BIOGRAPHICAL SKETCH

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NAME: Torres, Matthew

eRA COMMONS USER NAME (credential, e.g., agency login): MATT_TORRES

POSITION TITLE: Associate Professor

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE (if applicable)	END DATE MM/YYYY	FIELD OF STUDY
Humboldt State University, Arcata, CA	BS	05/1997	Biology
University of North Carolina at Chapel Hill, Chapel Hill, NC	PHD	05/2007	Biochemistry and Biophysics/Mass Spectrometry
University of North Carolina at Chapel Hill, Chapel Hill, NC	Postdoctoral Fellow	07/2012	Biochemistry/Cell Signaling

A. Personal Statement

Research: My research is centered on protein post-translational modifications (PTMs) – enzymatic and non-enzymatic chemical alterations to protein structure that are involved in every aspect of cell biology such as cell division, signal transduction, epigenetics, cellular trafficking and beyond. More recently, PTMs have become broadly appreciated for their involvement in phase separation of proteins. Over the last 19 years, I have focused on the detection and experimental investigation of PTMs, evidenced by a broad publication record ranging from mass spectrometry/proteomic method development to in vitro biochemistry and the dissection of molecular mechanisms in vivo. Currently, my lab integrates quantitative proteomics with bioinformatics, cell biology and biochemistry to understand how G proteins and their protein-protein interaction (PPI) networks are regulated by PTMs including phosphorylation, ubiquitination and acetylation. My lab has also developed novel computational tools and bioinformatic resources for the curation and prediction of functional PTM hotspots (SAPH-ire), which we have exploited to identify novel cell signaling regulatory circuits in eukaryotes. Through our work in the Southeast Center for Math and Biology, we have also studied the relationship between phosphorylation and protein intrinsic disorder via molecular dynamics simulation and generative machine learning.

Teaching/Mentorship: I have a demonstrated commitment to teaching and mentorship at Georgia Tech. I have trained 8 PhD students, 6 of which have graduated and moved into productive postdocs in biomedical fields. I have also mentored 8 postdocs, 12 MS students, 10 undergraduates (2 UG have published with me), and 4 high school students. My lab is devoted to supporting trainees to complete their degrees in a timely fashion and to promote excellence in research and development that includes the use of high standards of rigor and reproducibility. I focus heavily on science communication through the use of lab meetings and one-on-one speech coaching. I also teach a well-subscribed, self-developed course in Proteomics: Technologies and Applications.

Service: I am the faculty co-director for the Systems Mass Spectrometry Core Facility (Proteomics), which provides proteomics services to the Georgia Tech faculty. I am the founder and leader of the Molecular BioMedical (MBM) Research Community at Georgia Tech that supports 5-6 lunch seminars given by junior researchers in Biology, Chemistry, Physics and Engineering departments. The MBM also stewards an Appleton Endowment for research in Cancer and Related Topics, supports a student-led seminar series (outside speaker invitations/hosting), a top-up fellowship for incoming URM students, as well as faculty-invited speakers. Beyond my own lab and institution, I serve on the executive committee for the American Society for Pharmacology and Experimental Therapeutics (ASPET) and on the editorial board for the Journal of Biological Chemistry.

Four key publications that demonstrate our ongoing work in: (a) quantitative proteomics, (b) G protein signaling, (c) MS method development, and (d) protein bioinformatics and computational biology:

a. Montllor-Albalate C, Kim H, Thompson AE, Jonke AP, **Torres MP***, Reddi AR*. (2022). Sod1 integrates oxygen availability to redox regulate NADPH production and the thiol redoxome. *Proc Natl Acad Sci* USA. Jan 4;119(1). PMID: 34969852.
b. Su X[#], Pang Y, Li W[#], Gumbart J, Kelley J, **Torres M***. (2023). N-terminal intrinsic disorder is an ancestral feature of Gγ subunits that influences the balance between different Gβγ signaling axes in yeast. Journal of Biological Chemistry. 299(8):104947-.
c. Kim H[#], Moore CM, Mestre-Fos S, Hanna DA, Williams LD, Reddi AR*, **Torres MP***. (2023). Depletion Assisted Hemin Affinity (DAsHA) Proteomics Reveals an Expanded Landscape of Heme Binding Proteins in the Human Proteome. *Metallomics* 15(3): mfad004. PMID: 36669767.
d. Satalkar V[#], Degaga GD, Li W[#], Pang YT, McShan AC, Gumbart JC, Mitchell JC*, **Torres MP***. (2024) Generative β-hairpin design using a residue-based physicochemical property landscape. Biophys J. Feb 1. PubMed PMID: 38297834.

B. Positions, Scientific Appointments and Honors

Positions and Scientific Appointments

2023 -	Editorial Board Member, Journal of Biological Chemistry
2023 - 2023	Ad-hoc reviewer, S10 shared instrumentation grants, NIH
2023 - 2023	TRA R01 reviewer, NIH
2022 -	Molecular Pharmacology Division Executive Board Member, ASPET
2021 -	Founder, Molecular BioMedical (MBM) Research Community, Georgia Tech
2019 - 2022	Member, Q-Bios Program Graduate Committee, Georgia Tech
2019 - 2020	Ad-hoc reviewer for EBIT Study Section, NIH
2018 -	Associate Professor, Georgia Institute of Technology
2018 - 2018	Ad-hoc member, NIH Advisory Council Meeting
2017 -	Member, Quantitative Biosciences (Q-Bios) Program, Georgia Tech
2017 -	Member, American Society for Experimental Pharmacology & Therapeutics (ASPET)
2017 - 2021	Ad-hoc reviewer for MIST Study Section, NIH
2015 -	Co-Director, Systems Mass Spectrometry Core Facility (Proteomics Division), Georgia Tech
2015 -	Member, Integrated Cancer Research Center, Georgia Tech
2013 -	Member, IBB Core Facilities Adisory Board, Georgia Tech
2012 - 2018	Assistant Professor, Georgia Institute of Technology
2009 -	Member, American Society of Biochemistry and Molecular Biology (ASBMB)
2007 - 2012	Postdoctoral Fellow, Biochemistry Dept., UNC Chapel Hill (with Henrik Dohlman)
2002 -	Member, American Society for Mass Spectrometry (ASMS)
2001 - 2007	Graduate Student, Biochemistry, UNC Chapel Hill (with Christoph Borchers)
1997 - 2001	Research Associate I, then II, Microarray Research Division, Gene Logic Inc.
1997 - 1997	Research Associate, Lawrence Livermore National Lab (with Greg Lennon)

Honors

2010 - 2016	Pathway to Independence Award (K99/R00), NIH
2003 - 2006	Diversity Fellowship, UNC Chapel Hill, Ford Foundation
2022	Early Career Award, ASPET Molecular Pharmacology Div.
2018	CTL/BP Junior Faculty Teaching Excellence Award, Georgia Tech
2016	IBB Above and Beyond Award, Georgia Tech
2010	Awardee, Best thematic poster in "Systems Biology - Synthetic Biology & Signal Transduction", ASBMB
2010	Travel Award, ASBMB
2005	Travel Award for Outsanding Presentation - (Mathias Mann & Catherine Costello, Chairs), Keystone Symposium on Proteomics & Bioinformatics
1994	Science & Engineering Research Semester, Lawrence Livermore National Laboratory

C. Contribution to Science

Total of 55 Publications, Google Scholar h-index = 25, 2274 citations

*Corresponding Authorship; **Co-First Authorship; #Torres lab member; **Corresponding Author

My contributions to science (not including pre-graduate publications) fall within four major categories: 1. Mass spectrometry (MS)-based measurement of PTMs and PPIs; 2. G protein signaling - regulation by post-translational modifications (PTMs) and protein-protein interactions (PPIs); 3. MS method development; and 4. Bioinformatics and Computational Biology.

1. **MS Measurement of PTMs and PPIs** - Understanding the biological significance of PTMs and PPIs has been a long-term goal of mine since graduate school. At Georgia Tech, my lab uses MS to characterize (among other things) protein PTMs including cysteine oxidation (a,b), phosphorylation (c), as well as extracellular glutathionylation (d). These studies have been published in high profile journals and demonstrate my ability to apply sophisticated MS techniques for the analysis of PTMs and protein interactions in vivo and in vitro.

    a. Saccuzzo EG, Mebrat MD, Scelsi HF, Kim M, Ma MT, Su X[#], Hill SE, Rheaume E, Li R, **Torres MP**, Gumbart JC, Van Horn WD, Lieberman RL. (2024). Competition between inside-out unfolding and pathogenic aggregation in an amyloid-forming β-propeller. Nat Commun. 15(1):155. PubMed Central PMCID: PMC10762032.
    b. Montllor-Albalate C, Kim H[#], Thompson AE, Jonke AP, **Torres MP****, Reddi AR**. (2022). Sod1 integrates oxygen availability to redox regulate NADPH production and the thiol redoxome. Proc Natl Acad Sci U S A. 119(1) PubMed Central PMCID: PMC8740578.
    c. Mukherjee K[#], English N[#], Meers C, Kim H[#], Jonke A[#], Storici F, **Torres M****. (2020). Systematic analysis of linker histone PTM hotspots reveals phosphorylation sites that modulate homologous recombination and DSB repair. DNA Repair (Amst). 86:102763. PubMed Central PMCID: PMC6996138.
    d. Li W[#], Moretti L, Su X[#], Yeh CR, **Torres MP**, Barker TH. Strain-dependent glutathionylation of fibronectin fibers impacts mechano-chemical behavior and primes an integrin switch. Nat Commun. 2024 Oct 9;15(1):8751. doi: 10.1038/s41467-024-52742-3. PMID: 39384749; PMCID: PMC11479631.

2. **G protein signaling** – Regulation by PTMs and PPIs: I spent my post-doctoral career investigating the functional impact of phosphorylation and ubiquitination on the G protein alpha subunit of heterotrimeric G protein signaling systems. Longstanding evidence, which I published in a book chapter (a), has established G alpha subunits as prominent targets of phosphorylation and ubiquitination. While these modifications play an important role the pharmacology of G protein signaling systems, identifying the responsible enzymes is a continuous barrier to understanding the mechanisms of regulation. Through genetic and microscopy-based screening in the yeast model system, I discovered a mono-ubiquitin ligase – Rsp5 (ortholog of human Nedd4) – that is both necessary in vivo and sufficient in vitro for monoubiquitination of yeast G proteins including Galpha (d) and G beta subunits (not shown). My lab at Georgia Tech discovered a phospho-regulatory mechanism for G gamma subunits (identified using our custom machine learning tool, SAPH-ire), whereby phosphorylation of N-terminal intrinsically disordered tails on G gamma subunits controls G betagamma/effector binding and MAPK activation in yeast (c). We have recently shown that combinatorial phosphorylation of the G gamma N-terminal tail, controlled by multiple kinases that phosphorylate multiple sites, modulates both its structure and function (b). Most recently, we discovered that altered structures in the N-terminal intrinsically disordered region of the yeast G gamma subunit, Ste18, alters the signaling bias between G betagamma and two different effectors pathways (a). This work places G gamma subunits on the short list of proteins, like histones and GPCRs, for which combinatorial post-translational modification of intrinsically disordered terminal tails regulate biological function.

    a. Su X[#], Pang Y, Li W[#], Gumbart J, Kelley J, **Torres M****. (2023). N-terminal intrinsic disorder is an ancestral feature of Gγ subunits that influences the balance between different Gβγ signaling axes in yeast. Journal of Biological Chemistry. 299(8):104947-.

b. Nassiri Toosi Z[#], Su X[#], Austin R[#], Choudhury S[#], Li W[#], Pang Y, Gumbart J, **Torres M****. (2021). Combinatorial phosphorylation modulates the structure and function of the G protein γ subunit in yeast. Science Signaling. 14(688):-.

c. Choudhury S[#], Baradaran-Mashinchi P[#], **Torres MP****. (2018). Negative Feedback Phosphorylation of Gγ Subunit Ste18 and the Ste5 Scaffold Synergistically Regulates MAPK Activation in Yeast. Cell Rep. 23(5):1504-1515. PubMed Central PMCID: PMC5987779.

d. **Torres MP**, Lee MJ, Ding F, Purbeck C, Kuhlman B, Dokholyan NV, Dohlman HG. (2009). G Protein Mono-ubiquitination by the Rsp5 Ubiquitin Ligase. J Biol Chem. 284(13):8940-50. PubMed Central PMCID: PMC2659251.

3. **MS Method Development** - My lab's research is aimed, in part, at using mass spectrometry (MS) as a tool to detect, localize and quantify dynamic PTMs and PPIs. In this arena, we have published novel and highly cited methods useful for bottom-up MS analysis of the heme-protein interactome (a), phosphorylation (d) top-down proteomics (c). Through a collaborative effort with the Mechanical Engineering department at Georgia Tech, my lab has also helped to develop a novel device for improving nESI-MS sensitivity (called DRILL), which enhances MS detection of peptides from biological samples (b). In all cases, our role was to develop sample preparation methods for direct measurement by either MALDI or nESI-MS.

   a. Kim H[#], Moore CM, Mestre-Fos S, Hanna DA, Williams LD, Reddi AR*, **Torres MP***. (2023). Depletion Assisted Hemin Affinity (DAsHA) Proteomics Reveals an Expanded Landscape of Heme Binding Proteins in the Human Proteome. *Metallomics* 15(3): mfad004. PMID: 36669767.

   b. Kottke PA, Lee JY, Jonke AP[#], Seneviratne CA, Hecht ES, Muddiman DC, **Torres MP**, Fedorov AG. (2017). DRILL: An Electrospray Ionization-Mass Spectrometry Interface for Improved Sensitivity via Inertial Droplet Sorting and Electrohydrodynamic Focusing in a Swirling Flow. Anal Chem. 89(17):8981-8987. PubMed Central PMCID: PMC5587373.

   c. Ouvry-Patat SA*, **Torres MP***, Gelfand CA, Quek HH, Easterling M, Speir JP, Borchers CH. (2009). Top-down proteomics on a high-field Fourier transform ion cyclotron resonance mass spectrometer. Methods Mol Biol. 492:215-31. PubMed PMID: 19241035.

   d. **Torres MP**, Thapar R, Marzluff WF, Borchers CH. (2005). Phosphatase-directed phosphorylation-site determination: a synthesis of methods for the detection and identification of phosphopeptides. J Proteome Res. 4(5):1628-35. PubMed PMID: 16212415.

4. **Bioinformatics & Computational Biology** - My lab at Georgia Tech is also focused on understanding the diverse roles of PTM in regulating protein structure/function. Early in the process of establishing my lab, I published a highly cited review of the latest technology and methodologies for deciphering the role of combinatorial PTMs in simple and complex protein systems. Since then, a major focus of my lab has been to develop a heuristic computational tool for predicting when an experimentally-observed site of modification is likely to be functional. The tool (SAPH-ire) employs machine learning to characterize PTMs based on protein sequence, conservation, structure, and proteomics data (a,b). Since the start of this effort, we have predicted the probability of function for over 600,000 PTMs dispersed across >8000 protein families harboring more than 38,000 unique proteins. Ongoing work in our lab exploits SAPH-ire to probe the function of PTMs predicted by SAPH-ire to be functionally impactful. This tool can be used to direct experimental effort towards PTM hotspots with the greatest potential for functional impact. Most recently, we have begun to study the impact of phosphorylation on protein structure using molecular dynamics (c) and generative machine learning to generate phosphorylation-controled disordered regions (d).

   a. English N[#], **Torres M****. (2022). Enhancing the Discovery of Functional Post-Translational Modification Sites with Machine Learning Models - Development, Validation, and Interpretation. Methods Mol Biol. 2499:221-260. PubMed PMID: 35696084.

   b. Pennington KL, Chan TY, **Torres MP**, Andersen JL. (2018). The dynamic and stress-adaptive signaling hub of 14-3-3: emerging mechanisms of regulation and context-dependent protein-protein interactions. Oncogene. 37(42):5587-5604. PubMed Central PMCID: PMC6193947.

   c. Natarajan V[#], Satalkar V[#], Gumbart JC, **Torres M***. Molecular Dynamics Reveals Altered Interactions between Belzutifan and HIF-2 with Natural Variant G323E or Proximal Phosphorylation at T324. ACS Omega. 2024 Aug 26;9(36):37843-37855. PMID: 39281922; PMCID: PMC11391435.

d. Satalkar V[#], Degaga GD, Li W[#], Pang YT, McShan AC, Gumbart JC, Mitchell JC**, Torres MP**. (2024) Generative β-hairpin design using a residue-based physicochemical property landscape. Biophys J. Feb 1. PubMed PMID: 38297834.

Complete List of Published Work:
https://www.ncbi.nlm.nih.gov/myncbi/matthew.torres.1/bibliography/public/