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PROFESSIONAL TRAINING AND EMPLOYMENT HISTORY

- B. S. Biochemistry - April 1993, Brigham Young University, Provo, Utah.
- Ph. D. Biochemistry - July 23, 1998, University of Wisconsin-Madison, Madison Wisconsin, with Inorganic Chemistry Minor, Dissertation: The nickel processing system involved in the insertion of nickel into CO-dehydrogenase of Rhodospirillum rubrum. Dissertation Advisor; Paul W. Ludden.
- Postdoctoral Research - August 1998-August 2000, Princeton University, Department of Chemistry, Princeton New Jersey, Research areas: Photosynthesis, Biochemistry, Biophysical Chemistry, and Inorganic Chemistry. Postdoctoral advisor: G. Charles Dismukes.
- Assistant Professor - August 2000-May 2006, The University of New Mexico, Department of Chemistry, Albuquerque, NM. Bioinorganic chemistry.
- Assistant Professor - July 2006-2012, Brigham Young University, Department of Chemistry and Biochemistry, Provo, UT. Bioinorganic chemistry
- Associate Professor – August 2012-Present, Brigham Young University, Department of Chemistry and Biochemistry, Provo, UT. Bioinorganic chemistry

SUMMARY OF RESEARCH

Biological Trace Mineral Research.

Biological systems require trace amounts of transition metal ions to sustain life. Transition metal ions are required at the active sites of many enzymes for catalytic activity. In fact, transition metals catalyze some of the most energetically demanding reactions in biology. Unfortunately, these highly reactive metal ions also catalyze reactions that are dangerous for biological systems, especially if the metal ion is free in solution. For this purpose biology has evolved elaborate transition metal ion handling systems to bind and sequester transition metal ions in non-reactive environments to prevent these dangerous reactions from occurring. The Watt lab focuses on how metals are properly moved throughout the body.

A healthy individual possesses iron trafficking systems to absorb iron from the diet, transport iron in the bloodstream and deliver iron to cells that require iron. The failure or inhibition of these iron trafficking systems results in free iron that is a potent catalyst to form reactive oxygen species or oxidative stress.

The Watt lab studies diseases where iron trafficking is disrupted and oxidative stress is elevated. Such conditions include Alzheimer's disease, Parkinson's disease, kidney disease, Diabetes along with other conditions.

Anemia of Chronic Inflammation Caused by Hepcidin.

Hepcidin is an iron regulatory hormone induced by inflammation that degrades the iron transport protein ferroportin. Hepcidin causes a condition known as anemia of chronic inflammation. Ferroportin is required to transport iron into the bloodstream from the intestinal cells that absorb iron from the diet. Ferroportin also exports iron from the liver, and spleen into the bloodstream where transferrin binds iron and delivers iron to the bone marrow for red blood cell synthesis. The Watt lab has identified hepcidin inhibitors that prevent hepcidin production and stabilize ferroportin. Studies in rats show that iron delivery to the bone marrow is restored using these hepcidin inhibitors.

Alzheimer's Disease

Iron dysregulation is intimately connected to Alzheimer's disease (AD) but the direct connections are not clear. A new hypothesis relating to homocysteine disrupting iron loading into ferritin might explain the elevated cytosolic iron and oxidative stress. The inability to load iron into ferritin results in elevated cytosolic iron which upregulates expression of the Amyloid Precursor Protein (APP). Homocysteine also inhibits the phosphatase that dephosphorylates tau leading to elevated hyper-phosphorylated tau and tau tangles.

Diagnostics

Many inflammatory events accompany metal dysregulation in the body. Biomarkers for many diseases are known. Beneficial treatments that move these biomarkers towards healthy status need to be monitored by diagnostic tests. The Watt lab has developed several innovations to simplify the rapid diagnostic test called a lateral flow immunoassay (LFI). The test developed in the Watt lab is called the simple empowering LFI or seLFI because its lower production cost will allow it to be used daily to monitor markers of health. Additionally, we have developed an antibody pen that allows different markers to be tested depending on the current needs of the individual. We anticipate that these innovative tests will aid individuals and clinical practitioners to identify the most beneficial and effective treatment.

PUBLICATIONS

Articles in Refereed Journals:

1. Watt, R. K., Frankel, R. B., Watt, G. D., Redox Reactions of Apo Mammalian Ferritin, (1992) Biochemistry 31, 9673-9679.
2. Heqing, H., Watt, R. K., Frankel, R. B., Watt, G. D., Role of Phosphate in Fe2+ Binding to Horse Spleen Holoferritin, (1993) Biochemistry 32, 1681-1687.
3. Watt, R. K., Ludden, P. W., The Identification, Purification and Characterization of CooJ: A Nickel-Binding Protein that is Co-Regulated with the Nickel-Containing CO-Dehydrogenase from Rhodospirillum rubrum, (1998) J. Biol. Chem. 273, 10010-10025.

4. Johnson, J. L., Cannon, M., Watt, R. K., Frankel, R. B., Watt, G. D., Forming the phosphate layer in reconstituted horse spleen ferritin and the role of phosphate in promoting core surface redox reactions, (1999) Biochemistry, 38, 6706-6713.
5. Watt, R. K., Ludden, P. W., Nickel Transport in Rhodospirillum rubrum (1999) The Journal of Bacteriology 181, 4554-4560.
6. Büchel, C., Barber, J., Ananyev, G., Eshaghi, S., Watt, R., Dismukes, C., Photoassembly of the manganese cluster and oxygen evolution from monomeric and dimeric CP47-reaction centre photosystem II complexes, (1999) Proc. Natl. Acad. Sci. 96, 14288-14293.
7. Watt, R. K., Ludden, P. W., Nickel Binding Proteins. Cellular and Molecular Life Sciences (1999) 56, 604-625.
8. Song, Y. J., Challa, S. R., Medforth, C, J., Qiu, Y., Watt, R.K., Pena, D., Miller, J.E., van Swol, F. Shelnutt, J.A., Synthesis of peptide-nanotube platinum-nanoparticle composites. Chemical Communications; (2004), no.9, p.1044-1045.
9. Polanams, J., Ray, A. D., Watt R. K., Nanophase Iron Phosphate, Iron Arsenate, Iron Vanadate and Iron Molybdate Minerals Synthesized within the Protein Cage of Ferritin, Inorganic Chemistry, (2005) 44, 3204-3209.
10. Cutler, C., Bravo, A., Ray, A. D., Watt, R. K., Iron Loading into Ferritin can be Stimulated or Inhibited by the Presence of Cations and Anions: A Specific Role for Phosphate. Journal of Inorganic Biochemistry, (2005) 99, 2270-2275.
11. Zhang, B., Watt, R. K., Galvez, N., Dominguez-Vera, J. M., Watt, G. D., Rate of Iron Transfer through the Horse Spleen Ferritin Shell Determined by Formation of Prussian Blue and Fe-Desferrioxamine in the Ferritin Cavity. Biophysical Chemistry (2006) 120, (2) 96-105.
12. Tyryshkin, A. M., Watt, R. K., Baranov, S. V., Dasgupta, J., Hendrich, M. P., Dismukes, G. C., Spectroscopic evidence for Ca2+ involvement in the assembly of the Mn4Ca cluster in the photosynthetic water-oxidizing complex. Biochemistry (2006) 45, (43) 12876-12889.
13. Zhang, F., Gates, R. J., Smentkowski, V. S., Natarajan, S., Gale, B. K., Watt, R. K., Asplund, M. C., Linford, M. R., Direct Adsorption and Detection of Proteins, Including Ferritin, onto Microlens Array Patterned Bioarrays, J. Am. Chem. Soc. (2007), 129, 9252-9253.
14. Shin, K. M., Watt, R. K., Watt, G. D., Choi, S. H., Kim, H. H., Kim, S. I., Kim, S. J., Characterization of ferritin core on redox reactions as a nanocomposite for electron transfer. Electrochimica Acta (2010), 55, (10) 3486-3490.
15. Watt, R.K., Hilton, R. J., Graff, D. M., Oxido-Reduction is not the Only Mechanism Allowing Ions to Traverse The Ferritin Protein Shell (Invited Review), Biochim. Biophys. Acta (2010), 1800, 745-759.
16. Johnson J. Kenealey, J., Hilton, R.J., Bronsahan, D., Watt, R.K., Watt, G.D., Non-reductive iron release from horse spleen ferritin using desferoxamine chelation, J. Inorg. Biochem. (2011), 105, 202-207.

17. Watt, R.K., The many faces of the octahedral protein ferritin (Invited Review), BioMetals, (2011) 24 (3), 489-500.
18. Alejandro E. Yevenes, A. E., Marquez, V., Watt, R. K., Cloning and characterization of Chlorobium tepidum Ferritin, Biochimie (2011) 93 352-360.
19. Keyes, J. D., Hilton, R. J., Farrer, J., Watt, R. K., Ferritin as a Photocatalyst for Gold Nanoparticle Synthesis, Journal of Nanoparticle Research (2011) 13, 2563-2575.
20. Snow, C., Martineau, L. N., Hilton, R. J., Brown, S., Farrer, J., Boerio-Goates, J., Woodfield, B. F., Watt, R. K., Ferritin iron mineralization proceeds by different mechanisms in MOPS and imidazole buffers, J. Inorg. Biochem. (2011) 105, 972-977.
21. Orihuela, R., Fernández, B., Atrian, S., Watt, R. K., Domínguez-Vera, J. M., Capdevila, M. Ferritin and Metallothionein: Dangerous Liaisons. Chem. Comm. (2011) 28, 47(44). 12155-7.
22. López-Castro, J. D., Delgado, J. J., Perez-Omil, J. A., Gálvez, N., Cuesta, R., Watt R. K., Domínguez-Vera, J. M. A New Approach to the Ferritin Iron Core Growth: The Core Shape is a Fingerprint of the Protein Capsid Composition. Dalton Trans. (2012) **41**, 1320–1324.
23. Hilton, R. J., Andros, N. D., Watt, R. K., The Ferroxidase Center is Essential for Ferritin Iron Loading in the Presence of Phosphate and Minimizes Side Reactions that Form Fe(III)-Phosphate Colloids. BioMetals (2012) 25 (2), 259-273.
24. Hilton, R. J., Zhang, B., Watt, G. D., L. Naomi Martineau, Watt, R. K., Anion Deposition into Ferritin. J. Inorg. Biochem. (2012) 108, 8-14.
25. Hilton, R. J., Seare, M. C., Andros, N. D., Kenealley, Z., Watt, R. K., Phosphate Inhibits In Vitro Fe^{3+} Loading into Transferrin by Forming a Soluble Fe(III)-Phosphate Complex: A Potential Non-Transferrin Bound Iron Species. J. Inorg. Biochem. (2012) 110, 1-7.
26. Watt, R. K., A Unified Model for Ferritin Iron Loading by the Catalytic Center: Implications for Controlling "Free Iron" during Oxidative Stress. ChemBioChem (2013), 14, 415-419.
27. Watt, R. K., Petrucci, O. D., Smith, T., Ferritin as a model for developing 3rd generation nano architecture organic/inorganic hybrid photo catalysts for energy conversion, Catalysis, Science & Technology (2013) 3, 3103-3110.
28. Petrucci, O. D., Buck, D. C., Farrer, J. K., Watt, R. K., A ferritin mediated photochemical method to synthesize biocompatible catalytically active gold nanoparticles: size control synthesis for small (similar to 2 nm), medium (similar to 7 nm) or large (similar to 17 nm) nanoparticles. RSC Advances (2014) 4, (7) 3472-3481.
29. Colton, J. S., Erickson, S. D., Smith, T. J., Watt, R. K., Sensitive detection of surface- and size-dependent direct and indirect band gap transitions in ferritin. Nanotechnology (2014), 25, (13) Article number 135703.
30. Brito C., Matias, C., Gonzalez-Nilo, F. D., Watt, R. K., Yevenes, A., The C-terminal regions have an important role in the activity of the ferroxidase center and the stability of Chlorobium tepidum ferritin. Protein J. (2014), 33, 211-220.

31. Arenas-Salinas, M., Townsend, P. D., Brito, C., Marquez, V., Marabolli, V., Gonzalez-Nilo, F., Matias, C., Watt, R. K., Lopez-Castro, J. D., Dominguez-Vera, J., Pohl, E., Yevenes, A., The crystal structure of ferritin from *Chlorobium tepidum* reveals a new conformation of the 4-fold channel for this protein family. Biochimie (2014), DOI: 10.1016/j.bhichi.2014.07.019.
32. Erickson, S. D., Smith, T. J., Moses, L., Watt, R. K., Colton, J. S., Non-native Co, Mn, and Ti Oxyhydroxide Nanocrystals synthesized within the Protein Ferritin for High Efficiency Solar Energy Conversion. Nanotechnology (2015), 26, 015703.
33. Smith, T. J., Erickson, S. D., Matias Orozco, C., Fluckiger, A., Moses, L. M., Colton, J. S., Watt, R. K., Tuning the Band Gap of Ferritin Nanoparticles by Co-Depositing Iron with Halides or Oxo-anion. *J. Mater. Chem. A*, (2014), 2 (48) 20782-20788.
34. Swensen, A. C., Finnell, J. G., Matias, C, Gross, A. J., Prince, J. T., Watt, R. K., Price, J. C., Whole blood and urine bioactive Hepcidin-25 determination using liquid chromatography mass spectrometry. Analytical Biochemistry (2017), 517, 23-30.
35. Matias, C., Belnap, D. W., Smith, M. T., Stewart, M. G., Torres, I. F., Gross, A. J., Watt, R. K., Citrate and albumin facilitate transferrin iron loading in the presence of phosphate, J. Inorg. Biochem., 168 (2017) 107–113
36. Olsen C. R., Smith, T. J., Embley, J. S., Maxfield, J. H., Hansen, K. R., Peterson, J. R., Henrichsen, A. M., Erickson, S D., Buck, D. C., Colton, J. S., Watt, R. K., Permanganate-based synthesis of manganese oxide nanoparticles in ferritin, nanotechnology, 28 (2017), 195601, https://doi.org/10.1088/1361-6528/aa68ae.
37. Olsen, C.R., Embley, J. S., Hansen, K. R., Henrichsen, A. M., Peterson, J. R., Colton, J. S., Watt, R. K., Tuning Ferritin's band gap through mixed metal oxide nanoparticle formation, Nanotechnology, 28, (2017) 195604, https://doi.org/10.1088/1361-6528/aa68b0.
38. Hansen, K. R., Peterson, J. R., Perego, A., Shelley, M., Olsen, C. R., Perez, L. D., Hogg, H. L., Watt, R. K., Colton, J. S., (2018) Leas sulfide quantum dots inside ferritin: synthesis and application to photovoltaics. Applied Nanoscience, 8(7), 1687-1699.
39. Petrucci, O. D., Hilton, R. J, Farrer, J. K., Watt, R. K., A Ferritin Photochemical Synthesis of Monodispersed Silver Nanoparticles that Possess Antimicrobial Properties. Journal of Nanomaterials, Volume 2019, Article ID 9535708, 8 pages, https://doi.org/10.1155/2019/9535708.
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41. Souza E., Cho, K., Harris, S.T., Flindt, N. R., Watt, R. K., Pai, A. B., Hypoxia-inducible factor prolyl hydroxylase inhibitors: a paradigm shift for treatment of anemia in chronic kidney disease? Expert Opinions on Investigational Drugs (2020), https://doi.org/10.1080/13543784.2020.1777276.
42. Hedges, D.M., Yorgason, J.T., Perez, A.W., Schilaty, N.D., Williams, B.M., Watt, R.K., and Steffensen, S.C. Spontaneous formation of melanin from dopamine in the presence of iron. Antioxidants (2020) doi.org:10.3390/antiox9121285

43. Adhikari, R, Steed, K. S., Hutchinson, B, Wan, H., Mendoza, M.,Staudte, R., Atmojo, M., Cox, P., Barkdull, K., Harris, M., Watt, R., Bangerter, N., Wisco, J. Hippocampal T2 signal loss and decreased radial arm maze performance in transgenic murine model for AD. Brain and Nerves (2020) Vol. 5, pp. 1-8 doi: 10.15761/JBN.1000127.

Chapters Appearing in Edited Volumes:

1. Dismukes, G. C., Ananyev, G. M., Watt, R. K., The Assembly of the Inorganic Core and "Inorganic Mutants" of the Water Oxidizing Complex of Photosystem II: The Water/Plastoquinone Oxido-Reductase In Photosynthesis, T Wydrzynski and K. Satoh Editors; (2005), Springer, The Netherlands. Ch 30. Pp. 683-695.

Patent Applications:

1. Metal catalyzed hydrolysis of cellulose and hemicellulose to produce monomeric carbohydrates for transportation fuel and electrical production. Gerald D. Watt and Richard K. Watt. Patent No: US9,809,613 B2. Issued November 7, 2017.
2. Method and compositions for the treatment of anemia through the inhibition of furin. Richard K. Watt, Chad Hancock, Andrew Gross. Filed February 22, 2017.
3. Hepcidin Inhibitors that Stabilize Ferroportin: An Alternate Method to Release Iron from Tissue for Chelation Therapy in Iron Overload. Provisional patent filed August 8, 2018. 62/715,188.
4. Paper Lateral Flow Immunoassay. Provisional patent filed July 13, 2018. Richard Watt, Annie Pitts, Lara Grether, Kelly Pitts. 62/697,802.
5. The Development of a Biomarker-Antibody Pen, containing "Antibody Ink" or "Biomarker Ink" for the Deposition of Antibodies or Biomarkers on Surfaces, such as Paper, for Immunological Biomarker/Chemical Detection and Diagnostic Applications. Filed 7 Nov. 2018. Application number 62757029.
6. Hepcidin Filters for Removal of Hepcidin, Cytokines and other Molecules. Filed 6 February 2019. Application number 62802086.

Past and Present Consultant Positions, Collaborations and Joint Appointments

- Pfizer
- Rockwell Medical
- Clene NanoMedicine
- Groviv
- Adjunct Professor at Roseman School of Dentistry
- NASA
- China Lake Naval Weapons Laboratory
- Arlington Scientific
- Rocard Labs

Awards

BYU General Education Professorship – University Conference August 2021