



William H. Thiel, Ph.D.

Curriculum Vitae

CONTACT

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EDUCATION

Ph.D. *December 2008*

Vanderbilt University, Nashville TN
Department of Pharmacology

Bachelors of Science *May 2000*

Emory University, Atlanta GA

PROFESSIONAL MEMBERSHIPS

American Heart Association (AHA)
2011 - current

American Society of Gene and Cell
Therapy (ASGCT)
2009 – current

RESEARCH INTERESTS

My long-term goal is to decipher the mechanisms of cardiovascular disease development and progression using cell-targeting ligands (aptamers) and to develop novel treatments with these reagents. My specific focus areas include 1) use of vascular smooth muscle-specific aptamers to understand the complex mechanisms of neointimal formation after vascular injury; 2) developing cardiac-specific aptamers to study the mechanisms of cardiovascular disease and; 3) development of novel aptamer bioinformatics algorithms and methods to support aptamer discovery and target discovery.

PROFESSIONAL HISTORY

Assistant Professor *January 2019 – current*

University of Iowa, Iowa City IA

Department of Internal Medicine, Division of Cardiovascular Medicine

Research Assistant Professor *January 2015 – December 2018*

University of Iowa, Iowa City IA

Department of Internal Medicine, Hematology and Oncology

Advisors: Paloma H. Giangrande, Ph.D. and Francis J. Miller, M.D.

Research: Cardiovascular disease and aptamer technology

Postdoctoral Fellow *January 2009 – December 2014*

University of Iowa, Iowa City IA

Department of Internal Medicine, Hematology and Oncology

Advisor: Paloma H. Giangrande, Ph.D.

Research: VSMC-specific aptamers to study and treat neointimal formation following vascular injury

Graduate Student *August 2001 – December 2008*

Vanderbilt University, Nashville TN

Department of Pharmacology

Advisor: Mark E. Anderson, M.D., Ph.D.

Dissertation Committee: Alfred George M.D., (chair), Dan Roden M.D., Brian Wadzinski, Ph.D., and Roger Colbran, Ph.D.

Dissertation: "Pro-arrhythmic Defects in Timothy Syndrome Require Calmodulin Kinase II"

Research Technician *August 2000 – August 2001*

Emory University, Atlanta GA

Advisor: Stephen Traynelis, Ph.D.

Research: Homology modeling and molecular biology

Undergraduate Research *August 1997 – August 2000*

Emory University, Atlanta GA

Bio-molecular Computing Resource (BIMCORE)

Advisor: Kim Gernert, Ph.D.

Research: Web-based tutorials on crystal structures for the graduate school and homology modeling of protein structures

ACADEMIC AND PROFESSIONAL HONORS

2019

- Abstract accepted for oral presentation for the 2019 Arteriosclerosis, Thrombosis and Vascular Biology meeting in Boston.
- Ad hoc reviewer for *Molecular Therapy Nucleic Acids* journal and *Bioinformatics* journal.

2018

- American Heart Association Innovative Project Award (18IPA34170406) "Generation of Cardiac Specific Aptamer Ligands" funded with a percentile rank of 0.35%
- NHLBI R01 (HL139581-01A1) "Deciphering mechanisms of vascular disease with cell and process specific ligands" funded
- Member of the American Society of Gene and Cell Therapy New Investigator Committee
- Invited to serve as a mentor during the 2018 American Society of Gene and Cell Therapy meeting "Mentorship Event" for graduate students and postdoctoral fellows
- Invited to review the 2018 American Society of Gene and Cell Therapy meeting "Oligonucleotide Therapeutics II" poster session
- Ad hoc reviewer for *PLoS One* journal and *Molecular Therapy Nucleic Acids* journal

2017

- Member of the American Society of Gene and Cell Therapy New Investigator Committee
- Invited to serve as a mentor during the 2017 American Society of Gene and Cell Therapy meeting "Mentorship Event" for graduate students and postdoctoral fellows
- Invited to review the 2017 American Society of Gene and Cell Therapy meeting "Oligonucleotide Therapeutics I" poster session
- Ad hoc reviewer for *PLoS One* journal and *Molecular Therapy Nucleic Acids* journal

2016

- Co-chair of "Oligonucleotide Therapeutics I" session at 2016 American Society of Gene and Cell Therapy meeting
- Outstanding Poster Award at 2016 American Society of Gene and Cell Therapy meeting
- Invited to review the 2016 American Society of Gene and Cell Therapy meeting "Oligonucleotide Therapeutics II" poster session
- Ad hoc reviewer for *PLoS One* journal and *Cellular Physiology and Biochemistry* journal

2015

- Co-inventor of "Her2 Nucleic Acid Aptamers", Patent No: US9163242B2; Date of Grant: 10-20-2015
- Co-inventor of "Nucleic Acid Aptamers", Patent No: US9139835B2; Date of Grant: 09-22-2015
- Chair of "SELEX" session at 2015 Celebrating the 25th Anniversary of SELEX: An Aptamer Symposium
- Co-chair of "Aptamers" session at 2015 American Society of Gene and Cell Therapy meeting
- Ad hoc reviewer for *Bioinformatics* journal
- Best Basic Science Poster, 2015 University of Iowa Department of Internal Medicine Research Days

2014

- AHA Scientist Development Grant (14SDG18850071) "Inhibition of Vascular Disease with Cell-Targeted RNA Aptamers"
- Co-chair of "Clinical Trials with Oligonucleotides" session at 2014 American Society of Gene and Cell Therapy meeting
- Outstanding Poster Award at 2014 American Society of Gene and Cell Therapy meeting
- Invited to review the 2014 American Society of Gene and Cell Therapy meeting "Chemical/Molecular Conjugates and Physical Methods of DNA/DNA Delivery" poster session
- Best Basic Science Poster, 2014 University of Iowa Department of Internal Medicine Research Days
- Ad hoc reviewer for *Molecular Therapy Nucleic Acids* journal

2013

- Ad hoc reviewer for *PLoS One* journal

- Travel Award, 2013 American Society for Gene and Cell Therapy Annual Meeting
- AHA postdoctoral fellowship (13POST17070101) “Smooth Muscle Cell Targeted RNA Aptamers for the Treatment of Vascular Disease”

2012

- Best Basic Science Poster, 2012 University of Iowa Department of Internal Medicine Research Days

2011

- AHA postdoctoral fellowship (11POST7620018) “Smooth muscle cell-specific inhibition of NADPH oxidase to prevent vascular disease”

2009

- University of Iowa Cardiovascular IRF (HL007121) “Smooth muscle cell-specific inhibition of NADPH oxidase to prevent vascular disease”
- Ad hoc reviewer for *Circulation* journal

2008

- Publication Thiel WH *et al.* *Circulation* 2008 Nov. 10 evaluated by Faculty of 1000 as recommended

CONTRIBUTIONS TO SCIENCE WITH SELECT PUBLICATIONS

Vascular smooth muscle cell RNA aptamers for the treatment of cardiovascular disease: Cardiovascular disease (CVD) is the leading cause of mortality in many countries. Many vascular disorders are caused by pathological vascular smooth muscle cell (VSMC) remodeling following injury. An ideal therapeutic intervention would target the VSMCs without impairing the injured vessel re-endothelialization. However, current therapies do not selectively prevent pathological VSMC remodeling leading to impaired re-endothelialization, late stent thrombosis and death. Thus, there is a clear need for cell-targeted treatment and prevention options of pathological VSMC remodeling. As a postdoc I, with guidance from Dr. Paloma Giangrande and in collaboration with Dr. Francis Miller, developed VSMC specific RNA aptamers. These VSMC-specific aptamers exhibited up to 20-fold greater internalization in cultured VSMCs as compared to endothelial cells. We most recently reported on a VSMC-specific anti-migratory aptamer that inhibits VSMC migration to multiple agonists, including platelet-derived growth factor-BB (PDGF-BB), and prevents neointimal formation in vivo following acute vascular injury. I have identified two additional VSMC-targeting aptamers that modulate VSMC, but not EC, proliferation and apoptosis through unknown mechanisms originating at the cell surface. These data serve as the basis for my recently funded R01 from the NIH/NHLBI. These VSMC-targeting aptamers present a significant advance in the development of VSMC-targeting drugs to specifically modulating VSMC pathological remodeling and improve the safety and efficacy of DES.

- Thiel WH, Esposito CL, Dickey DD, Dassie JP, Long ME, Adam J, Streeter J, Schickling B, Takapoo, M, Flenker KS, Klesney-Tait J, Francis V, Miller FJ Jr, Giangrande PH. Smooth Muscle Cell-targeted RNA Aptamer Inhibits Neointimal Formation. *Molecular Therapy*. 2016 Apr;24(4):779-87. PMID: 26732878; PMCID: PMC4886937.
- Thiel WH, Thiel KW, Flenker KS, Bair T, Dupuy AJ, McNamara JO 2nd, Miller FJ Jr, Giangrande PH. Cell-internalization SELEX: method for identifying cell-internalizing RNA aptamers for delivering siRNAs to target cells. *Methods Molecular Biology*. 2015;1218:187-99. PMID: 25319652; PMCID: PMC4435695
- Thiel WH, Bair T, Peek AS, Liu X, Dassie J, Stockdale KR, Behlke MA, Miller FJ Jr, Giangrande PH. Rapid identification of cell-specific, internalizing RNA aptamers with bioinformatics analyses of a cell-based aptamer selection. *PLoS One*. 2012; 7(9):e43836. PubMed PMID: 22962591; PubMed Central PMCID: PMC3433472.

Innovation in aptamer bioinformatics: Aptamers are small (20-100 nucleotide) DNA or RNA oligonucleotides that specifically bind target molecules with high affinity. Aptamers are enriched for a target cell/protein through a process termed SELEX, Systematic Evolution of Ligands by EXponential enrichment. Because aptamers are comprised of nucleic acids, the identity of the enriched aptamer sequences may be identified using high-throughput sequencing (HTS). From these HTS aptamer data, I developed several novel approaches in

aptamer bioinformatics. This includes 1) the first mathematical formula to ascertain the progress of an aptamer selection by using HTS data to calculate sequence enrichment; 2) the first documentation of PCR bias during aptamer selection by analyzing both targeted and non-targeted aptamer selections; 3) separating selected aptamers from non-selected aptamers by comparing the abundance and persistence of an aptamer sequence throughout a selection; 4) using the non-enriched starting aptamer library as a bioinformatics negative control to identify selected aptamers; and 5) developing a clustering algorithm that generates networks of related aptamers using sequence similarity by edit distance and structure similarity by tree distance to identify candidate aptamer sequences. Most recently, I reported the adaptation of conventional HTS genomic tools, such as the Galaxy Webserver, to analyze aptamer HTS datasets. I am currently collaborating with the University of Iowa Institute for Clinical and Translational Science (ICTS) on integrating the most recent version of the aptamer clustering algorithm into a web-based application. This collection of work with aptamer bioinformatics has established myself as an expert and facilitates several collaborations as I continue to innovate.

- Thiel WH*, Galaxy Workflows for Web-based Bioinformatics Analysis of Aptamer High-throughput Sequencing Data. *Molecular Therapy Nucleic Acids*. 2016 Aug; 5(8): e345. PMID: PMC5023399. (*corresponding author)
- Thiel WH*, Giangrande PH. Analyzing HT-SELEX data with the Galaxy Project tools - A web based bioinformatics platform for biomedical research. *Methods*. 2015 Oct 20. pii: S1046-2023(15)30127-4. doi: 10.1016/j.ymeth.2015.10.008. PMID: 26481156. (*corresponding author)
- Thiel WH, Bair T, Peek AS, Liu X, Dassie J, Stockdale KR, Behlke MA, Miller FJ Jr, Giangrande PH. Rapid identification of cell-specific, internalizing RNA aptamers with bioinformatics analyses of a cell-based aptamer selection. *PLoS One*. 2012; 7(9):e43836. PMID: 22962591; PMID: PMC3433472.
- Thiel WH, Bair T, Wyatt Thiel K, Dassie JP, Rockey WM, Howell CA, Liu XY, Dupuy AJ, Huang L, Owczarzy R, Behlke MA, McNamara JO, Giangrande PH. Nucleotide Bias Observed with a Short SELEX RNA Aptamer Library. *Nucleic Acid Therapeutics* 2011 Aug. 21(4):253-63. PMID: 21793789, PMID: PMC3198618

Novel methodology facilitating aptamer discovery: Congruent with my development of novel aptamer bioinformatics tools and methodologies, I have also innovated techniques used in aptamer discovery. Recently, I developed a rapid and high-throughput method to test aptamer binding and internalization on cells. The Aptamer Fluorescence Binding and Internalization (AFBI) assay may be used to measure dissociation constants of aptamers on cells and the internalization time course. The AFBI assay is a rapid, high-throughput assay that requires minimal reagents as compared to conventional assays such as RT-qPCR and flow cytometry. I have used this assay to explore optimal aptamer folding. These experiments yielded unexpected results that may explain some controversies within the aptamer field. I anticipate publishing these data within the next year. Most recently, I have been exploring the adaptation of CRISRP-Cas9 technology with aptamer technology to facilitate the identification of aptamer targets.

- Thiel WH*, Giangrande PH. AFBI assay - Aptamer Fluorescence Binding and Internalization assay for cultured adherent cells. *Methods*. 2016 Jul 1;103:180-7. PMID: 26972784. PMID: PMC4921262 (*corresponding author)
- Thiel WH, Thiel KW, Flenker KS, Bair T, Dupuy AJ, McNamara JO 2nd, Miller FJ, Giangrande PH. Cell-Internalization SELEX: Method for Identifying Cell-Internalizing RNA Aptamers for Delivering siRNAs to Target Cells. *Methods Mol Biol*. 2015;1218:187-99. PMID:25319652. PMID: PMC4435695

The role of calmodulin-dependent kinase II (CaMKII) in cardiovascular disease: Ca²⁺ activated signaling pathways coordinate contraction in the heart, but these pathways cause disease upon excessive activation. Intracellular Ca²⁺ activates the multifunctional Ca²⁺ and calmodulin-dependent protein kinase II (CaMKII) and activated CaMKII increases Ca²⁺ entry, by a feed-forward process, through voltage-gated (CaV1.2) Ca²⁺ channels in cardiac myocytes. When I first began my graduate work with Dr. Mark Anderson, I studied excitation contraction coupling of cardiomyocytes following myocardial infarction. We found that inhibition of CaMKII preserved cellular contraction following myocardial infarction. These findings were a part of the larger study showing that CaMKII inhibition protects against structural heart disease. This work was followed by my investigation of CaMKII activation with the CaV1.2 Timothy Syndrome mutation. I developed an adult rat

ventricular myocyte model of Timothy Syndrome by lentivirus-mediated exogenous expression of CaV1.2. I modified the lentivirus to enable packaging of a wild type or Timothy Syndrome (G406R) CaV1.2 containing a dihydropyridine resistance mutation (T1066Y). These exogenous CaV1.2 channels could be specifically studied by silencing endogenous CaV1.2 channels with the dihydropyridine nifedipine. Using this model of Timothy Syndrome, I found that the CaV1.2 Timothy Syndrome expressing cardiac myocytes exhibited increased CaMKII activity, increased number of afterdepolarizations, enhanced I_{Ca} facilitation and augmented intracellular Ca^{2+} handling. Inhibition of CaMKII prevented the Long-QT arrhythmia inducing afterdepolarizations. From these data we developed a revised mathematical model of Timothy Syndrome. This work was accompanied by a review within *Circulation* (London B. Understanding cardiac calcium channelopathies. *Circulation*, 2008 Nov25;118(22) PMID: 19029476) and is listed with *Faculty of 1000* as recommended reading as an interesting hypothesis, new finding and novel drug target. Most recently I have been developing a new project to integrate my background in cardiac biology with aptamer technology to develop cardiac-specific aptamer ligands. Specifically, these cardiac-specific aptamer ligands will serve as a novel strategy to identify druggable cardiac proteins and serve as a basis to deliver therapeutics specifically to the heart. This project is supported by an Innovative Project Award from American Heart Association and the grant proposal was reviewed with significant enthusiasm with a percentile rank of 0.35%.

- Thiel WH, Chen B, Hund TJ, Koval OM, Purohit A, Song LS, Mohler PJ, Anderson ME. Proarrhythmic defects in timothy syndrome require calmodulin kinase II. *Circulation*. 2008;118:2225-2234. PMID: 19001023, PMCID: PMC3226825
- Zhang R, Khoo MS, Wu Y, Yang Y, Grueter CE, Ni G, Price EE Jr, Thiel W, Guatimosim S, Song LS, Madu EC, Shah AN, Vishnivetskaya TA, Atkinson JB, Gurevich VV, Salama G, Lederer WJ, Colbran RJ, Anderson ME. Calmodulin kinase II inhibition protects against structural heart disease., *Nat Med*. 2005 Apr;11(4):409-17. PMID: 15793582
- Zhang R, Dzhura I, Grueter CE, Thiel W, Colbran RJ, Anderson ME., A dynamic alpha-beta inter-subunit agonist signaling complex is a novel feedback mechanism for regulating L-type Ca^{2+} channel opening. *FASEB J.*, 2005 Sep;19(11):1573-5. PMID: 15994413

COMPLETE LIST OF PEER-REVIEWED PUBLICATIONS

1. Udofot O, Lin LH, Thiel WH, Erwin M, Turner E, Miller FJ, Giangrande PH, Yazdani SK. "Delivery of cell-specific aptamers to the arterial wall with an occlusion perfusion catheter." *Molecular Therapy Nucleic Acids*, 2019 (in press)
2. Urak KT, Blanco GN, Shubham S, Lin LH, Dassie JP, Thiel WH, Chen Y, Sonkar VK, Lei B, Murthy S, Gutierrez WR, Wilson ME, Stiber JA, Klesney-Tait J, Dayal S, Miller FJ Jr, Giangrande PH. "RNA inhibitors of nuclear proteins responsible for multiple organ dysfunction syndrome." *Nat Commun*. 2019 Jan 10;10(1):116. PMID: 30631065
3. Guo A, Wang Y, Chen B, Wang Y, Yuan J, Zhang L, Hall D, Wu J, Shi Y, Zhu Q, Chen C, Thiel WH, Zhan X, Weiss RM, Zhan F, Musselman CA, Pufall M, Zhu W, Au KF, Hong J, Anderson ME, Grueter CE, Song LS. E-C coupling structural protein junctophilin-2 encodes a stress-adaptive transcription regulator. *Science*. 2018 Dec 21; 362(6421). PMID 30409805
4. Meng X, Yang S, Li Y, Li Y, Devor EJ, Bi J, Wang X, Umesalma S, Quelle DE, Thiel WH, Thiel KW, Leslie KK. "Combination of Proteasome and Histone Deacetylase Inhibitors Overcomes the Impact of Gain-of-Function p53 Mutations." *Dis Markers*. 2018 Dec 17;2018:3810108. PMID: 30647797
5. Ruiz CD, Vargas MR, Thiel WH, Bruno MA, Giangrande PH, Mestre MB. Aptamers as Diagnostic Tools in Cancer. *Pharmaceuticals (Basel)*. 2018 Sep 11;11(3). PMID: 30208607
6. Nguyen EK, Koval OM, Noble P, Broadhurst K, Allamargot C, Wu M, Strack S, Thiel WH, Grumbach IM. CaMKII (Ca²⁺/Calmodulin-Dependent Kinase II) in Mitochondria of Smooth Muscle Cells Controls Mitochondrial Mobility, Migration, and Neointima Formation. *Arterioscler Thromb Vasc Biol*. 2018 Jun;38(6):1333-1345. PMID: 29599132
7. Thiel WH, Esposito CL, Dickey DD, Dassie JP, Long ME, Adam J, Streeter J, Schickling B, Takapoo, M, Flenker KS, Klesney-Tait J, Franciscis V, Miller FJ Jr, Giangrande PH. Smooth Muscle Cell-targeted RNA

- Aptamer Inhibits Neointimal Formation. *Molecular Therapy*. 2016 Apr;24(4):779-87. PMID: 26732878; PMCID: PMC4886937.
8. Thiel WH*, Galaxy Workflows for Web-based Bioinformatics Analysis of Aptamer High-throughput Sequencing Data. *Molecular Therapy Nucleic Acids*. 2016 Aug; 5(8): e345. PMID: 28131286; PMCID: PMC5023399. (*corresponding author)
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 9. Thiel WH*, Giangrande PH. AFBI assay - Aptamer Fluorescence Binding and Internalization assay for cultured adherent cells. *Methods*. 2016 Jul 1;103:180-7. PMID: 26972784. PMCID: PMC4921262 (*corresponding author)
 10. Thiel WH*, Giangrande PH. Analyzing HT-SELEX data with the Galaxy Project tools - A web based bioinformatics platform for biomedical research. *Methods*. 2015 Oct 20. PMID: 26481156. PMCID: PMC4792767. (*corresponding author)
 - Google Scholar: cited by 19
 11. Thiel WH, Thiel KW, Flenker KS, Bair T, Dupuy AJ, McNamara JO 2nd, Miller FJ Jr, Giangrande PH. Cell-internalization SELEX: method for identifying cell-internalizing RNA aptamers for delivering siRNAs to target cells. *Methods Molecular Biology*. 2015;1218:187-99. PMID: 25319652; PMCID: PMC4435695
 - Google Scholar: cited by 27
 12. Streeter J, Schickling BM, Jiang S, Stanic B, Thiel WH, Gakhar L, Houtman JC, Miller FJ Jr. Phosphorylation of Nox1 regulates association with NoxA1 activation domain. *Circ Res*. 2014 Nov 7;115(11):911-8. PMID: 25228390. PMCID: PMC5025877.
 13. Gourronc FA, Rockey WM, Thiel WH, Giangrande PH, Klingelutz AJ. Identification of RNA aptamers that internalize into HPV-16 E6/E7 transformed tonsillar epithelial cells. *Virology*. 2013 Nov;446(1-2):325-33. PMID: 24074596. PMCID: PMC3812236.
 14. Streeter J, Thiel WH, Brieger K, Miller Jr. FJ. Opportunity Nox: The future of NADPH oxidases as therapeutic targets in cardiovascular disease. *Cardiovascular Therapeutics*. 2013 Jun;31(3):125-37. PMID: 22280098.
 15. Thiel WH, Bair T, Peek AS, Liu X, Dassie JD, Stockdale KR, Behlke MA, Miller FJ Jr., Giangrande PH. Rapid identification of cell-specific, internalizing RNA aptamers with bioinformatics analyses of a cell-based aptamer selection. *PLoS One* 2012, Sept;7(9). PMID: 22962591. PMCID: PMC3433472.
 - Top 10% PLoS One most cited articles
 - Google Scholar: cited by 87
 16. Thiel KW, Hernandez LI, Dassie JP, Thiel WH, Liu X, Stockdale KR, Rothman AM, Hernandez FJ, McNamara JO 2nd, Giangrande PH. Delivery of chemo-sensitizing siRNAs to HER2+ breast cancer cells using RNA aptamers. *Nucleic Acids Research* 2012, Mar;30:1-19. PMID: 22467215. PMCID: PMC3401474.
 17. Berezhnoy A, Stewart CA, McNamara II JO, Thiel W, Giangrande P, Trinchieri G, Gilboa E. Isolation and Optimization of Murine IL-10 Receptor Blocking Oligonucleotide Aptamers Using High-throughput Sequencing. *Molecular Therapy* 2012 Jun;20(6):1242-50. PMID: 22434135 PMCID: PMC3369303
 18. Thiel WH, Bair T, Wyatt Thiel K, Dassie JP, Rockey WM, Howell CA, Liu XY, Dupuy AJ, Huang L, Owczarzy R, Behlke MA, McNamara JO, Giangrande PH. Nucleotide Bias Observed with a Short SELEX RNA Aptamer Library. *Nucleic Acid Therapeutics* 2011 Aug. 21(4):253-63. PMID: 21793789 PMCID: PMC3198618
 - Google Scholar: cited by 51
 19. Thiel WH, Chen B, Hund TJ, Koval OM, Purohit A, Song LS, Mohler PJ, Anderson ME. Proarrhythmic defects in timothy syndrome require calmodulin kinase II. *Circulation*. 2008;118:2225-2234. PMID: 19001023 PMCID: PMC3226825
 - Associated comment: London B. "Understanding cardiac calcium channelopathies." *Circulation*. 2008 Nov 25;118(22):2221-2.
 - Evaluated by Faculty of 1000 as recommended

20. Zhang R, Dzhura I, Grueter CE, Thiel W, Colbran RJ, Anderson ME., A dynamic alpha-beta inter-subunit agonist signaling complex is a novel feedback mechanism for regulating L-type Ca²⁺ channel opening. *FASEB J.*, 2005 Sep;19(11):1573-5. PMID: 15994413.
21. Zhang R, Khoo MS, Wu Y, Yang Y, Grueter CE, Ni G, Price EE Jr, Thiel W, Guatimosim S, Song LS, Madu EC, Shah AN, Vishnivetskaya TA, Atkinson JB, Gurevich VV, Salama G, Lederer WJ, Colbran RJ, Anderson ME. Calmodulin kinase II inhibition protects against structural heart disease., *Nat Med.* 2005 Apr;11(4):409-17. PMID: 15793582.
22. Low CM, Lyuboslavsky P, French A, Le P, Wyatte K, Thiel WH, Marchan EM, Igarashi K, Kashiwagi K, Gernert K, Williams K, Traynelis SF, Zheng F., Molecular determinants of proton-sensitive N-methyl-D-aspartate receptor gating. *Mol Pharmacol.* 2003 Jun;63(6):1212-22. PMID: 12761330.
23. Tobiason DM, Buchner JM, Thiel WH, Gernert KM, Karls AC, Conserved amino acid motifs from the novel Piv/MooV family of transposases and site-specific recombinases are required for catalysis of DNA inversion by Piv. *Mol Microbiol.* 2001 Feb;39(3):641-51. PMID: 11169105.

NCBI MyBibliography list of published work:

<http://www.ncbi.nlm.nih.gov/sites/myncbi/william.thiel.1/bibliography/47569381/public/?sort=date&direction=ascending>.

ABSTRACTS

1. Giangrand PH, Miller FJ, Thiel WH. "VSMC Specific Aptamer Ligands for the Next Generation of DES to Prevent Neointimal Formation." American Society for Gene and Cell Therapy (ASGCT) May, 2018 Chicago IL
2. Urak KT, Blanco G, Lin LH, Dassie J, Shubham S, Thiel WH, Chen Y, Sokar V, Lei B, Gutierrez W, Wilson M, Dayal S, Miller FJ, Giangrande PH. "RNA Inhibitors of Nuclear Proteins Implicated in Multiple Organ Dysfunction Syndrome." American Society for Gene and Cell Therapy (ASGCT) May, 2018 Chicago IL
3. Veeramani S, Blackwell SE, Thiel WH, Giangrande PH, Weiner GJ. "Targeting human T regulatory cells with novel Interleukin 2 alpha - IL2 complex-specific RNA aptamer." AACR Annual Meeting 2017; April 1-5, 2017; Washington, DC
4. Bair T, Wertz JS, Miller RJ, Schappet J, Giangrande PH, Thiel WH. "AptaMetrics: A Web-based Aptamer Bioinformatics Platform." Oligonucleotide Therapeutics Society (OTS) September, 2016 Montreal
5. Dickey DD, Giangrande PH, Thiel WH. "Optimizing Conditions for Aptamer Folding Using a High-Throughput Aptamer Fluorescence Binding and Internalization (AFBI) Assay." American Society for Gene and Cell Therapy (ASGCT) May, 2016 Washington DC
6. Veeramani S, Blackwell SE, Thiel WH, Giangrande PH, Weiner GJ. "Novel IL-2Ralpha (CD25)-Binding RNA Aptamer to Target T Regulatory Cells." American Society of Hematology (ASH) Annual Meeting 2016
7. Bair T, Miller RJ, Schappet J, Giangrande PH, Thiel WH. "AptmR: A High Throughput Rational Aptamer Truncation Algorithm" American Society for Gene and Cell Therapy (ASGCT) May, 2015 New Orleans
8. Thiel WH, Esposito CL, Dickey DD, Dassie JP, Long ME, Adam J, Streeter J, Schickling B, Takapoo M, Flenker KS, Klesney-Tait J, de Franciscis V, Miller FJ Jr., Giangrande PH. "Vascular Smooth Muscle Cell RNA Aptamers for the Treatment of Cardiovascular Disease" American Society for Gene and Cell Therapy (ASGCT) May, 2015 New Orleans
9. Thiel WH, Dickey DD, Streeter J, Schickling B, Dassie JP, Takapoo M, Liu X, Miller FJ Jr., Giangrande PH. "Cell-targeted RNA-based therapies for cardiovascular disease." American Society for Gene and Cell Therapy (ASGCT) May, 2014 Washington DC
 - Winner of Outstanding Poster Award for the Cardiovascular and Pulmonary Therapies Session
10. Thiel WH, Takapoo M, Jiang S, Streeter J, Stanic B, Liu X, Miller FJ Jr., Giangrande PH. "Smooth Muscle Cell Targeted RNA Aptamers for the Treatment of Vascular Disease." American Society for Gene and Cell Therapy (ASGCT) May, 2013 Salt Lake City, UT
 - Travel award recipient

11. Thiel WH, Bair T, Peek AS, Stanic B, Takapoo M, Streeter J, Liu X, Behlke MA, Miller FJ Jr., Giangrande PH. "VSMC-Targeted Aptamer-siRNA Chimeras as Inhibitors of Intimal Hyperplasia." American Heart Association (AHA) November, 2012 Los Angeles, CA
12. Thiel WH, Bair T, Peek AS, Stanic B, Takapoo M, Streeter J, Liu X, Behlke MA, Miller FJ Jr., Giangrande PH. VSMC-Targeted Aptamer-siRNA Chimeras as Inhibitors of Intimal Hyperplasia. RNAIowa, Symposium, October, 2012 University of Iowa
13. Thiel WH, Bair T, Peek AS, Stanic B, Takapoo M, Streeter J, Liu X, Behlke MA, Miller Jr. FJ, Giangrande PH. Aptamer-siRNA Chimera Inhibitors of Intimal Hyperplasia. American Society for Gene and Cell Therapy (ASGCT) May, 2012 Philadelphia, PA
14. Thiel WH, Bair T, Peek AS, Stanic B, Takapoo M, Streeter J, Liu X, Behlke MA, Miller Jr. FJ, Giangrande PH. "Aptamer-siRNA Chimera Inhibitors of Intimal Hyperplasia." University of Iowa Department of Internal Medicine Research Days, February, 2012 University of Iowa
 - Winner for Best Basic Science Poster
15. Thiel WH, Stanic B, Streeter J, Liu X, Miller Jr. FJ, Giangrande PH. RNA Inhibitors of Intimal Hyperplasia. American Society for Gene and Cell Therapy (ASGCT) May, 2011 Seattle, WA
16. Thiel WH, Thiel KW, Dassie JP, Liu X, Stockdale KR, Rockey WM, McNamara II JO, Giangrande PH. "Methods for isolating cell-internalizing RNA aptamers for targeted siRNA delivery." American Society for Gene and Cell Therapy (ASGCT) May, 2010 Washington, DC
17. Thiel KW, Thiel WH, Xiuying L, Dassie JP, Stockdale KR, Rockey WM, McNamara II JO, Giangrande PH. "Delivery of chemo-sensitizing siRNAs to HER2-positive breast cancer cells using RNA aptamers." American Society for Gene and Cell Therapy (ASGCT) May 19-22, 2010 Washington, D
18. Thiel KW, Thiel WH, Liu X, Nannapaneni K, Scheetz K, Peek AS, McNamara JO II, and Giangrande PH. "Development of Novel RNA-Based Therapeutics for HER2-Positive Cancers." 2009, Midwest Breast Cancer Research Symposium
19. Thiel WH, Mohler PJ, Purohit A, Anderson ME., "Timothy Syndrome mutation causes action potential prolongation and afterdepolarizations in adult cardiomyocytes." 2007 Heart Rhythm Society Meeting

PATENTS

1. HER2 NUCLEIC ACID APTAMERS. US9163242B2. Inventors: Paloma H. Giangrande, James O. McNamara, Kristina Wyatt Thiel, William H. Thiel, William M. Rockey. Publication date: 2015-10-20. The present invention relates to optimized HER2 aptamers and methods of using these aptamers.
2. NUCLEIC ACID APTAMERS. US9139835B2. Inventors: Paloma H. Giangrande, Francis Miller, William Thiel. Publication date: 2015-09-22. The present invention relates to optimized aptamers and methods of using these aptamers.
3. Novel Approach to Identify RNA Aptamer Sequences Specific for Receptor-Ligand Complexes as Demonstrated Through Identification of Aptamers Targeting T Regulatory Cells. Provisional patent disclosure (November 2016). Inventors: Sue E. Blackwell, Suresh Veeramani, Paloma H. Giangrande, William H. Thiel, George J. Weiner.

INVITED TALKS

January 2019

University of Iowa Division of Pulmonary, Critical Care & Occupational Medicine, Pulmonary Research Conference, "Cell-Specific Aptamer Ligands to Treat Cardiovascular Disease."

February 2018

University of Iowa Division of Cardiology, Abboud Cardiovascular Center Works in Progress, "Cardiac Specific Aptamer Ligands to Treat Cardiovascular Disease."

March 2018

University of Iowa Research Seminar Series, "Cell-Specific Aptamer Ligands to Treat Cardiovascular Disease."

May 2016

American Society for Gene and Cell Therapy (ASGCT) annual meeting, Washington DC

“Optimizing Conditions for Aptamer Folding Using a High-Throughput Aptamer Fluorescence Binding and Internalization (AFBI) Assay.”

August 2015

Department of Internal Medicine Research Days, University of Iowa
“Vascular Smooth Muscle Cell RNA Aptamers for the Treatment of Cardiovascular Disease”

May 2015

American Society for Gene and Cell Therapy (ASGCT) annual meeting, New Orleans, LA
“AptmR: A High Throughput Rational Aptamer Truncation Algorithm”

May 2015

American Society for Gene and Cell Therapy (ASGCT) annual meeting, New Orleans, LA
“Vascular Smooth Muscle Cell RNA Aptamers for the Treatment of Cardiovascular Disease”

June 2014

University of Missouri, hosted by Donald Burke, Ph.D.
“Aptamers, Cardiovascular Disease and Bioinformatics”

March 2014

Department of Internal Medicine Research Days, University of Iowa
“Cell-targeted RNA-based Therapies for Cardiovascular Disease”

May 2013

American Society for Gene and Cell Therapy (ASGCT) annual meeting, Salt Lake City, UT
“Smooth Muscle Cell Targeted RNA Aptamers for the Treatment of Vascular Disease.”

November 2012

American Heart Association (AHA) annual meeting, Los Angeles, CA
“VSMC-Targeted Aptamer-siRNA Chimeras as Inhibitors of Intimal Hyperplasia.”

October 2012

RNAIowa Symposium, University of Iowa
“VSMC-Targeted Aptamer-siRNA Chimeras as Inhibitors of Intimal Hyperplasia.”

February 2012

Department of Internal Medicine Research Days, University of Iowa
“Aptamer-siRNA Chimera Inhibitors of Intimal Hyperplasia.”

RESEARCH SUPPORT

Current

- 07/2018 – 06/2023 NHLBI R01 (HL139581-01A1) “Deciphering mechanisms of vascular disease with cell and process specific ligands”
- 07/2018 – 06/2020 American Heart Association Innovative Project Award (18IPA34170406) “Generation of Cardiac Specific Aptamer Ligands”

Completed

- 01/2014 – 12/2018 American Heart Association Scientist Development Grant (14SDG18850071) “Inhibition of Vascular Disease with Cell-Targeted RNA Aptamers”
- 07/2013 – 12/2013 American Heart Association postdoctoral fellowship (13POST17070101) “Smooth Muscle Cell Targeted RNA Aptamers for the Treatment of Vascular Disease”
- 07/2011 – 06/2013 American Heart Association postdoctoral fellowship (11POST7620018) “Smooth muscle cell-specific inhibition of NADPH oxidase to prevent vascular disease”
- 01/2009 – 03/2011 University of Iowa Cardiovascular IRF (HL007121) “Smooth muscle cell-specific inhibition of NADPH oxidase to prevent vascular disease”
- 01/2007 – 12/2007 Renewal of American Heart Association predoctoral fellowship (0710144Z) “L-type Calcium Channel Regulation by CaMKII”
- 07/2004 – 06/2006 American Heart Association predoctoral fellowship (0415229B) “L-type Calcium Channel Regulation by CaMKII”
- 05/2002 – 05/2004 Vanderbilt University, Pharmacology Training Grant

05/2001 – 05/2002

Vanderbilt University, IGP Training Grant

TEACHING AND MENTORING EXPERIENCE

Teaching

August 1997 – August 2000

Emory University, Atlanta GA

I created an interactive web-based tutorial on sodium channel structure for the graduate school. I assisted Kim Gernert Ph.D. as a Teacher's Assistant of a graduate dry laboratory course in using Rasmol software to explore protein crystal structures.

Mentoring

Dario Ciancio *June 2017 – November 2017*

Visiting graduate student from Catholic University of Cuyo, San Juan, Argentina

I have been mentoring Dario Ciancio in conducting a cell-based aptamer selection and internalization assays.

Ofonime Udofot, Ph.D. *November 2016 – September 2018*

Postdoctoral Fellow under Paloma Giangrande, Ph.D.

I have been mentoring Dr. Udofot in SELEX, cell-based aptamer assays, molecular biology and data analysis.

Kevin Urak *January 2015 – August 2018*

Graduate student under Paloma Giangrande, Ph.D.

I mentored Kevin Urak in preparation of aptamer libraries for high throughput sequencing and the subsequent aptamer bioinformatics of an aptamer selection.

Radhika Patel *August 2016 – November 2016*

Graduate student rotating with Paloma Giangrande, Ph.D.

I mentored Radhika Patel in molecular biology and cell-based assays.

Justin Dassie, Ph.D. *August 2009 – December 2014*

Graduate student and postdoctoral fellow under Paloma Giangrande, Ph.D.

I mentored Dr. Dassie in cell-based assays and preparation of aptamer libraries for high throughput sequencing along with the subsequent aptamer bioinformatics of an aptamer selection.

Greg Thomas, Ph.D. *August 2010 – December 2012*

Graduate student under Paloma Giangrande, Ph.D.

I mentored Dr. Thomas in cell-based assays and molecular biology.

Jeff Erickson, Ph.D. *November 2005 – December 2007*

Postdoctoral Fellow under Mark Anderson, M.D. Ph.D.

I mentored Dr. Erickson in biochemical kinase assays and molecular biology.

Anil Purohit, M.D. *August 2006 – November 2007*

Medical resident of the Department of Internal Medicine at the University of Iowa conducting research under Mark Anderson M.D., Ph.D.

I mentored Dr. Purohit in the isolation, culturing and whole-cell voltage clamp of adult cardiomyocytes and subsequent data analysis using pCLAMP software.