Joshua A. Weiner

Dartmouth College
Molecular and Cellular Biology Program
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Education

Dartmouth College, Hanover, New Hampshire, 2008-2014
Ph.D. in Biochemistry, Successfully completed June 30th, 2014

University of New England, Biddeford, Maine, 2004-2008
B.A. in Biochemistry
B.A. in Marine Biology

Awards and Affiliations

MCB Training grant (US NIH #5T32GM008704-13), 2010-2012.
Nomination for the Albert J. Ryans Fellowship, 2012
Dartmouth Graduate Studies Graduate Travel Award, 2014
Biophysical Society Member, 2014
Maine Space Grant (NASA), 2007-2008

Research Experience

Doctoral Research (Research Advisor: Dr. Dale F. Mierke)
Department of Chemistry, Dartmouth College, 2009-2014

Engineering of the Parathyroid Hormone Receptor

- Optimized expression and purification of a soluble, engineered PTH1R protein (natural abundance and ^{13}C, ^{15}N labeled).
- Characterized ePTH1R using circular dichroism, size-exclusion chromatography, and crosslinking.
- Developed point mutants of ePTH1R using site directed mutagenesis.
- Characterized ePTH1R interactions with NHERF by pull-down and NMR.
- Performed backbone assignment using double and triple resonance NMR experiments.
- Evaluated bioactivity using GTP binding and turn-over assays.
- Determined that ePTH1R mimics characteristics of the native receptor and is more amenable to small molecule HTS and biochemical techniques.
- Discovered that both ePTH1R and wtPTH1R bind GTP

Endothelin A and B Receptors

- Optimized expression and purification of recombinantly expressed peptides.
- Optimized expression and purification of engineered soluble Endothelin receptors.

- Investigated hetero- and homo-dimerization using crosslinking, size-exclusion chromatography and pull-down.
- Investigated bio-activity of engineered receptors using GTP binding and turnover assays.
- Characterized the carboxyl terminus of the Endothelin A (ETA) receptor in solution using NMR and created a homology model based on the Bradykinin Receptor.

Undergraduate Research (Research Advisor: Dr. Mark Sweezy)
Department of Chemistry, University of New England, 2006-2008

Role of Rad51 in Homologous Recombination

- Expressed and purified Rad51 in *E. Coli.*
- Characterized protein DNA complexes using Atomic Force Microscopy.
- Evaluated Rad51-DNA complexes using EMSA.
- Determined that Rad51 binds DNA and may aid in formation of holiday junctions during homologous recombination in *Schizosaccharomyces pombe*.

Research Interests

- Improve protein expression and purification methodologies for challenging proteins, such as low solubility and integral membrane proteins.
- Characterize biophysical properties of GPCR's through structural and biochemical methodologies
- Develop new technologies for the identification, production and isolation of biological therapeutics, such as antibodies and vaccines

Teaching Experience

Teaching Assistant, Biochemistry (BIO41), Dartmouth College, 2009: Led weekly hour long recitation sections which taught additional application of class material and grading. Continued to assist from 2010-2013.

Tutor, Chemistry and Physics, University of New England, 2006-2008: Worked one on one and ran large (30+ student) question and answer sessions, as well as designing and administering problems sets.

University Services

MCB Committee, Dartmouth College, 2011-2012: Member of a 10 person committee responsible for important decisions regarding the Molecular and Cellular Biology program at Dartmouth, including but not limited to graduate student recruitment and selection, disciplinary action, course approval, and interviewing.

President and Member of Outing and Scuba Clubs, University of New England, 2006-2008

Orientation Leader, University of New England, 2005-2008

Skills

- Cloning and Expression- *E. Coli*, isotopic (^{13}C, ^{15}N) labeling, mammalian cell culture (CHO, COS7, HEK)
- Purification- FPLC based methods (IEC, GST, Streptavidin, Ni-NTA, Intein/Chitin, SEC) refolding, and membrane preparations
- Analysis- High throughput robotics (TECAN), Protein-Protein interactions, confocal microscopy, EMSA, AFM, UV/VIS, NMR & In Cell NMR, Circular dichroism, fluorescence methodologies (FRET, FP)
- Computational Skills- Energy minimization and molecular dynamics, protein modeling and analysis

Publications and Presentations

Thomas C. Scanlon, Charlotte C. Teneback, Avinash Gill, Jenna L. Bement, **Joshua A. Weiner**, John W. Lamppa, Laurie W. Leclair, Karl E. Griswold Enhanced Antimicrobial Activity of Engineered Human Lysozyme. *ACS Chemical Biology* 2010 5 (9), 809-818

Amacher, J. F., Cushing, P. R., **Weiner, J. A**. & Madden, D. R. (2011). A Crystallization and preliminary diffraction analysis of the CAL PDZ domain in complex with a selective peptide inhibitor Acta Cryst. F67, 600-603.

Weiner, J.A., Plati, J., Mao, L., Pellegrini, M., Mierke, D.F. Biochemical Characterization of the G Protein Coupled Receptor PTH1R and its Role in Calcium Regulation. Poster session presented at: 22nd Molecular Pharmacology Gordon Research Conference; 2011 January 9-14; Ventura, CA

Weiner, J.A., Mao, L., Pellegrini, M., Mierke, D.F. Engineering the parathyroid hormone receptor for small molecule screening and structural studies using a soluble template. Poster session presented at: 6th Phosphorylation & G-Protein Mediated Signaling Networks Gordon Research Conference and Research Seminar; 2012 June 9-15; Biddeford, ME.

Joshua A. Weiner, Christopher O. Audu, Kristina Seitler, Maria Pellegrini, Dale F. Mierke. Engineering the Endothelin A and B Receptors using a Soluble Template for Structural Analysis and Small Molecule Screening. *Biophysical Journal* 106(2) pp. 102a - 103a. Poster and abstract presented at BPS 2014 meeting, 2014 January 28th; San Francisco

J.A. Weiner, L. Mao, M. Pellegrini, K.H. Ahn, D. Kendall, D.F. Mierke. A Novel Technique for the Investigation of G Protein Coupled Receptors: Engineering the Parathyroid Hormone receptor for small molecule and ligand screening using a soluble template. Manuscript in preparation

J.A. Weiner, C. Audu, M. Pellegrini, K Zeigler, D.F. Mierke. NMR based Structural Characterization of the Endothelin A Receptor and modeling of the Endothelin A/B receptors. Manuscript in preparation