# RAUNAK SHRESTHA, PhD

Curriculum Vitae [Last Updated: September 26, 2018]

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#### RESEARCH STATEMENT

My primary research goals are directed towards understanding the complex nature of cancer by computationally modelling cancer omics data. My research is primarily focused on development and application of computational methods integrating cancer omics data so as to enable precision oncology. The methods I develop leverage complex network approaches which helps to bring these multi-dimensional data into a single-analysis framework.

My current research focuses on exploring this idea analyzing the genotype-phenotype relationships in cancer to prioritize cancer driver genes and precision therapeutics. Most recently, my research led to define a novel molecular subtype as well as biomarker stratifying this subtype of a rare cancer of abdomen potentially vulnerable to immunotherapy.

Furthermore, I would like to understand the spatial heterogeneity in cancer. I believe, communication between tumor and its micro-environment and vice versa is critical for cancer progression and therapeutic resistance. Using integrated single-cell multi-omics analysis, I would like to study how tumor-microenvironment communication shapes cancer evolution and how we can leverage this knowledge to develop novel cancer therapeutics.

### POST-SECONDARY EDUCATION

SEPT 2012 - AUG 2018 Doctor of Philosophy in BIOINFORMATICS, University of British Columbia, Canada

under CIHR Bioinformatics Training Program

Advisors: Dr. Colin C. Collins and Dr. S. Cenk Sahinalp

Thesis Title: "Computational Prioritization of Cancer Driver Genes for Precision Oncology"

SEPT 2011 - AUG 2012 Master of Science in BIOINFORMATICS, Simon Fraser University, Canada

under CIHR Bioinformatics Training Program

(Transferred to PhD program)

2005 - 2009 Bachelors of Technology (B.Tech.) in BIOTECHNOLOGY, Kathmandu University, Nepal

### RESEARCH & TRAINING EXPERIENCE

SEPT 2018 - Current Post-doctoral Research Fellow, Laboratory for Advanced Genome Analysis,

Vancouver Prostate Centre, Vancouver, BC, Canada

SEPT 2012 - Aug 2018 PhD Candidate, Laboratory for Advanced Genome Analysis,

Vancouver Prostate Centre, Vancouver, BC, Canada

MAY - Aug 2012 Graduate Research Student, Laboratory for Advanced Genome Analysis,

Vancouver Prostate Centre, Vancouver, BC, Canada

SEPT 2011 - MAY 2012 Graduate Research Student,

Simon Fraser University, Burnaby, BC, Canada

JULY 2009 - JULY 2011 Research Associate, Center for Molecular Dynamics Nepal, Kathmandu, Nepal

# **SELECTED PUBLICATIONS**

- [1] R. Shrestha, E. Hodzic, T. Sauerwald, P. Dao, K. Wang, J. Yeung, S. Anderson, F. Vandin, G. Haffari, C. C. Collins, and S. C. Sahinalp. HIT'nDRIVE: patient-specific multidriver gene prioritization for precision on-cology. Genome Research, 27(9):1573–1588, sep 2017. ISSN 1549-5469. doi: 10.1101/gr.221218.117. URL https://www.ncbi.nlm.nih.gov/pubmed/28768687
- [2] R. Shrestha, E. Hodzic, J. Yeung, K. Wang, T. Sauerwald, P. Dao, S. Anderson, H. Beltran, M. A. Rubin, C. C. Collins, G. Haffari, and S. C. Sahinalp. HIT'nDRIVE: Multi-driver Gene Prioritization Based on Hitting Time. Research in Computational Molecular Biology: 18th Annual International Conference, RECOMB 2014, Pittsburgh, PA, USA, April 2-5, 2014, Proceedings, pages 293–306, 2014. doi: 10.1007/978-3-319-05269-4\_23. URL http://dx.doi.org/10.1007/978-3-319-05269-4\_23
- [3] R. Shrestha, N. Nabavi, Y.-Y. Lin, F. Mo, S. Anderson, S. Volik, H. H. Adomat, D. Lin, H. Xue, X. Dong, R. Shukin, R. H. Bell, B. McConeghy, A. Haegert, S. Brahmbhatt, E. Li, H. Z. Oo, A. Hurtado-Coll, L. Fazli, J. Zhou, Y. McConnell, A. McCart, A. Lowy, G. B. Morin, M. Daugaard, S. C. Sahinalp, F. Hach, S. Le Bihan, M. E. Gleave, Y. Wang, A. Churg, and C. C. Collins. Integrated Multi-omics Molecular Subtyping Predicts Therapeutic Vulnerability in Malignant Peritoneal Mesothelioma. bioRxiv preprint, 2018. doi: 10.1101/243477. URL https://doi.org/10.1101/2434777. (Submitted)
- [4] E. Hodzic, <u>R. Shrestha</u>\*, K. Zhu, K. Cheng, C. C. Collins, and S. C. Sahinalp. Combinatorial detection of conserved alteration patterns for identifying cancer subnetworks. *bioRxiv preprint*, 2018. doi: 10.1101/369850. URL https://doi.org/10.1101/369850. (*Submitted*) \*As joint first author

### **RELEVANT PUBLICATIONS**

- [1] M. A. Reyna, D. Haan, M. Paczkowska, L. P. Verbeke, M. Vazquez, A. Kahraman, S. Pulido Tamayo, J. Barenboim, L. Wadi, P. Dhingra, R. Shrestha, G. Getz, M. S. Lawrence, J. S. S. Pedersen, M. A. Rubin, D. A. Wheeler, S. Brunak, J. M. Izarzugaza, E. Khurana, K. Marchal, C. von Mering, S. C. Sahinalp, A. Valencia, J. Reimand, J. M. Stuart, B. J. Raphael, and PCAWG. Pathway and network analysis of more than 2,500 whole cancer genomes. bioRxiv preprint, 2018. doi: 10.1101/385294. URL https://doi.org/10.1101/385294. (Submitted)
- [2] H. Sharifi-Noghabi, Y. Liu, N. Erho, <u>R. Shrestha</u>, M. Alshalalfa, E. Davicioni, C. C. Collins, and M. Ester. *Deep Genomic Signature for early metastasis prediction in prostate cancer. bioRxiv preprint*, 2018. doi: 10.1101/276055. URL https://doi.org/10.1101/276055. (Submitted)
- [3] Y. Feng, <u>R. Shrestha</u>, R. H. Bell, S. Volik, N. Erho, Y. Sun, V. Hayes, S. Ren, and C. C. Collins. *Metagenomic and metatranscriptomic analysis of human prostate microbiota from patients with prostate cancer.* (Submitted), 2018
- [4] M. Yamada, J. Tang, J. Lugo-Martinez, E. Hodzic, R. Shrestha, H. Ouyang, P. Radivojac, C. Sahinalp, F. Menczer, Y. Chang, A. Saha, H. Mamitsuka, and D. Yin. *Ultra High-Dimensional Nonlinear Feature Selection for Big Biological Data*. IEEE Transactions on Knowledge and Data Engineering, 30(7):1352–1365, 2018. ISSN 1041-4347. doi: 10.1109/TKDE.2018.2789451. URL https://doi.org/10.1109/TKDE.2018.2789451
- [5] E. E. Gill, L. S. Chan, G. L. Winsor, N. Dobson, R. Lo, S. J. Ho Sui, B. K. Dhillon, P. K. Taylor, <u>R. Shrestha</u>, C. Spencer, R. E. W. Hancock, P. J. Unrau, and F. S. L. Brinkman. *High-throughput detection of RNA processing in bacteria*. **BMC Genomics**, 19(1):223, 2018. ISSN 1471-2164. doi: 10.1186/s12864-018-4538-8. URL http://www.ncbi.nlm.nih.gov/pubmed/29587634
- [6] I. S. U. Luk, R. Shrestha, H. Xue, Y. Wang, F. Zhang, D. Lin, A. Haegert, R. Wu, X. Dong, C. C. Collins, A. Zoubeidi, M. E. Gleave, P. W. Gout, and Y. Wang. BIRC6 Targeting as Potential Therapy for Advanced, Enzalutamide-Resistant Prostate Cancer. Clinical Cancer Research, 23(6):1542–1551, mar 2017. ISSN 1078-0432. doi: 10.1158/1078-0432.CCR-16-0718. URL http://www.ncbi.nlm.nih.gov/pubmed/27663589

- [7] A. W. Wyatt, F. Mo, K. Wang, B. McConeghy, S. Brahmbhatt, L. Jong, D. M. Mitchell, R. L. Johnston, A. Haegert, E. Li, J. Liew, J. Yeung, R. Shrestha, A. V. Lapuk, A. McPherson, R. Shukin, R. H. Bell, S. Anderson, J. Bishop, A. Hurtado-Coll, H. Xiao, A. M. Chinnaiyan, R. Mehra, D. Lin, Y. Wang, L. Fazli, M. E. Gleave, S. V. Volik, and C. C. Collins. Heterogeneity in the inter-tumor transcriptome of high risk prostate cancer. Genome Biology, 15(8):426, Aug 2014. ISSN 1474-760X. doi: 10.1186/s13059-014-0426-y. URL http://www.ncbi.nlm.nih.gov/pubmed/25155515
- [8] K. Wang, R. Shrestha, A. W. Wyatt, A. Reddy, J. Lehár, Y. Wang, A. Lapuk, and C. C. Collins. A meta-analysis approach for characterizing pan-cancer mechanisms of drug sensitivity in cell lines. PloS One, 9(7):e103050, 2014. ISSN 1932-6203. doi: 10.1371/journal.pone.0103050. URL http://www.ncbi.nlm.nih.gov/pubmed/25036042

#### **THESIS**

• R. Shrestha. Computational Prioritization of Cancer Driver Genes for Precision Oncology. PhD thesis, The University of British Columbia, 2018. URL https://open.library.ubc.ca/cIRcle/collections/24/items/1.0370936. Advisors: Dr. Colin C. Collins & Dr. S. Cenk Sahinalp

### **CONFERENCE PRESENTATIONS**

#### **Selected Oral Presentations**

- Inactivation of BAP1 Predicts a Distinct Immunogenic Class of Malignant Peritoneal Mesothelioma. Terry Fox Seminar, Vancouver Prostate Centre. September 28, 2018, Vancouver General Hospital, Vancouver, Canada.
- BAP1 Loss Predicts Therapeutic Vulnerability in Malignant Peritoneal Mesothelioma. 14<sup>th</sup> International Conference of the International Mesothelioma Interest Group (iMig2018). May 2-5, 2018, Ottawa, Canada
- HIT'nDRIVE: Patient-Specific Multi-Driver Gene Prioritization for Precision Oncology. 8<sup>th</sup> Annual Scientific Meeting, Terry Fox Research Institute. November 4, 2017, Vancouver, Canada
- Translating Big-Data to Precision Oncology. Terry Fox Seminar, Vancouver Prostate Centre. February 17, 2017, Vancouver General Hospital, Vancouver, Canada.
- HIT'nDRIVE: Patient-Specific Multi-Driver Gene Prioritization for Precision Oncology. Vancouver Bioinformatics User Group (VanBUG). November 3, 2016, Vancouver, Canada
- HIT'nDRIVE: Patient-Specific Multi-Driver Gene Prioritization for Precision Oncology. 10<sup>th</sup> Annual Lorne D. Sullivan Lectureship & Research Day. June 21, 2016, Vancouver General Hospital, Vancouver, Canada.
- HIT'nDRIVE: Patient-Specific Multi-Driver Gene Prioritization to Guide Precision Cancer Medicine. Workshop on Network Biology (Algorithmic Challenges in Genomics). April 11-15, 2016, Simons Institute for the Theory of Computing, UC Berkeley, Berkeley, CA, USA. https://simons.berkeley.edu/talks/raunak-shrestha-04-12-16
- Computational Detection and Prioritization of Driver Alterations in Cancer. Terry Fox Seminar, Vancouver Prostate Centre. November 3, 2014, Vancouver General Hospital, Vancouver, Canada.
- HIT'nDRIVE: Multi-Driver Gene Prioritization based on Hitting Time. 18<sup>th</sup> Annual International Conference on Research in Computational Molecular Biology (RECOMB). April 2-5, 2014, Pittsburgh, PA, USA.

Analysis of KatG Ser315Thr Mutation in Multidrug Resistant Mycobacterium tuberculosis and SLC11A1
 Polymorphism in Multidrug Resistance Tuberculosis in Central Development Region of Nepal Using
 PCR-RFLP Technique: A Pilot Study. 2<sup>nd</sup> International Symposium on Biotechnology. June 29-30, 2010,
 Kathmandu, Nepal

#### **Selected Poster Presentations**

- Raunak Shrestha, Ermin Hodzic, Thomas Sauerwald, Phuong Dao, Kendric Wang, Jake Yeung, Shawn Anderson, Fabio Vandin, Gholamreza Haffari, Colin C. Collins and S. Cenk Sahinalp.(2017). HIT'nDRIVE: Patient-Specific Multi-Driver Gene Prioritization for Precision Oncology. 4th Canadian Cancer Research Conference, November 4-7, 2017, Vancouver, BC, Canada.
- Raunak Shrestha, Ermin Hodzic, Thomas Sauerwald, Phuong Dao, Kendric Wang, Jake Yeung, Shawn Anderson, Fabio Vandin, Gholamreza Haffari, Colin C. Collins and S. Cenk Sahinalp.(2017). HIT'nDRIVE: Patient-Specific Multi-Driver Gene Prioritization for Precision Oncology. Genome Informatics, November 1-4, 2017, Cold Spring Harbor Laboratory, NY, USA.
- Raunak Shrestha, Ermin Hodzic, Thomas Sauerwald, Phuong Dao, Kendric Wang, Jake Yeung, Shawn Anderson, Fabio Vandin, Gholamreza Haffari, Colin C. Collins and S. Cenk Sahinalp.(2016). HIT'nDRIVE: Patient-Specific Multi-Driver Gene Prioritization for Precision Oncology. The 27<sup>th</sup> International Conference on Genome Informatics, October 3-5, 2016, Fudan University, Shanghai, China.
- Noushin Nabavi, **Raunak Shrestha**, Yuzhuo Wang and Colin C. Collins (2016). Characterization of intertumor heterogeneity in Malignant Mesothelioma. 13<sup>th</sup> International Conference of the International Mesothelioma Interest Group (iMIG 2016), May 1-4, 2016, Birmingham, UK. (As a first co-author).
- Raunak Shrestha, Ermin Hodzic, Fan Mo, Anna Lapuk, S. Cenk Sahinalp and Colin C. Collins (2015). Computational Detection and Prioritization of Driver Alterations in Prostate Cancer from Multi-Omics Data. Eighth Annual Prostate Cancer Program Retreat (SPORE), March 15-17, 2015, Fort Lauderdale, Florida, USA. (Selected among the top-eight poster of the conference.)
- Raunak Shrestha, Kendric Wang, S. Cenk Sahinalp, Anna Lapuk and Colin Collins (2013). Exploring the Biology of Prostate Cancer Progression using Systems Biology Approach. The Eleventh Asia Pacific Bioinformatics Conference, January 21-23, 2013, Vancouver, Canada.

### AWARDS AND HONORS

2018	UBC Translational Cancer Genomics Travel Award (iMig2018).
2016-2018	Mitacs Accelerate PhD Fellowship.
2015-2016	Prostate Cancer Foundation - British Columbia (PCF-BC) Research Awards - 2015.
2014-2016	Faculty of Science Graduate Award, University of British Columbia.
2014	International Society for Computational Biology (ISCB) Travel Fellowship (RECOMB-2014).
2011-2013	CIHR Bioinformatics Training Program for Health Research.

### TECHNICAL SKILLS

Programming Languages R, perl, python, C, C++

Web Development php, HTML/5, CSS, JavaScript, R-shiny

Databases & Query Languages MySQL

Others CPLEX, GitHub

Molecular Biology Experienced in routine genomics & proteomics laboratory works

### **SOFTWARE PACKAGES**

• HIT'nDRIVE (https://github.com/sfu-compbio/hitndrive)

• cd-CAP (https://github.com/ehodzic/cd-CAP)

# STUDENTS MENTORED

- Hossein Sharifi-Noghabi (Ph.D. Student, Computer Science. Simon Fraser University, Canada)
- Jingchao Wei (Ph.D. Candidate, Urology, Central South University, China)

# ACADEMIC PAPERS PEER REVIEWED

(number of reviews parenthesized)

Nature Communications	(3)
Bioinformatics	(2)
BMC Genomics	(1)
BMC Bioinformatics	(1)
Research in Computational Molecular Biology (RECOMB)	
International Conference on Intelligent Systems for Molecular Biology (ISMB)	
The Asia Pacific Bioinformatics Conference (APBC)	
Workshop on Algorithms in Bioinformatics (WABI)	(1)
International Conference on Computational Advances in Bio and medical Sciences (ICCABS)	
Nepal Journal of Biotechnology	

# PROFESSIONAL MEMBERSHIPS

- Vancouver Bioinformatics User Group (VanBUG): Development Group
- Biotechnology Society of Nepal (BSN): Life time Member and Former Executive Member

# REFERENCES

References can be made available upon request

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