Sheeno Thyparambil, Ph.D.

Senior Director R&D mProbe, Rockville, MD 20850

Profile: Award winner, innovative and accomplished leader with extensive background in personalized medicine and molecular diagnostics. Dedicated to proteomic biomarker discovery and validation in clinical setting as evidenced by 28 US issued patents. Developed and implemented high complexity proteomic assays in a clinical lab environment. Experience with regulated environments including GLP, CAP and CLIA. Comprehensive experience authoring, editing, and proofreading scientific research documents and presentation materials. Strong interpersonal and communication skills for bridging between scientific and business concepts, negotiating timelines and facilitating collaboration.

Expertise includes:

- 15+ years of Mass spectrometry experience
- Clinical Validation of biomarkers
- Molecular Oncology

Molecular OncologyStrategic Planning

2019- Present

Patent

PROFESSIONAL EXPERIENCE

mProbe, Inc, Rockville, MD Senior Director (R&D)

Scientific and Strategic leader for organization wide oncology R&D efforts Lead the business efforts of Oncology diagnostics Product Line Responsible for integration of proteomics and metabolomics efforts at mProbe.

NantOmics LLC, Rockville MD (formerly OncoPlex Diagnostics, Rockville)	2009 - 2019
Principal Scientist, Product Development	2015 - 2019
Senior Scientist, Mass Spectrometry	2010 - 2015
Scientist, Mass Spectrometry	2009 - 2010

Founding mass spectrometrist and co-inventor on multiple patents. Key contributor to company buildout on strategy, hiring and logistics. Responsible for providing analytical leadership during the development of proteomic assays. Responsible for pioneer clinical validation study. Support regulatory submissions as a subject matter expert. Collaborative, cross-functional team player including members from proteomic/genomic sciences, pathology and medical affairs. Identify and establish relationships with industry and academic partners.

- Founding mass spectrometrist at OncoplexDx/NantOmics.
- Reduced an innovative technology to clinical practice. Developed the first tissue proteomic clinical assay from FFPE tissue.
- 29 US issued patents.
- Awarded inaugural (2017) NantHealth Presidential Award for Scientific achievement
- Developed and implemented high complexity proteomic assays in a clinical lab environment. Analytically validated three hundred (300+) new assays over 9 years of work.
- Responsible for implementing 30 biomarkers on the clinical report.
- Managed the release of the next 40 biomarkers on the clinical report by interfacing with Molecular Oncology, Mass Spectrometry, Operations and Medical Director.
- Published (joint first author) the first clinical validation paper on mass spec based approach to identify durable responders to trastuzumab from FFPE tissue
- Manage the business development collaboration with external pharma partners

- Authored the mass spectrometry portions of key clinical documents including, clinical study protocols and clinical study reports.
- Support regulatory submissions as a subject matter expert and contribute scientific and technical sections of key regulatory documents including premarket approval (PMA) of Class III medical devices documents.
- Communicated research findings through preparation and publication of eight (8) original manuscripts.
- Established multiple collaborations with KOLs across Europe and US.
- Worked within a cross functional team to provide internal and external medical affairs support.
- Involved in key hiring decisions for ~90% of the scientific team across Mass Spectrometry and Bioinformatics.

Myeloma Institute of Research and Therapy, Univ. of Arkansas for Medical Sciences (UAMS) 2008 to 2009 Post-doctoral Fellow

- Biomarker discovery from serum or bone marrow samples of multiple myeloma patients treated with VTD (Velcade, Thalidomide, Dexamethsone) regimen.
- Post-translation modifications (PTM) research of treated patients using mass spectrometry based approaches (Orbitrap).
- Integration of proteomic data with genomic information to elucidate pathways that are key in resistance to VTD therapy.

Food and Drug Administration (FDA)/National Center for Toxicology Research (NCTR) Degree Granting Institute: UAMS 2008 to 2009

Pre-doctoral Fellow

- Joint program by UAMS (didactic) and NCTR/FDA (research)
- Research conducted in the Division of Systems Toxicology
- Oakridge Institute for Science and Education (ORISE) fellowship
- Co-authored one of the earliest works on systems biology integrating proteomic, genomic and metabonomic approaches to elucidate the impact of valproic acid in hepatotoxicity
- Biomarker discovery and validation of hepatocellular carcinoma biomarkers from human liver samples (tissue and serum)
- Authored a book chapter on primary liver carcinogenesis

RELEVANT EDUCATION

Ph.D. (Biochemistry and Molecular Biology), University of Arkansas for Medical Sciences

PROFESSIONAL AFFILIATIONS

American Society of Clinical Oncology (ASCO)

American Association for Cancer Research (AACR)

American Society for Mass spectrometry (ASMS)

SELECTED PUBLISHED WORKS

Amodio V, Yaeger R, Arcella P, Cancelliere C, Lamba S, Lorenzato A, Arena S, Montone M, Mussolin B, Bian Y, Whaley A, Pinnelli M, Murciano-Goroff YR, Vakiani E, Valeri N, Liao WL, Bhalkikar A, **Thyparambil S**, Zhao HY, de Stanchina E, Marsoni S, Siena S, Bertotti A, Trusolino L, Li BT, Rosen N, Di Nicolantonio F, Bardelli A, Misale S. EGFR blockade reverts resistance to KRAS G12C inhibition in colorectal cancer. Cancer Discov. 2020 May 19:CD-20-0187.

Li BT, Michelini F, Misale S, Cocco E, Baldino L, Cai Y, Shifman S, Tu HY, Myers ML, Xu C, Mattar M, Khodos I, Little M, Qeriqi B, Weitsman G, Wilhem CJ, Lalani AS, Diala I, Freedman RA, Lin NU, Solit DB, Berger MF, Barber PR, Ng T, Offin M, Isbell JM, Jones DR, Yu HA, **Thyparambil S**, Liao WL, Bhalkikar A, Cecchi F, Hyman DM, Lewis JS, Buonocore DJ, Ho AL, Makker V, Reis-Filho JS, Razavi P, Arcila ME, Kris MG, Poirier JT, Shen R, Tsurutani J, Ulaner GA, de Stanchina E, Rosen N, Rudin CM, Scaltriti M. HER2-Mediated Internalization of Cytotoxic Agents in ERBB2 Amplified or Mutant Lung Cancers. Cancer Discov. 2020 May;10(5):674-687. doi: 10.1158/2159-8290.CD-20-0215. Epub 2020 Mar 25

Schaff LR, Yan D, **Thyparambil S**, Tian Y, Cecchi F, Rosenblum M, Reiner AS, Panageas KS, Hembrough T, Lin AL. Characterization of MGMT and EGFR protein expression in glioblastoma and association with survival. J Neurooncol. 2020 Jan;146(1):163-170. doi: 10.1007/s11060-019-03358-x. Epub 2019 Dec 10. PMID: 31823165; PMCID: PMC6939885.

Serna G, Ruiz-Pace F, Cecchi F, Fasani R, Jimenez J, **Thyparambil S**, Landolfi S, Elez E, Vivancos A, Hembrough T, Tabernero J, Dienstmann R, Nuciforo P. Targeted multiplex proteomics for molecular prescreening and biomarker discovery in metastatic colorectal cancer. Sci Rep. 2019 Sep 19;9(1):13568. doi: 10.1038/s41598-019-49867-7. PMID: 31537838; PMCID: PMC6753065.

An E, Ock CY, Kim TY, Lee KH, Han SW, Im SA, Kim TY, Liao WL, Cecchi F, Blackler A, **Thyparambil S**, Kim WH, Burrows J, Hembrough T, Catenacci D, Oh DY, Bang YJ. Quantitative proteomic analysis of HER2 expression in the selection of gastric cancer patients for trastuzumab treatment. Ann Oncol. 2016 Sep 29. pii:mdw442. [Epub ahead of print]

Sellappan S, Blackler A, Liao WL, O'Day E, Xu P, **Thyparambil S**, Cecchi F, Hembrough T, Catenacci DV. Therapeutically Induced Changes in HER2, HER3, and EGFR Protein Expression for Treatment Guidance. J Natl Compr Canc Netw. 2016 May;14(5):503-7.

Hembrough T, Liao WL, Hartley CP, Ma PC, Velcheti V, Lanigan C, **Thyparambil S**, An E, Monga M, Krizman D, Burrows J, Tafe LJ. Quantification of Anaplastic Lymphoma Kinase Protein Expression in Non-Small Cell Lung Cancer Tissues from Patients Treated with Crizotinib. Clin Chem. 2016 Jan;62(1):252-61.

Catenacci DV, Liao WL, Zhao L, Whitcomb E, Henderson L, O'Day E, Xu P, **Thyparambil S**, Krizman D, Bengali K, Uzzell J, Darfler M, Cecchi F, Blackler A, Bang YJ, Hart J, Xiao SY, Lee SM, Burrows J, Hembrough T. Mass-spectrometry-based quantitation of Her2 in gastroesophageal tumor tissue: comparison to IHC and FISH. Gastric Cancer. 2016 Oct;19(4):1066-79.

Nuciforo P, **Thyparambil S***, Aura C, Garrido-Castro A, Vilaro M, Peg V, Jimenez J, Vicario R, Cecchi F, Hoos W, Burrows J, Hembrough T, Ferreres JC, Perez-GarciaJ, Arribas J, Cortes J, Scaltriti M. High HER2 protein levels correlate withincreased survival in breast cancer patients treated with anti-HER2 therapy. Mol Oncol. 2016 Jan;10(1):138-47.

*Joint first authors

Catenacci DV, Liao WL, **Thyparambil S**, Henderson L, Xu P, Zhao L, Rambo B, Hart J, Xiao SY, Bengali K, Uzzell J, Darfler M, Krizman DB, Cecchi F, Bottaro DP, Karrison T, Veenstra TD, Hembrough T, Burrows J. Absolute quantitation of Met using mass spectrometry for clinical application: assay precision, stability, and correlation with MET gene amplification in FFPE tumor tissue. PLoS One. 2014 Jul 1;9(7):e100586.

Hembrough T, **Thyparambil S**, Liao WL, Darfler MM, Abdo J, Bengali KM, HewittSM, Bender RA, Krizman DB, Burrows J. Application of selected reaction monitoring for multiplex quantification of clinically validated biomarkers in formalin-fixed, paraffin-embedded tumor tissue. J Mol Diagn. 2013 Jul;15(4):454-65.

Hembrough T, **Thyparambil S**, Liao WL, Darfler MM, Abdo J, Bengali KM, Taylor P, Tong J, Lara-Guerra H, Waddell TK, Moran MF, Tsao MS, Krizman DB, Burrows J.Selected Reaction Monitoring (SRM) Analysis of Epidermal Growth Factor Receptor (EGFR) in Formalin Fixed Tumor Tissue. Clin Proteomics. 2012 May 3;9(1):5.

Ahmed BA, Bukhari IA, Jeffus BC, Harney JT, **Thyparambil S**, Ziu E, Fraer M, Rusch NJ, Zimniak P, Lupashin V, Tang D, Kilic F. The cellular distribution of serotonin transporter is impeded on serotonin-altered vimentin network. PLoS One.2009;4(3):e4730.

Gomes AV, Zong C, Edmondson RD, Li X, Stefani E, Zhang J, Jones RC, **Thyparambil S**, Wang GW, Qiao X, Bardag-Gorce F, Ping P. Mapping the murine cardiac 26S proteasome complexes. Circ Res. 2006 Aug 18;99(4):362-71. Epub 2006 Jul 20.

Schnackenberg LK, Jones RC, **Thyparambil S**, Taylor JT, Han T, Tong W, Hansen DK, Fuscoe JC, Edmondson RD, Beger RD, Dragan YP. An integrated study of acute effects of valproic acid in the liver using metabonomics, proteomics, and transcriptomics platforms. OMICS. 2006 Spring;10(1):1-14.

Gomes AV, Zong C, Edmondson RD, Berhane BT, Wang GW, Le S, Young G, Zhang J, Vondriska TM, Whitelegge JP, Jones RC, Joshua IG, **Thyparambil S**, Pantaleon D, Qiao J, Loo J, Ping P. The murine cardiac 26S proteasome: an organelle awaiting exploration. Ann N Y Acad Sci. 2005 Jun;1047:197-207.

BOOK CHAPTERS

Thyparambil S, Edmondson RD, Dragan YP, Primary Liver Cancer: Chemical Carcinogenesis. *Hepatocellular Carcinoma. Diagnosis and Treatment 2nd Edition Ed Brian Carr 2010: 55-108*

SELECTED PATENTS

Issued (US) : 29 Pending (US): 4

Krizman DB, Hembrough T, An E, **Thyparambil S**. SRM/MRM assay for mesothelin (MSLN) protein. US Patent 10,078,08. Issued September 18, 2018.

Krizman DB, Hembrough T, An E, **Thyparambil S**. SRM/MRM assay for the 6-O-methylguanine-DNA methyltransferase (MGMT) protein. US Patent 10,060,927. Issued September 18, 2018.

Krizman DB, Liao WL, **Thyparambil S**, Hembrough T. SRM/MRM assay for the insulin receptor protein. US Patent 9,255,934. Issued August 7, 2018.

Krizman; DB, Hembrough T, **Thyparambil S**. Her3 protein SRM/MRM assay. US Patent 9,869,680. Issued January 16, 2018.

Krizman DB, Hembrough T, T**hyparambil S**, Liao WL. SRM assay to indicate cancer therapy. US Patent 9,840,728. Issued December 12, 2017

Krizman DB, Hembrough T, **Thyparambil S**, Liao WL. SRM/MRM assay for the fatty acid synthase protein. US Patent 9,804,164. Issued October 31, 2017

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Krizman DB, Liao WL, **Thyparambil S**, Hembrough T. SRM/MRM assay for the receptor tyrosine-protein kinase erbB-4 protein (HER4). US patent 9,470,696. Issued October 18, 2016

Krizman DB, Hembrough T, **Thyparambil S**, Liao WL. MRM/SRM assay for death receptor 5 protein. US Patent 9,442,119. September 13, 2016

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Krizman DB, Hembrough T, **Thyparambil S**, Liao WL. cMET protein SRM/MRM assay. US Patent 9,372,195. Issued June 21, 2016

Krizman DB, Hembrough T, **Thyparambil S**, Liao WL. Multiplex MRM assay for evaluation of cancer. US Patent 9,360,487. Issued June 7, 2016

Krizman DB, Hembrough T, **Thyparambil S**, Liao WL. SRM/MRM assay for the fatty acid synthase protein. US Patent 9,309,554. Issued April 12, 2016

Krizman DB, Liao WL, **Thyparambil S**, Hembrough. SRM/MRM assay for subtyping lung histology. US Patent 9,261,506. Issued February 16, 2016

Krizman; DB, Hembrough T, **Thyparambil S**. Methods for measuring the level of insulin-like growth factor 1 receptor (IGF1R) protein using SRM/MRM assay. U.S. Patent 8,728,753. Issued May 20, 2014.