

## Faculty Profile

 

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### Mark (Marty) Pagel

Associate Professor

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### Honors

- Arizona Engineering Faculty Fellow, 2012
- Sydney E. Salmon Distinguished Junior Investigator Award, Arizona Cancer Center, Tucson, AZ, 2010
- Case School of Engineering Graduate Teaching Award, CWRU, Cleveland, OH, 2006
- Young Investigator Award, Contrast Media Research 2005 Symposium, 2005
- Early Career Recognition Award, Pharmacia Corp., St. Louis, MO, 2003
- John C. Sowden Prize in Chemistry, Washington University, St. Louis, MO, 1988

### Education and Appointments

- B.A., Chemistry 1988, Washington University, St. Louis, MO
- B.A., Biology 1988, Washington University, St. Louis, MO
- PhD, Chemistry 1993, University of California, Berkeley CA

### Research Interests

- Biochemistry
- Physical
- Bioanalytical
- Chemical Biology
- Spectroscopy/molecular Structure

### Research Summary

Dr. Marty Pagel directs the Contrast Agent Molecular Engineering Laboratory (CAMEL) in the University of Arizona Cancer Center.

**Research Mission** The Contrast Agent Molecular Engineering Laboratory (CAMEL) develops chemical agents that change the contrast of biomedical images. These contrast agents are designed to respond to molecular biomarkers of biological processes and pathologies. This molecular information is used to predict response to therapy before the therapy is applied, monitor the delivery of therapy to targeted tissues, and evaluate the early-stage effects of the therapy. These diagnostic methods that affect the choice of therapy are designed to provide personalized medicine for each individual patient.

CAMEL primarily focuses on the development of contrast agents for Magnetic Resonance Imaging (MRI). In particular, CAMEL has developed a new type of MRI contrast agent that can detect molecular biomarkers through Chemical Exchange Saturation Transfer (CEST). CAMEL has also developed CEST MRI methods for pre-clinical and clinical studies, and has also developed methods that rapidly synthesize CEST contrast agents. CAMEL also develops contrast agents for optical

imaging, particularly focusing on applications of optical imaging that use multiple agents to improve the specificity of molecular imaging. CAMEL is affiliated with the Department of Biomedical Engineering and the Biomedical Engineering Graduate Interdisciplinary Program, the Department of Chemistry and Biochemistry, the Department of Medical Imaging, the University of Arizona Cancer Center, and the Institute for Collaborative BioResearch (BIO5) at the University of Arizona in Tucson, AZ. These affiliations reflect the interdisciplinary research approach undertaken by CAMEL and the supportive environment for biomedical research at the University of Arizona.

### Teaching Mission

CAMEL supports the teaching and training mission of the University of Arizona. The CAMEL laboratories provide an outstanding training environment for graduate and undergraduate students from a variety of disciplines, including biomedical engineering, chemistry & biochemistry, and cancer biology. In addition, Dr. Pagel regularly teaches a graduate-level course for biomedical engineers, BME 510: "Cell Biology for Engineers", which covers basic cell biology from a quantitative, design-driven perspective. Dr. Pagel also teaches an undergraduate-level course for chemists and biochemists, CHEM 481: "Biophysical Chemistry" that covers quantum mechanics and spectroscopy as applied to biochemistry and biotechnology. These multidisciplinary teaching roles further strengthen the teaching mission of CAMEL.

### History

CAMEL was first established in the Department of Biomedical Engineering at Case Western Reserve University in 2003. Dr. Marty Pagel started this research program after leaving the pharmaceutical industry to return to academia, to contribute to the high-risk high-reward field of molecular imaging. CAMEL pioneered the development of responsive CEST MRI contrast agents in 2003-2005, and demonstrated the first in vivo MRI studies with paramagnetic CEST agents in 2006-2007. CAMEL also developed new synthesis methods to create new types of MRI contrast agents.

In 2008, Dr. Pagel moved CAMEL to the University of Arizona, in Tucson AZ. This transition provided CAMEL with resources and opportunities to collaborate with cancer biology researchers in the University of Arizona Cancer Center, and access to resources in the Departments of Biomedical Engineering, Chemistry & Biochemistry, and Medical Imaging. The combination of these diverse resources and multidisciplinary collaborators has been essential to the continued productivity of CAMEL. Furthermore, the collaborative research environment at the University of Arizona has greatly facilitated the expansion of CAMEL's research interests into optical imaging and clinical imaging. CAMEL has found an ideal home in the desert!

## Selected Publications

1. Yoo B, Pagel MD. A facile synthesis of  $\alpha$ -amino-DOTA as a versatile molecular imaging probe. *Tetrahedron Lett*, 2006, 47: 7327-7330.
2. Yoo B, Pagel MD. A PARACEST MRI contrast agent to detect enzyme activity. *J. Am. Chem. Soc.*, 2006, 128(43):14032-14033.
3. YooB, Pagel MD. Peptidyl Molecular Imaging Contrast Agents Using a New Solid Phase Peptide Synthesis Approach. *Bioconj. Chem.*, 2007,18: 903-911.
4. Yoo B, Raam M, Rosenblum R, Pagel MD. Enzyme-responsive PARACEST MRI contrast agents: A new biomedical imaging approach for studies of the proteasome. *Contrast Media Molec. Imag.*, 2007, 2:189-198.
5. Liu G, Lu Y, Pagel MD. Design and characterization of new irreversible responsive PARACEST MRI contrast agent that detects nitric oxide. *Magn. Reson. Med.*, 2007, 58:1249-1256.
6. Yoo B, Pagel MD. An overview of responsive MRI contrast agents for molecular imaging. *Front. Bioscience*, 2008, 13:1733-1752.
7. Sheth VR, van Heeckeren RC, Wilson AG, van Heeckeren AM, Pagel MD, Monitoring Infection and Inflammation in Murine Models of Cystic Fibrosis with Magnetic Resonance Imaging, *J Magn Reson Imaging*, 2008, 28(2):527-532.
8. Liu G, Ali, M, Yoo B, Griswold MA, Tkach JA, Pagel MD. PARACEST MRI With Improved Temporal

9. Ali MM, Yoo B, Pagel MD. Tracking the relative in vivo pharmacokinetics of nanoparticles with PARACEST MRI. *Molec Pharmaceutics*, 2009, 6(5):1409-1416.
10. Yoo B, Sheth V, Pagel MD. An amine-derivatized, DOTA-loaded polymeric support for Fmoc Solid Phase Peptide Synthesis. *Tet Lett*, 2009, 50:4459-4462.
11. Ali MM, Liu G, Shah T, Flask CA, Pagel MD. Using Two Chemical Exchange Saturation Transfer Magnetic Resonance Imaging Contrast Agents for Molecular Imaging Studies. *Acc Chem Res*, 2009, 42(7):915-924.
12. Shah T, Lu L, Dell K, Pagel MD, Griswold M, Flask CA. CEST-FISP: A Novel Technique for Rapid Chemical Exchange Saturation Transfer (CEST) MRI at 7T. *Magn Reson Med* 2011, 65:432-437.
13. Li Y, Sheth VR, Liu G, Pagel MD. A self-calibrating PARACEST MRI contrast agent that detects esterase enzyme activity. *Contrast Media Molec. Imaging*, 2011, 6(4):219-228.
14. Pagel MD. The hope and hype of multimodality imaging contrast agents. *Nanomed.*, 2011, 6(6):945-948.
15. Pagel MD. Responsive paramagnetic chemical exchange saturation transfer MRI contrast agents. *Imaging Med.*, 2011, 3(4):377-380.
16. Josan JS, De Silva CR, Yoo B, Lynch RM, Pagel MD, Vagner J, Hruby VJ. Fluorescent and lanthanide labeling for ligand screens, assays, and imaging. *Methods Molecular Biol.*, 2011, 716:89-126.
17. Sheth VR, Li Y, Chen LQ, Howison CM, Flask CA, Pagel MD. Measuring in vivo tumor pHe with CEST-FISP MRI. *Magn. Reson. Med.*, 2012, 67:760-768.
18. Liu G, Li Y, Sheth VR, Pagel MD. Imaging in vivo extracellular pH with a Single PARACEST MRI Contrast Agent. *Molecular Imaging*, 2012, 11(1):47-57.
19. Sheth VR, Liu G, Li Y, Pagel MD. Improved pH measurements with a single PARACEST MRI contrast agent. *Contrast Media Molec. Imaging*, 2012, 7:26-34.
20. Cardenas-Rodriguez J, Li Y, Galons JP, Connell H, Pagel MD, Baker AF. Imaging biomarkers to monitor response to the hypoxia-activated prodrug TH-302 in the MiaPaCa2 flank xenograft model. *Magn. Reson. Imaging*, 2012, 30:1002-1009.
21. Ali MM, Bhuiyan MPI, Janic B, Varma NRS, Mikkelsen T, Ewing JR, Knight RA, Pagel MD, Arbab AS. A nano-sized PARACEST-fluorescence imaging contrast agent facilitates & validates in vivo CEST MRI detection of glioma. *Nanomed.*, 2012, in press. Epub published 8/14/12.
22. Zhang X, Pagel MD, Baker AF, Gillies RJ. Reproducibility of MR perfusion imaging with Gd-DTPA and P792. *Magn. Reson. Med.*, 2012, in press.
23. Stephen R, Pagel MD, Brown K, Baker AF, Meuillet EJ, Gillies RJ. Monitoring the development of xenograft triple negative breast cancer models using diffusion-weighted MRI. *Exp. Biol. Med.*, 2012, in press.
24. Cardenas-Rodriguez J, Howison CM, Pagel MD. A linear algorithm of the reference region model for DCE-MRI is robust and relaxes requirements for temporal resolution. *MRI*, 2013, 31(4):497-507. PMID 23228309.
25. Yoo B, Pagel MD. Lanthanide-Mediated Dephosphorylation Used for Peptide Cleavage during Solid Phase Peptide Synthesis. *Molecules*, 2013, 18, 3894-3905. PMID 23549296.
26. Hingorani DV, Randtke EA, Pagel MD. A CatalyCEST MRI Contrast Agent That Detects the Enzyme-Catalyzed Creation of a Covalent Bond. *J Am Chem Soc*, 2013, 135 (17):6396-6398. PMID 23601132.
27. Cardenas-Rodriguez J, Howison CM, Matsunaga TO, Pagel MD. A reference agent model for DCE MRI can be used to quantify the relative vascular permeability of two MRI contrast agents. *MRI*, 2013, 31:900-910. PMID 23583323.
28. Yoo B, Sheth VR, Howison CM, Douglas MJK, Pineda CT, Maine EA, Baker AF, Pagel MD.

Detection of In Vivo Enzyme Activity with CatalyCEST MRI. *Mag Reson Med*, 2013, available online. PMID 23640714.

29. Randtke EA, Chen LQ, Correales LR, Pagel MD. The Hanes-Woolf Linear QUESP Method Improves the Measurements of Fast Chemical Exchange Rates with CEST MRI. *Magn Reson Med*, 2013, epub ahead of print, PMID 23780911.

30. Hingorani DV, Gonzalez SI, Li JF, Pagel MD. Sensing Lanthanide Metal Content in Biological Tissues with Magnetic Resonance Spectroscopy. *Sensors*, 2013, 13:13732-13743. PMID 24152931.

31. Rantke EA, Chen LQ, Pagel MD. The reciprocal linear QUEST analysis method facilitates the measurements of chemical exchange rates with CEST MRI. *Contrast Media Molec Imaging*, 2013, in press.

32. Chen LQ, Howison CM, Jeffery JJ, Robey IF, Kuo PH, Pagel MD. Evaluations of extracellular pH within in vivo tumors using acidoCEST MRI. *Magn Reson Med*, 2013, in press.

33. Jeffery JJ, Lux K, Vogel JS, Herrera WD, Greco S, Woo HH, AbuShahin N, Pagel MD, Chambers SK. Autocrine inhibition of the c-fms proto-oncogene reduces breast cancer bone metastasis assessed with in vivo dual-modality imaging. *Exp. Bio. Med.*, 2013, accepted for publication.

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