

**William Keun Chan Park, Ph.D.**

Assistant Professor (Research)/ Research Associate II  
Department of Diagnostic Imaging  
Alpert Medical School at Brown University/ Rhode Island Hospital  
55 Claverick Street, Providence RI 02903  
Ph) 401-444-5010  
[William\\_keun\\_chan\\_park@brown.edu](mailto:William_keun_chan_park@brown.edu)  
[kpark@lifespan.org](mailto:kpark@lifespan.org)

**RESEARCH SUMMARY AND ACCOMPLISHMENTS IN 2016-Present**

The 2016-present period was a pivotal year for me because it brought to fruition an extremely exciting outcome as a result of my many years of investigation and collaboration efforts: the discovery and development of a novel **Thermal Accelerant (TA)** that has the potential to play an essential role in solid tumor treatment by **Image-Guided Thermal Ablation (IGTA)**. My newly discovered TA has several properties that are uniquely beneficial to IGTA: 1. The capacity to augment microwave energy; 2. Produce a highly visible contrast in Ultrasound (US), MRI and Computer-aided Tomography (CT or CAT); and 3. Its optimum viscosity allows TA to remain at the target area in the body (e.g., the liver); Lastly, it is non-toxic. I have led the effort in my laboratory and successfully demonstrated the unique properties of TA so as to augment the applied MW energy for ablation from a distance unattainable under normal MWA conditions. In the ensuing animal studies the team, lead by Dr. Dupuy and I, demonstrated that the outer-boundary of a tumor can be ablated completely and also addressed the issue of the heat sink effect, both causes of local tumor recurrence.

I have produced multiple presentations on the TA discovered and developed in my laboratory: four publications in peer-reviewed journals; three oral presentations: one at RSNA 2016; two talks at the SPIE BIOS 2017 conference that included a keynote address; one poster at the 2017 National Center Image-guided Therapy Workshop sponsored by Harvard Medical School; two posters at the 2016 World Conference of Interventional Oncology (one was awarded first place); Furthermore, two patents have been filed, one for US Utility and the other for PCT (Dec 23, 2016) based on the previous provisional patents: Park et al. 62/387,250; 62/381,251.

Based on this intellectual property, a commercial entity (a.k.a. Theromics) has formed. I am currently participating in the IRB preparation for the Investigational Device Exemption (IDE) status. Once this is completed, the 510(k) approval from the FDA will be sought for commercialization of TA.

## EDUCATION

- The Scripps Research Institute, Post-doctoral fellow, **1995-1996**: Design and synthesis of neamine-containing inhibitors towards the Rev Responsive Element of HIV RNA.
- University of Ottawa, Ph.D., Synthetic organic chemistry: Glyco-dendrimer, **1992-1994**.
- Queen's University, B.S., Chemistry (hon.) **1984-1989**; M.S., Physical organic chemistry, **1990-1992**.

## RESEARCH EXPERIENCE

### Rhode Island Hospital / Alpert Medical School at Brown University (2011-present)

- Discovery and development of a novel thermal accelerant (TA) that is useful for image-guided thermal ablation of solid tumors.
- Design of a novel iron-based MRI contrast agent that is capable of detecting and visualizing prostate cancer.
- Novel hyperthermia strategy of eradication of tumor cells that are labeled by the iron-containing contrast agent.
- Modulation of de novo ceramide biosynthesis by small molecules.

### University of Rhode Island, Kingston, RI (2010)

- Proposed and initiated research program in Pharmacy, to discover hexokinase II inhibitors that are selectively transported to tumor cell interior through GLUT1.

### P&H Therapeutics Inc., Providence, RI (2007-2009)

- Successfully designed and synthesized PNH101, a potent renin inhibitor that is considered to be one of the safest anti-hypertensive drug targets.
- The synthesis was accomplished in Professor DeBoef's laboratory. In addition, interacted closely with graduate students in the lab (e.g., mentored and provided guidance to students).
- Utilization of INBRE facility in Department of Pharmacy for characterization of compounds.
- Accomplished the milestone to meet the required efficacy (> 15 mmHg blood pressure drop @ 30 mpk) of PNH101 in an animal model through an academic Contract Research Organization (CRO), In Vivo Pharmacology Center at Michigan State University.
- Designed and synthesized PNH 200 series analogs to strengthen and expand PNH's patent position.
- Collaborations with Pfizer: received human renin-related materials and know-how that are essential to establish in vitro assay.

Pfizer Inc., PGRD Michigan Laboratory, Ann Arbor, MI (2001-2007)

- Actively involved in various Candidate Alert Notice (CAN)-seeking activities for the Serine Palmitoyl CoA Transferase (SPT) project: Established an IP position and coordinated patent preparation for the project, involved in managing a CRO in India, generated ideas for back-up chemical matters. The project achieved a CAN status in 2006.
- Proposed ideas for five new projects based on multiple pharmacological target strategy: Identified chemical matters exhibit simultaneous activities towards hypertension and diabetes or obesity targets.
- Project leader for an early stage project, i.e., Serine Palmitoyl CoA Transferase (SPT) Project. Discovered small-molecule chemical matters through open access screening laboratory (OASL). Eliminated selectivity, reactive metabolites and safety concerns by key structural changes. Achieved pre-CAN milestone in June, 2005 and subsequently CAN status in 2006.
- A subgroup leader for a late discovery project, i.e., Statin Plus Project: Impacted the team by proposing a comprehensive design for central chemical scaffolds, e.g., imidazoles, pyrazoles and pyrroles by using docking scores. Designed and synthesized imidazole-core statin analogs. The synthetic methodology was adopted by a Kilo-lab chemistry group. Key compounds passed preclinical and First-In-Human (FIH) requirements and are currently at First-In-Patient (FIP) stage.
- Designed and synthesized 4-sulfamoyl pyrrole statin analogs targeting desired hepatoselectivity. The key compounds revealed the greatly improved selectivity for hepatocytes over myocytes in vitro.
- Therapeutically Aligned Combinatorial Chemistry (TACC) group leader supporting multiple oncology projects i.e., IGF1R, HDAC and CDK4.

Ontogen Inc., Carlsbad, California (1998-2001)

- Design and synthesis of diverse chemical libraries using parallel synthetic methodologies, i.e., tetrahydroquinolines via a multiple component reaction (MCR) approach and 3-aminopropanols via reduction of isoxazolines.
- Participated in development of supercritical fluid chromatography (SFC) separation technology of chemical libraries.

BIJ BioScience Institute, San Diego, California (1996-1997)

- Proposed high-throughput screening ideas in search of immunosuppressant agents using BiaCORE as a screening tool.
- Lead research and business activities of the Institute at its infancy.

**BUSINESS EXPERIENCE**

P&H Therapeutics Inc., Providence, RI (2007-2009)

- Founder and acting COO of the company: a S-corp., Delaware incorporation.
- Rewarded with \$500K Slater Technology Fund.
- Initiated a corporate relationship with Pfizer for an asset out-licensing deal.
- Presented P&H business plans to investors including Novartis, J&J and Pfizer.
- Established and managed academic and commercial CROs (e.g., Michigan State University, Valesco, MedPace).

## TEACHING EXPERIENCE

- Lecturer for Organic Chemistry at URI Providence **2009-2010**.
- Laboratory Instructor of organic chemistry at URI Summer **2009**.

## PATENTS

Thermal Accelerant Composition and Methods of Use. William K.C. Park, Damian E. Dupuy, (Filed, US Utility and PCT **No 62/171,609 Dec 2016**).

Ferritin-based Tumor targeting agent, and Imaging and treatment methods. William K.C. Park, David R. Mills, Edward G. Walsh, (Extended Provisional, **2012**), **No 61691346**.

A Substituted (S)-Benzoxazinone, William Keun Chan Park and Daniel Holsworth, (**2009**) non-provisional US patent (filed 06/13/**2009**).

Substituted Bezoxazinones. William Keun Chan Park and Daniel Holsworth, (**2008**), PCT/US 09/35178.

Inhibitors of Serine Palmitoyltransferase. Bolton, Gary, Louis Hutchings, Richard, Henry, Korht, Jeffrey, Thomas, Park, William, Keun, Chan, VanHuis, Chad, Alan, (**2008**), WO/2008/084300

Novel pyrazole-based HMG-CoA reductase inhibitors. Choi, Chulho; Bowles, Daniel Merritt; Hutchings, Richard H.; Park, William K. C.; Pfefferkorn, Jeffrey A. U.S. Pat. Appl. Publ. (**2006**), 76 pp. US 2006111422 A1.

Preparation of novel imidazoles as HMG-CoA reductase inhibitors for use in treating hyperlipidemia and other diseases. Bolton, Gary Louis; Bowles, Daniel Merritt; Boyles, David Christopher; Hutchings, Richard H.; Park, William K. C. (USA). U.S. Pat. Appl. Publ. (**2005**), 90 pp. US 2005239857 A1.

Preparation of 7-(1-pyrrolyl)-3,5-dihydroxyheptanoic acid derivatives as HMG-CoA reductase inhibitors. Kennedy, Robert Michael; Park, William Keun-Chan; Roth, Bruce David; Song, Yuntao; Trivedi, Bharat K., U.S. Pat. Appl. Publ. (**2005**), 83 pp. US 2005043364 A1.

Preparation of pyrrole derivatives as HMG-CoA reductase inhibitors. Kennedy, Robert Michael; Park, William Keun-Chan; Roth, Bruce David; Song, Yuntao; Trivedi, Bharat Kalidas. PCT Int. Appl. (**2005**), 149 pp. WO 2005014539 A2.

## PUBLICATIONS

William Keun Chan Park; Aaron Wilhelm Palmer Maxwell; Victoria Elizabeth Frank; Michael Patrick Primmer; Scott Andrew Collins; Grayson Luderman Baird; Damian Edward Dupuy, Evaluation of A Novel Thermal Accelerant (TA) for Augmentation of Microwave Energy during Image-guided Tumor Ablation. *Theranostics* **2017**; 7(4): 1026-1035.

William K C Park; Aaron W P Maxwell; Shaolei Lu; Kara Lombardo; Michael P Primmer; Tiffany Borjeson; Grayson L Baird; Damian E Dupuy, The *in vivo* performance of a novel thermal accelerant used for augmentation of microwave energy delivery within biologic tissues during image-guided thermal ablation: A porcine study, *Accepted in International Journal of Hyperthermia* **2017**.

William K. C. Park, Aaron W P Maxwell; Victoria E. Frank, Michael P. Primmer, Scott A. Collins, Damian E. Dupuy, A Novel Thermal Accelerant for Augmentation of Microwave Energy during Image-guided Tumor Ablation, *Proceedings of SPIE Photonics West Bios*, **2017**;10066:1006602-9.

William K. C. Park, David R. Mills, Sierin Lim, Barindra Sana, Victoria E. Frank, Brendan M. Kenyon, Grayson L. Baird, Kate E. Brilliant, Edward G. Walsh, Damian E. Dupuy, A Ferritin-Based Nanoconjugate MRI Contrast Agent Targeting Necl-5 as a Tumor Specific Marker: A Potential Thermal Accelerant for Microwave Ablation, *Proceedings of SPIE Photonics West Bios*, **2017**;10066: 100660H-1-9.

William K. C. Park, Aaron M.P. Maxwell, Victoria E. Frank, Michael P. Primmer, Scott A. Collins, Damian E. Dupuy, A Novel Thermal Accelerant for Augmentation of Microwave Energy during Image-guided Tumor Ablation, Abstract in *Journal of Vascular and Interventional Radiology*, Jan **2016**.

William K. C. Park, David R. Mills, Sierin Lim, Barindra Sana, Victoria E. Frank, Brendan M. Kenyon, Grayson L. Baird, Kate E. Brilliant, Edward G. Walsh, Damian E. Dupuy, A Ferritin-Based Nanoconjugate MRI Contrast Agent Targeting Necl-5 as a Tumor Specific Marker, Abstract in *Journal of Vascular and Interventional Radiology*, Jan **2016**.

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William K.C. Park, Robert M. Kennedy, Scott D. Larsen, Steve Miller, Bruce D. Roth, Yuntao Song, Bruce A. Steinbaugh, Kevin Sun, Bradley D. Tait, Mark C. Kowala, Bharat K. Trivedi, Bruce Auerbach, Valerie Askew, Lisa Dillon, Jeffrey C. Hanselman, Zhiwu Lin, Gina H. Lu, Andrew Robertson and Catherine Sekerke, Hepatoselectivity of statins: Design and synthesis of 4- sulfamoyl pyrroles as HMG-CoA reductase inhibitors, *BioOrganic Medicinal Chemistry Letters*, **2008**, 18(3) 1151.

Jeffrey A. Pfefferkorn, Chulho Choi, Scott D. Larsen, Bruce Auerbach, Richard Hutchings, William Park, Valerie Askew, Lisa Dillon, Jeffrey C. Hanselman, Zhiwu Lin, Gina H. Lu, Andrew Robertson, Catherine Sekerke, Melissa S. Harris, Alexander Pavlovsky, Graeme Bainbridge, Nicole Caspers, Mark Kowala, and Bradley D. Tait, Pyrazoles as Hepatoselective HMG-CoA Reductase Inhibitors: Discovery of (3R,5R)-7-[2-(4-Fluorophenyl)-4-isopropyl-5-(4-methyl-benzylcarbamoyl)-2H-pyrazol-3-yl]-3,5-dihydroxyheptanoic Acid (PF-3052334) as a Candidate for the Treatment of Hypercholesterolemia, *J. Med. Chem.* **2008** 51, 31.

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Roy, Rene; Park, William, K. C.; Zanini, Diana; Foxall, Carrol; Srivastava, Om P., Dendritic 3'-sulfo-LewisX-(Glc) as potent L- and E-selectin antagonists. *Carbohydrate Letters*, **1997**, 2(4), 259-266.

Park, William K. C.; Auer, Manfred; Jaksche, Herbert; Wong, Chi-Huey., Rapid Combinatorial Synthesis of Amino Glycoside Antibiotic Mimetics: Use of a Polyethylene Glycol-Linked Amine and a Neamine-Derived Aldehyde in Multiple Component Condensation as a Strategy for the Discovery of New Inhibitors of the HIV RNA Rev Responsive Element. *Journal of the American Chemical Society*, **1996**, 118(42), 10150-10155.

Roy, Rene; Park, William K. C.; Srivastava; Om P.; Foxall, Carrol. Combined glycomimetic and multivalent strategies for the design of potent selectin antagonists. *Bioorganic & Medicinal Chemistry Letters*, **1996**, 6(12), 1399-1402.

Park, W. K. C.; Meunier, S. J.; Zanini, D.; Roy, R. Chemoselective deprotection of thioacetates with hydrazinium acetate. *Carbohydrate Letters*, **1995**, 1(3), 179-184.

Zanini, D.; Park, W. K. C.; Meunier, S. J.; Wu, Q.; Aravind, S.; Kratzer, B.; Roy, R. Syntheses and biological properties of glycodendrimers. *Polymeric Materials Science and Engineering* **1995**, 73 82-3.

Zanini, Diana; Park, William K. C.; Roy, Rene, Synthesis of novel dendritic glycosides. *Tetrahedron Letters*, **1995**, 36(41), 7383-6.

Roy, Rene; Park, William K. C.; Wu, Qingquan; Wang, Sho-Nong. Synthesis of hyper-branched dendritic lactosides. *Tetrahedron Letters*, **1995**, 36(25), 4377-80.

Park, William K. C.; Aravind, Sivasubramanian; Romanowska, Anna; Renaud, Jocelyn;

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## PRESENTATIONS

**Keynote Address:** William K. C. Park\*, Aaron Wilhelm Palmer Maxwell, Victoria E. Frank, Michael P. Primmer, Scott A. Collins, Damian E. Dupuy, A Novel Thermal Accelerant for Augmentation of Microwave Energy during Image-guided Tumor Ablation, SPIE Photonics West Conference, San Francisco, CA January **2017**.

**Oral Presentation:** William K. C. Park\*, David R. Mills, Sierin Lim, Barinda Sana, Victoria E. Frank, Brendan M. Kenyon, Grayson L. Baird, Kate E. Brilliant, Edward G. Walsh, Damian E. Dupuy, A Ferritin-Based Nanoconjugate MRI Contrast Agent Targeting Necl-5 as a Tumor Specific Marker: A Potential MWA TA, SPIE Photonics West Conference, San Francisco, CA January **2017**.

**Poster Presentation:** William K. C. Park\*, Aaron Wilhelm Palmer Maxwell, Victoria E. Frank, Michael P. Primmer, Scott A. Collins, Damian E. Dupuy, Evaluation of a Novel Thermal Accelerant for Augmentation of Microwave Energy during Image-guided Tumor Ablation, The 9<sup>th</sup> National Center for Image-guided Therapy Workshop, Bethesda MD March **2017**.

**Poster Presentation:** Kara A Lombardo\*, William K. C. Park, Victoria E. Frank, Michael P. Primmer, Scott A. Collins, Damian E. Dupuy, Shaolei Lu, Pathologic Evaluation of a Novel Thermal Accelerant used in Microwave Ablation of Tumor, The United States and Canadian Academy of Pathology Annual Meeting, San Antonio TX March 4-10 **2017**.

**Lecture:** William K. C. Park, Damian E. Dupuy\*, Aaron Wilhelm Palmer Maxwell, Shaolei Lu, Grayson L Baird, Edward L Walsh, Victoria E Frank, Michael P Primmer, Evaluation of a Novel Thermal Accelerant for Augmentation of Microwave Energy during Image-guided Tumor Ablation, RSNA National Scientific Assembly Annual Meeting, Chicago IL, Nov 27-Dec 2, **2016**.

**Poster Presentation:** William K. C. Park\*, Aaron W.P. Maxwell, Victoria E. Frank, Michael P. Primmer, Scott A. Collins, Damian E. Dupuy, A Novel Thermal Accelerant for

Augmentation of Microwave Energy during Image-guided Tumor Ablation, World Conference of Interventional Oncology, Boston MA June **2016**.

**Poster Presentation:** William K. C. Park\*, David R. Mills, Sierin Lim, Barinda Sana, Victoria E. Frank, Brendan M. Kenyon, Grayson L. Baird, Kate E. Brilliant, Edward G. Walsh, Damian E. Dupuy, A Ferritin-Based Nanoconjugate MRI Contrast Agent Targeting Necl-5 as a Tumor Specific Marker, World Conference of Interventional Oncology, Boston MA June **2016**.

William K. C. Park\*; Gary L. Bolton; Mark M. Bush; Kevin J. Filipiski; Richard H. Hutchings; Jeffery T. Kohrt; Bruce A. Steinbaugh; Chad Van Huis, Discovery of PF-03384148 as an inhibitor of Serine Palmitoyl Transferase (SPT) and its analogs. *PGRD Michigan Medicinal Chemistry Symposium 2006*.

William K. C. Park\* Gary L. Bolton, Dan M. Bowles, David Boyles, James B. Dunbar, Richard Hutchings, Robert M. Kennedy. PF-00261809, An Imidazole-4-Carboxamide Statin: From Conception to Preparative Synthesis. *PGRD Michigan Medicinal Chemistry Symposium 2005*.

Bruce J. Auerbach, Sandra Bak Mueller, Edwin Davila-Delgado, Lisa M. Dillon, James B. Dunbar Jr., Jeffrey C. Hanselman, Tanoya L. Harris, Robert M. Kennedy, Zhiwu Lin, Gina H. Lu, Holly M. Meade, Thomas E. Mertz, Steven R. Miller, Karl F. Olsen, William K. C. Park, Alexander G. Pavlovsky, Andrew W. Robertson, Bruce D. Roth, Catherine S. Sekerke, Yuntao Song, Bruce A. Steinbaugh\*, Bharat K. Trivedi, Xiangyang Xu, Kristin H. Yuille. Synthesis and SAR of Sulfonamide Analogues for a Novel Statin Using Munchnone Chemistry. *PGRD Michigan Medicinal Chemistry Symposium 2004*.

Park, William K. C.\* ; Ling, Jing; Gritzen, Colleen; Short, Kevin M. Synthesis of 3-aminopropanols on solid support by reduction of isoxazolidines. Department of Chemistry, Ontogen Corporation, Carlsbad, CA, USA. Abstracts of Papers, 224th ACS National Meeting, Boston, MA, United States, August 18-22, **2002**, ORGN-144.

Park, William K C.\*; Short, Kevin M.; Jones, Todd K.; Ripka, William C. Novel and facile formylation methodology of N-alkyl anilines by using a combination of  $\text{RSO}_2\text{Cl}$  (R = alkyl or aryl) and DMF. Department of Chemistry, Ontogen Corporation, Carlsbad, CA, USA. Abstracts of Papers, 221st ACS National Meeting, San Diego, CA, United States, April 1-5, **2001**, ORGN-145.

Park, William K C.\*; Short, Kevin M.; Ripka, William C.; Jones, Todd K. Methodology toward the solid phase production of a library of tetrahydroquinolines. Department of Chemistry, Ontogen Corporation, Carlsbad, CA, USA. Abstracts of Papers, 221st ACS National Meeting, San Diego, CA, United States, April 1-5, **2001**, ORGN-143.

Priestley, E.\* Scott; Hendrix, Martin; Alper, Phil B.; Park, William K. C.; Wong, Chi-Huey., A chemical approach to aminoglycoside-RNA recognition. Department Chemistry, The Scripps Research Institute, La Jolla, CA, USA. Book of Abstracts, 213th ACS National Meeting, San Francisco, April 13-17, **1997**, CARB-073.

Park, W. K. C.\*; Zanini, D.; Meunier, S. J.; Wu, Q.; Aravind, S.; Kratzer, B.; Roy, R., Syntheses and biological properties of glycodendrimers. Department Chemistry, University Ottawa, Ottawa, ON, Can. Book of Abstracts, 210th ACS National Meeting, Chicago, IL, August 20-24, 1995, (Pt. 2), PMSE-043.

## **RESEARCH SUPPORT**

***Title:*** “Benzoxazinone Derivatives, as A Small-Molecule Renin Inhibitor”

Principal Investigator: William K C Park

Agency: Slater Technology Fund

1/1/07-12/31/09

***Title:*** “A Targeted, Iron-based MRI contrast for Tumor Detection and Therapy”

Principal Investigator: William K C Park

Agency: Rhode Island Medical Imaging

12/1/11-11/30/12

***Title:*** “A Targeted, Iron-based MRI contrast for Prostate Cancer Detection and Therapy”

Principal Investigator: William K C Park

Agency: Lifespan

09/1/12-08/31/13

***Title:*** “The Combined Use of Cesium X (X=halides or anions) and a Reverse-Phase Transition Gel for Image-Guided, Effective Thermal Ablation of Solid Tumors”

Principal Investigator: William K C Park

Agency: JISP NIH/NIGMS (COBRE grant P30GM110759)

09/1/15-08/31/16