BIOGRAPHICAL SKETCH

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NAME: Hatice Ülkü Osmanbeyoğlu

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

POSITION TITLE: Assistant Professor, Biomedical Informatics, University of Pittsburgh

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)*	Completion Date MM/YYYY	FIELD OF STUDY
Northeastern University	BS	05/04	Computer Engineering
Carnegie Mellon University	MS	09/06	Electrical and Computer Engineering
University of Pittsburgh	MS	04/09	Bioengineering
University of Pittsburgh	PhD	12/12	Biomedical Informatics
Memorial Sloan Kettering Cancer Center	Postdoctoral	03/13-11/18	Computational and Systems Biology

A. Personal Statement

My research has focused on developing computational methods to study and model transcriptional regulatory mechanisms and dissect the dysregulation of gene expression in cancer. I have expertise in applying machine learning methods to analyze numerous next generation sequencing data types (such as DNase-seq, ATAC-seq, transcription factor and histone modification ChIP-seq, RNA-seq, and sc-RNA-seq). In particular, I have recently developed a novel computational approach, patient-specific inference of networks informed by chromatin (PSIONIC) by integrating transcriptomic and epigenomic data from bulk RNA-seq and cell line ATAC-seq (assay for transposase-accessible chromatin using sequencing) to predict patient-specific transcriptional regulatory networks. We will extend and develop this framework for predicting profile-specific transcriptional regulatory networks both in patient and single cell levels and then studying the transcriptional dependencies in the tumor milieu associated with lymph node metastasis in HPV-negative oral squamous cell carcinoma using existing datasets and ultimately identify clinically relevant biomarkers and therapeutic targets in collaboration with Dr. Duvvuri's lab.

a. **Osmanbeyoglu HU**, Pelossof R, Bromberg JF, Leslie CS (2014) Linking signaling pathways to transcriptional response in breast cancer. Genome Res 24(11):1869-80. PMID: 25183703
b. **Osmanbeyoglu HU**, Toska E, Chan C, Baselga J, Leslie CS (2017) Pan-cancer modeling predicts the context-specific impact of somatic mutations on transcriptional programs. Nature Communications 8, 14249.
c. **Osmanbeyoglu, H.U**., Shimizu F, Rynne-Vidal A, Jelinic P, Mok SC, Chiosis G, Levine DA, Leslie CS. Chromatin-informed inference of transcriptional programs in gynecologic and basal breast cancers. BioRxiv 333757 **[Preprint]**. May 30, 2018. Available from: https://doi.org/10.1101/333757

B. Positions and Honors

Positions and Employment

2018 – Present	Assistant Professor, Department of Biomedical Informatics, University of Pittsburgh, Pittsburgh, PA
2018 – Present	Member, UPMC Hillman Cancer Center, Pittsburgh, PA
2016 – 2018	Postdoctoral Research Associate, Department of Computational and Systems Biology, Memorial Sloan Kettering Cancer Center, New York, NY
2013 – 2016	Postdoctoral Research Scholar, Department of Computational Biology, Memorial Sloan Kettering Cancer Center, New York, NY
2009 – 2012	Graduate Researcher, Department of Biomedical Informatics, University of Pittsburgh, Pittsburgh, PA
2006 – 2012	Graduate Researcher, Department of Bioengineering, University of Pittsburgh, Pittsburgh, PA
2004 – 2005	Test Engineer, Ambient Corporation, Boston, MA

Other Experience and Professional Memberships

2006 – Present	Member, International Society for Computational Biology
2012	Judge, Pittsburgh Regional Science Fair (PSEF), Pittsburgh, PA, USA
2012	Judge, Intel's International Science & Engineering Fair, Pittsburgh, PA, USA
2013 – 2014	Representative, NCI's Integrative Cancer Biology Program's Early Stage Investigators Steering Committee Meeting
2017	Referee of the Women in Machine Learning Workshop
2017 – Present	Member, American Association for Cancer Research
2017	Member, Program Committee, Workshop on Computation Biology, Sydney, Australia
2017 – Present	Referee of the PLOS Computational Biology
2019	Referee of the IEEE/ACM Transactions on Computational Biology and Bioinformatics
2019	Referee of the Clinical Colorectal Cancer

Honors

2002 – 2004	Dean's List, Northeastern University, Boston, MA
2003	Outstanding Junior Award, Northeastern University, Boston, MA
2004	Sears B. Condit Award, Northeastern University, Boston, MA
2004	Winner, Computer Engineering Capstone Design Group Competition, Northeastern University, Boston, MA
2011	Doctoral Comprehensive Exam passed with High Honors, University of Pittsburgh, PA
2012	Finalist, Best Trainee Paper Award, University of Pittsburgh, PA
2012	NSF Travel Award to the Research in Computational Molecular Biology Conference
2012	Travel Award to the Machine Learning Summer School
2012	Travel Award to the Workshop for Women in Machine Learning
2012	Finalist, Best Performer in Phase 2 of DREAM7 Challenge, Breast Cancer Prognosis
2014	Travel Award to the Intelligent Systems for Molecular Biology (ISMB) Conference
2016	NIH/NCI K99/R00 Pathway to Independence Award
2017	Memorial Sloan Kettering Postdoctoral Research Award
2017	NCI Scholarship for Experimental Models of Human Cancer Course at The Jackson Laboratory
2017	EMBL Corporate Partnership Fellowship for Cancer Genomics conference at EMBL, Germany

C. Contributions to Science

1. **Modeling gene regulatory programs and cancer systems biology**. I have developed novel integrative algorithms for modeling gene regulatory programs using large-scale tumor data sets where multiple parallel sources of molecular profiling data are available. Distinguishing features of my methods are the use of regulatory sequence information together with modern supervised learning algorithms to train the models. For instance, I developed a novel statistical approach for exploiting parallel proteomics and mRNA expression data generated for large tumor sets through projects such as The Cancer Genome Atlas

(TCGA) to link dysregulation of upstream signaling pathways with altered transcriptional response via the transcriptional circuitry. I used these models to mechanistically interpret the cancer-specific impact of somatic alterations in terms of dysregulated transcription factors (TFs) and signaling pathways. These studies demonstrate the power of integrative "big" data analysis for cancer research.

d. **Osmanbeyoglu HU**, Pelossof R, Bromberg JF, Leslie CS (2014) Linking signaling pathways to transcriptional response in breast cancer. Genome Res 24(11):1869-80. PMID: 25183703
e. **Osmanbeyoglu HU**, Toska E, Chan C, Baselga J, Leslie CS (2017) Pan-cancer modeling predicts the context-specific impact of somatic mutations on transcriptional programs. Nature Communications 8, 14249.
f. Nargund AM, Pham CG, Dong Y, Wang PI, **Osmanbeyoglu HU**, Xie Y, Aras O, Han S, Oyama T, Takeda S, Ray CE, Dong Z, Berge M, Hakimi AA, Monetta S, Lekaye CL, Koutcher JA, Leslie CS, Creighton CJ, Weinhold N, Lee W, Tickoo SK, Wang Z, Cheng EH, Hsieh JJ (2017) The SWI/SNF Protein PBMR1 Restrains VHL Loss-Driven Clear Cell Kidney Cancer, Cell Reports 18, 2893-2906.
g. Iyer A, **Osmanbeyoglu HU**, Leslie CS (2017) Computational methods to dissect gene regulatory networks in cancer. Current Opinion in Systems Biology, 2:115-122.
h. Nargund AM, **Osmanbeyoglu HU**, Cheng EH, Hsieh JJ (2017) SWI/SNF tumor suppressor gene PBRM1/BAF180 in human clear cell kidney cancer. *Molecular & Cellular Oncology*, Vol 4, Iss 4.

2. **Epigenetics of breast cancer and drug response.** I have expertise in the analysis of many next generation sequencing data types (DNase-seq, ATAC-seq, transcription factor and histone modification ChIP-seq, RNA-seq, GRO-seq) as well as high throughput chromatin conformation capture technologies (especially ChIA-PET). During my graduate studies, I integrated diverse high throughput data to understand estrogen receptor (ER)-mediated transcription in breast cancer. This work provides insights into dysregulation of expression programs in ER-positive breast cancer. Later, I applied my expertise, in collaboration with Dr. José Baselga's laboratory, to investigate the epigenetic mechanisms leading to the activation of ER-dependent transcription upon PI3Kα inhibition in breast cancer models. Our study also revealed that understanding then interaction between cell signaling and epigenetic regulation at a systems level is critical for design of therapeutics.
   a. **Osmanbeyoglu HU**, Hartmaier RJ, Oesterreich S, Lu X (2012) Improving ChIP-seq peak-calling for functional co-regulator binding by integrating multiple sources of biological information. BMC Genomics 13 Suppl 1: S1. PMCID: PMC3439677
   b. **Osmanbeyoglu HU**, Lu KN, Oesterreich S, Day RS, Benos PV, Coronnello C, Lu X (2013) Estrogen represses gene expression through reconfiguring chromatin structures. Nucleic acids research 41(17):8061-71. PMID: 23821662
   c. Toska E, **Osmanbeyoglu HU***, Castel P*, Chan C, Dickler M, Hendrickson RC, Scaltriti M, Leslie CS, Armstrong SA, Baselga J (2017) PI3K pathway regulates ER-dependent transcription in breast cancer through the epigenetic regulator KMT2D, Science, 355 (6331), 1324-1330.
   d. Watters RJ, Hartmaier RJ, **Osmanbeyoglu HU**, Gillihan RM, Rae J, Liao L, Chen K, Li W, Lu X, Oesterreich S (2017) Steroid receptor coactivator-1 can regulate osteoblastogenesis independently of estrogen, Molecular and Cellular Endocrinology, 448:21-27.

3. **Omics approaches in immunology and immunotherapy.** I am also involved in many collaborative projects in immunology. For example, I developed an analysis pipeline for sequencing data sets that profile the *T cell* receptor (TCR) repertoire in collaboration with the laboratory of Dr. Alexander Rudensky (HHMI and MSKCC). We investigated the genetic control of regulatory T cell development and, in particular, its selection of the TCR repertoire. Through our study of CNS3, a cis-regulatory element in the Foxp3 locus, we found a previously unrecognized mechanism that diversifies Treg cell TCR repertoire and its significance in achieving sufficient self-tolerance. I also worked with the laboratory of Dr. Ming Li (MSKCC) on elucidating the role of Ets family TFs in T cell homeostasis. Our work dissected novel transcriptional programs regulating immune responses in anticipation of future T-cell-based immunotherapies. In these projects, I led high throughput data analysis.
   a. Feng Y, Veeken J, Shugay M, Putintseva EV, **Osmanbeyoglu HU**, Dikiy S, Hoyos BE, Moltedo B,Hemmers S, Treuting P, Leslie CS, Chudakov M, Rudensky AY (2015) A mechanism for expansion of regulatory T-cell repertoire and its role in self-tolerance. Nature, 528(7580):132-136.

b. Luo C, **Osmanbeyoglu HU**, Do MH, Bivona MR, Toure A, Kang D, Xie Y, Leslie CS, Li M (2017) Ets transcription factor GABP controls T cell homeostasis and immunity. Nature Communications 8,1062.

4. **Developing machine-learning algorithms for biomedical applications.** I designed machine-learning algorithms that can be used when labeled data is scarce and difficult to obtain experimentally in the case of transmembrane helix prediction and host-viral protein-protein interaction prediction. I also utilized natural language processing methods to compare the pattern landscape of microbial proteomes.

   a. **Osmanbeyoglu HU**, Wehner JA, Carbonell JG, Ganapathiraju MK (2010) Active machine learning for transmembrane helix prediction. BMC Bioinformatics 11 Suppl 1: S58. PMCID: PMC3009531
   b. Chalancon G, Kosloff M, **Osmanbeyoglu HU**, Saraswathi S (2010) PLoS Computational Biology conference postcards from ISMB 2010. PLoS Comput Biol 6: e1002000.
   c. **Osmanbeyoglu HU**, Ganapathiraju MK (2011) Rapid deployment of viral-human interactome prediction for new viruses. Proc of the American Medical Informatics Association Summit on Translational Bioinformatics.
   d. **Osmanbeyoglu HU**, Ganapathiraju MK (2011) N-gram analysis of 970 microbial organisms reveals presence of biological language models. BMC Bioinformatics 12: 12. PMCID: PMC3027111

5. **Clinical informatics.** Point-of-care documentation has been identified as a patient safety measure for improving accuracy and timeliness of data. During my PhD training, I worked with a team to evaluate the barriers that nurses and nurse aide/clinical technicians encounter for electronic point-of-care documentation we conducted surveys on a telemetry unit of a hospital.
   a. Kohle-Ersher A, Chatterjee P, **Osmanbeyoglu HU**, Hochheiser H, Bartos C (2012) Evaluating the Barriers to Point-of-Care Documentation for Nursing Staff. Comput Inform Nurs 30: 126-133.

Complete List of Published Work in Google Scholar:
https://scholar.google.com/citations?user=YzCsmdgAAAAJ&hl=en

D. Additional Information: Research Support and/or Scholastic Performance

K99/R00 CA207871 Osmanbeyoglu (PI) 07/01/16-11/30/21
Algorithms to link signaling pathways with transcriptional programs for precision medicine
Role: PI
In this project, we are developing algorithmic approaches linking signaling to transcriptional response for precision medicine. We use novel statistical modeling approaches to integrate publicly available transcriptomic, proteomic and genomic data across tumor types with epigenomic data in appropriate cell lines to study altered transcriptional programs and signaling pathways in cancer. With these methods in hand, we study the impact of common and cancer-specific transcription factor and signaling regulators on clinical outcome and drug response. We expect that our results will lead to new insights in cancer biology and facilitate the design of clinical trials that match actionable oncogenic signatures with personalized therapies.