cells and Skews Their Differentiation Toward Goblet Cells. Gastroenterology. 2023 Jun;164(7):1137-1151.

Peer Reviewed Reviews:

14. **Wang J**, Song Y, Wang Q, Kralik PM, Epstein PN. Causes and characteristics of diabetic cardiomyopathy. Rev Diabet Stud. 2006 Fall;3(3):108-17.

15. Song Y, **Wang J**, Li XK, Cai L. Zinc and the diabetic heart. Biometals. 2005 Aug;18(4):325-32.