MICHAEL J. KNAPP

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Research Experience:

Associate Professor (2009 – present), Assistant Professor (2002 – 2009), University of Massachusetts–Amherst

Molecular Mechanisms of Hypoxia Sensing

Enzymology of human HIF-hydroxylases; O_2-activation in α-ketoglutarate-dependent Fe(II) oxygenases; Uncoupled O_2-activation; hypoxia.

Charge transfer in protein-nanoparticle hybrid materials

Kinetics of interprotein electron-transfer on nanoparticle surfaces; protein-nanoparticle dynamics; bio-nanotechnology.

Fluorescence sensing

Developing small molecules for detection of explosives and environmental contaminants. Inorganic synthesis, lifetime and steady-state fluorescence measurements.

NIH Postdoctoral Fellow, University of California, Berkeley 1998–2002
Advisor: Professor Judith P. Klinman
Hydrogen tunneling and O_2 reactivity of lipoxygenase.

Research Assistant, University of California, San Diego 1993–1998
Advisor: Professor David N. Hendrickson
Electronic structure and magnetic exchange interactions in metal clusters.

Education:

Ph.D., Chemistry; University of California, San Diego 1998
Advisor: Professor David N. Hendrickson
Thesis title: "Spectroscopic Properties of Iron-Sulfur Model Systems: High-Field EPR and Electronic Structure Calculations"

B.S., Biochemistry and Cell Biology; University of California, San Diego 1993
Advisor: Professor Paul Saltman

Research Interests:

Enzymology of oxygen sensing; relevant to angiogenesis and cancer metastasis
Interprotein charge-transfer reactions

Research Group Summary

Graduate students (all Ph.D. track)

Vanessa Chaplin 12/12 - present

Undergraduate students

2 current

Graduated students

Christina Martin (2015, defended PhD)
Cornelius Taabazuing (2015 PhD)
John Hangasky (2014 PhD)
Meaghan Valliere (PS Honors thesis)
Serap Pektas (2013, PhD)
Kate Liedell (2013, BS Honors thesis)
Tyler ONeil (2013, BS Honors thesis)
Jaqueline Dorhout (B.S. honors thesis, 2012)
Shannon Coates,(02/2006- 06/11) PhD
Evren Saban, (02/2006 – 05/11) PhD
Breanne Holmes (02/2010 – 08/2011) M.S.
Yuan-Han (Robert) Chen, 2003 – 2009, PhD.
Adrienne Gilbert-Carver, 02/04 – 05/09, PhD.
Halil Bayraktar (02/2004 – 06/2008) PhD.
Meaghan Germain (02/2004 – 06/2008) Ph.D.
Tom Vargo, (B.S. honors thesis, 2006)
Todd Ratacjzak (B.S. honors thesis, 2006)

Teaching Experience:

University of Massachusetts, Amherst 2002 – present

Undergraduate:

General Chemistry; Honors General Chemistry
Intermediate Descriptive Inorganic Chemistry – lab and lecture
Inorganic Chemistry
Caveman Chemistry- Honors Colloquium for Int. Inorg. Chem.
FFYS: Chemical Technology of AmerIndians
FFYS: Nuclear Chemistry

Graduate:

Coordination Chem.
Metals in Biology
CORE
Enzymology
Journal clubs: EPR as a Research Technique; Reaction Mechanisms; Bioinorganic chemistry; Zebrafish and Metalloenzymes

Awards and Memberships:

NIH Postdoctoral Fellowship
NIH Predoctoral Trainee
Member, American Chemical Society
Division of Inorganic Chemistry
Division of Biological Chemistry

Reviewer for:

Funding Agencies: NSF, NIH, ACS-PRF, Burroughs Welcome Fund
Journals: Inorg. Chem., Biochemistry, Trends in Biotech., PNAS, J. Am. Chem. Soc., Chem. Soc. Rev., Org. Lett., Photosynth. Res., Biochemistry, Chem. Commun. J. Inorg. Biochem.

Sponsored Research

Active

2R01-GM077413-06 (renewal) Knapp (PI) 2015 – 2019
National Institutes of Health
"Molecular Mechanisms of Hypoxia Sensing by the HIF-hydroxylases,"
$1.1M (total) 4-years ($190K direct, year 1)

Completed

1R01-GM077413 Knapp (PI) 2007-2012
National Institutes of Health
"Molecular Mechanisms of Hypoxia Sensing by the HIF-hydroxylases,"
$722K (direct)

Michael J. Knapp (PI) 2013 –2015
Rays of Hope (subaward)
"Sulfur metabolites increase cancer risk by disrupting the HIF pathway"
$ 25,000 total (no indirect)

Michael J Knapp, PI 08/13 – 07/13
Proctor and Gamble, "Screening HIF hydroxylase inhibitors"
$7500 total

Mellon Mutual Mentoring Chambers (PI), Knapp (co-PI) 06/08 – 12/09
"Chemical Biology Group"
$10,000 (total) 1-year

PRF40033-G4 Knapp (PI) 9/1/03–8/31/05
American Chemical Society – Petroleum Research Fund
"Quantum Effects in Catalysis: H-Atom Transfer in C-H Oxidation"
Explored the relevance of tunneling as an alternative catalytic strategy.
$35,000 total

IRG 93-033 3/1/05 – 2/28/06
American Cancer Society – Individual Allocation from Institutional Research Grant
"Protein Conformation Changes in Hypoxia Sensing"
Seed grant to develop biophysical and kinetic studies of FIH.
$20,000 (total)

FRG/Healy Endowment (internal) Knapp (PI) 6/1/05 – 5/31/06
University of Massachusetts, Amherst
"Inhibiting Protein-Protein Recognition with Nanomaterials"
The goal of this study is to develop high-throughput screening assay for inhibitors of protein-protein recognition.
$30,000 (total)

FRG (internal) Knapp (PI) 11/01/03 – 4/1/04
University of Massachusetts, Amherst
"Enzymology of Oxygen-Dependent Gene Regulation"
This grant provided seed money to develop heterologous expression of HIF hydroxylases.
$12,000 (total)

Publications

(44) Taabazuing, CY; Fermann, J; Garman, S; Knapp, MJ. "Substrate promotes productive gas binding in the αKG-dependent oxygenase FIH" Biochemistry, (2015). Revision requested.

(43) CY Taabazuing, JA Hangasky, MJ Knapp. "Oxygen sensing strategies in mammals and bacteria." J Inorg Biochem. **133**(2014):63-72.

(42) Light KM, Hangasky JA, Knapp MJ, Solomon EI.* "First- and second-sphere contributions to Fe(ii) site activation by cosubstrate binding in non-heme Fe enzymes." Dalton Trans. **43**(2014):1505-8.

(41) Pektas S, **Knapp MJ**.*, "Substrate preference of the HIF-prolyl hydroxylase-2 (PHD2) and substrate-induced conformational change." J Inorg Biochem. 2013 Sep;126:55-60.

(40) K. Light, J.A. Hangasky, M.J. Knapp,* E.I. Solomon,* "Spectroscopic Studies of the Mononuclear Nonheme FeII Enzyme FIH: Second–Sphere Contributions to Reactivity." J Am Chem Soc. (2013) 135(26):9665-74.

(39) J.A. Hangasky, C.Y. Taabazuing, M.A. Valliere and M.J. Knapp.* "Imposing function down a (cupin)-barrel: seconday structure and metal stereochemistry in the alpha-KG-dependent oxygenases." Metallomics(2013)

(38) J.A. Hangasky, E. Saban and M.J. Knapp.* "Kinetic evidence of aquo release from the Fe(II) alpha-KG dependent hydroxylase, factor inhibiting HIF." Biochemistry (2012).

(37) S.C. Flagg, N. Giri, S. Pektas, M.J. Maroney and M.J. Knapp.* "Inverse Solvent Isotope Effects Demonstrate Slow Aquo Release from Hypoxia Inducible Factor-Prolyl Hydroxylase (PHD2)." Biochemistry **51**(2012): 6654-6666.

(36) S.C. Flagg, C.B. Martin, C.Y. Taabazuing, B.E. Holmes and M.J. Knapp.* "Screening chelating inhibitors of HIF-Prolyl Hydroxylase Domain 2 (PHD2) and Factor Inhibiting HIF (FIH)." J. Inorg. Biochem. **113**(2012): 25-30.

(35) E. Saban, Y.-H. Chen, J. A. Hangasky, C. Y. Taabazuing, B. E. Holmes, M. J. Knapp,* "The Second Coordination Sphere of FIH Controls Hydroxylation," *Biochemistry,* **2011** *50* (21), 4733–4740.

(34) E. Saban,, S. C. Flagg, M. J. Knapp,* "Uncoupled O2-activation in the human HIF-asparaginyl hydroxylase, FIH, does not produce reactive oxygen species," *J. Inorg. Biochem.* **2011** *105* 630–636.

(33) Germain, M.E.; Knapp, M.J.* "Optical Explosives Detection: from Color Changes to Fluorescence Turn-On," *Chem. Soc. Rev.* **2009** *38*(9), 2543-2555.

(32) Carver, A.C.; De, M.; Bayraktar, H.; Rana, S.; Rotello, V.M.; Knapp, M. J.*; "Intermolecular Electron-Transfer Catalyzed on Nanoparticle Surfaces," *J. Am. Chem. Soc.*, **2009**, *131*(11), 3798-3799.

(31) Carver, A. C.; Knapp, M. J.* "Electron and energy transfer reactions of $[Ru(bpy)_3]^{2+*/3+}$ with copper-phenolates," *Polyhedron* **2008**, *27*, 3313-3317.

(30) Chen, Y.-H.; Comeaux, L. M.; Herbst, R. M.; Saban, E.; Kennedy, D. C.; Maroney, M. J.; Knapp, M. J.* "Coordination changes and auto-hydroxylation of FIH-1: uncoupled O_2-activation in a human hypoxia sensor," *J. Inorg. Biochem.* **2008**, *102* 2120–2129. *Part of the "Young Investigators Issue*."

(29) Germain, M. E.; Knapp, M. J.* "Turn-on fluorescence detection of H_2O_2 and TATP," *Inorg. Chem.* **2008**, *47*, 9748-9750.

(28) Germain, M. E.; Vargo, T. R.; McClure, B. A.; Rack, J. J.; Van Patten, P. G.; Odoi, M.; Knapp, M. J.* "Quenching Mechanism of Zn(Salicylaldimine) by Nitroaromatics," *Inorg. Chem.* **2008**, *47*, 6203-6211.

(27) Germain, M. E.; Knapp, M. J.* "Discrimination of nitroaromatics and explosives mimics by a fluorescent Zn(salicylaldimine) sensor array," *J. Am. Chem. Soc.* **2008**, *130*, 5422-5423.

(26) Chen, Y.-H.; Comeaux, L. M.; Eyles, S. J.; Knapp, M. J.* "Auto-hydroxylation of FIH-1, an Fe(II), α-ketoglutarate dependent human hypoxia sensor," *Chem. Commun.* **2008**, 4768 - 4770.

(25) Bayraktar, H.; Srivastava, S.; You, C. C.; Rotello, V. M.*; Knapp, M. J.* "Controlled nanoparticle assembly through protein conformational changes," *Soft Matter* **2008**, *4*, 751-756. ***Cover article***

(24) Sandanaraj, B. S.; Bayraktar, H.; Krishnamoorthy, K.; Knapp, M. J.*; Thayumanavan, S.* "Recognition and modulation of cytochrome c's redox properties using an amphiphilic homopolymer," *Langmuir* **2007**, *23*, 3891-3897.

(23) Germain, M. E.; Vargo, T. R.; Khalifah, P. G.; Knapp, M. J.* "Fluorescent Detection of Nitroaromatics and 2,3-Dimethyl 2,3-dinitrobutane (DMNB) by a Zinc Complex: (salophen)Zn," *Inorg. Chem.* **2007**, *46*, 4422-4429.

(22) Bayraktar, H.; You, C. C.; Rotello, V. M.*; Knapp, M. J.* "Facial control of nanoparticle binding to cytochrome c," *J. Am. Chem. Soc.* **2007**, *129*, 2732-2733.

(21) You, C. C.; Agasti, S. S.; De, M.; Knapp, M. J.; Rotello, V. M.* "Modulation of the catalytic behavior of alpha-chymotrypsin at monolayer-protected nanoparticle surfaces," *J. Am. Chem. Soc.* **2006**, *128*, 14612-14618.

(20) Bayraktar, H.; Ghosh, P. S.; Rotello, V. M.*; Knapp, M. J.* "Disruption of protein-protein interactions using nanoparticles: inhibition of cytochrome c peroxidase," *Chem. Commun.* **2006**, 1390-1392.

(19) Knapp, M. J.; Meyer, M. M.; Klinman, J. P. In *Handbook of Hydrogen Transfer, Vol; 2: Biological Aspects of Hydrogen Transfer*; Schowen, R. L., Klinman, J. P., Eds.; VCH: Weinheim, 2006.

(18) Knapp, M. J.; Klinman, J. P. "Kinetic studies of oxygen reactivity in soybean lipoxygenase-1," *Biochemistry* **2003**, *42*, 11466-11475.

(17) Sanudo, E. C.; Grillo, V. A.; Knapp, M. J.; Bollinger, J. C.; Huffman, J. C.; Hendrickson, D. N.; Christou, G. "Tetranuclear manganese complexes with dimer-of-dimer and ladder structures from the use of a bis-bipyridyl ligand," *Inorg. Chem.* **2002**, *41*, 2441-2450.

(16) Knapp, M. J.; Rickert, K.; Klinman, J. P. "Temperature-dependent isotope effects in soybean lipoxygenase-1: Correlating hydrogen tunneling with protein dynamics," *J. Am. Chem. Soc.* **2002**, *124*, 3865-3874.

(15) Knapp, M. J.; Klinman, J. P. "Environmentally coupled hydrogen tunneling - Linking catalysis to dynamics," *Eur. J. Biochem.* **2002**, *269*, 3113-3121.

(14) Francisco, W. A.; Knapp, M. J.; Blackburn, N. J.; Klinman, J. P. "Hydrogen tunneling in peptidylglycine alpha-hydroxylating monooxygenase," *J. Am. Chem. Soc.* **2002**, *124*, 8194-8195.

(13) Knapp, M. J.; Seebeck, F. P.; Klinman, J. P. "Steric control of oxygenation regiochemistry in soybean lipoxygenase-1," *J. Am. Chem. Soc.* **2001**, *123*, 2931-2932.

(12) Krzystek, J.; Telser, J.; Knapp, M. J.; Hendrickson, D. N.; Aromi, G.; Christou, G.; Angerhofer, A.; Brunel, L. C. "High-frequency and -field electron paramagnetic

resonance of high-spin manganese(III) in axially symmetric coordination complexes," *Appl. Magn. Reson.* **2001**, *21*, 571-585.

(11) Maes, E. M.; Knapp, M. J.; Czernuszewicz, R. S.; Hendrickson, D. N. "Ligand conformational effects on the resonance Raman signature of $[Fe_4S_4(SAryl)_4]^{2-}$ clusters," *J. Phys. Chem. B* **2000**, *104*, 10878-10884.

(10) Knapp, M. J.; Krzystek, J.; Brunel, L. C.; Hendrickson, D. N. "High-frequency EPR study of the ferrous ion in the reduced rubredoxin model $[Fe(SPh)_4]^{2-}$," *Inorg. Chem.* **2000**, *39*, 281-288.

(9) Brechin, E. K.; Knapp, M. J.; Huffman, J. C.; Hendrickson, D. N.; Christou, G. "New hexanuclear and octanuclear iron(III) oxide clusters: octahedral $[Fe_6O_2]^{14+}$ species and core isomerism in $[Fe_8O_4]^{16+}$ complexes," *Inorg. Chim. Acta* **2000**, *297*, 389-399.

(8) Knapp, M. J.; Krzystek, J.; Brunel, L. C.; Hendrickson, D. N. "High-field EPR study of resonance-delocalized $[Fe_2(OH)_3(tmtacn)_2]^{2+}$," *Inorg. Chem.* **1999**, *38*, 3321-3328.

(7) Grant, C. M.; Stamper, B. J.; Knapp, M. J.; Folting, K.; Huffman, J. C.; Hendrickson, D. N.; Christou, G. "Syntheses, crystal structures and properties of mononuclear chromium(III) and dinuclear vanadium(III) and copper(II) complexes with a bis-bipyridyl ligand," *J. Chem. Soc. Dalton* **1999**, 3399-3405.

(6) Aromi, G.; Knapp, M. J.; Claude, J. P.; Huffman, J. C.; Hendrickson, D. N.; Christou, G. "High-spin molecules: Hexanuclear Mn-III clusters with $[Mn_6O_4X_4]^{6+}$ (X = Cl-, Br-) face-capped octahedral cores and S=12 ground states," *J. Am. Chem. Soc.* **1999**, *121*, 5489-5499.

(5) Seela, J. L.; Knapp, M. J.; Kolack, K. S.; Chang, H. R.; Huffman, J. C.; Hendrickson, D. N.; Christou, G. "Structural and magnetochemical properties of mono-, di-, and trinuclear Manganese(III) dithiolate complexes," *Inorg. Chem.* **1998**, *37*, 516-525.

(4) Grant, C. M.; Knapp, M. J.; Streib, W. E.; Huffman, J. C.; Hendrickson, D. N.; Christou, G. "Dinuclear and hexanuclear iron(III) oxide complexes with a bis(bipyridine) ligand: A new $[Fe_6(mu_3\text{-}O)_4]^{10+}$ core," *Inorg. Chem.* **1998**, *37*, 6065-6070.

(3) Grant, C. M.; Knapp, M. J.; Huffman, J. C.; Hendrickson, D. N.; Christou, G. "A new structural type in iron carboxylate cluster chemistry via use of bis-bipyridine ligands: $[Fe_6O_4Cl_4(O_2CPh)_4L\text{-}2][FeCl_4]_2$," *Chem. Commun.* **1998**, 1753-1754.

(2) Aromi, G.; Claude, J. P.; Knapp, M. J.; Huffman, J. C.; Hendrickson, D. N.; Christou, G. "High-spin molecules: Hexanuclear $[Mn_6O_4Cl_4(Me_2dbm)6]$ (Me_2dbmH = 4,4 '-dimethyldibenzoylmethane) with a near tetrahedral $[Mn_6O_4Cl_4]^{6+}$ core and a S=12 ground state," *J. Am. Chem. Soc.* **1998**, *120*, 2977-2978.

(1) Grillo, V. A.; Knapp, M. J.; Bollinger, J. C.; Hendrickson, D. N.; Christou, G. "Bis(bipyridine) ligands in manganese carboxylate cluster chemistry: Self-assembly of a cluster complex with two butterfly-like $[Mn_4(mu_3\text{-}O)_2]^{8+}$ cores," *Angew. Chem. Int. Ed.* **1996**, *35*, 1818-1820.