

Achal Neupane
Date: September 30, 2019

Dear Search Committee:

I am writing to express my interest in the advertised Postdoctoral Associate position at University of XX. I am a PhD candidate at South Dakota State University (Brookings, SD, USA) and will be graduating with a specialization in bioinformatics in May, 2020. I have previously worked on a variety of bioinformatics projects at both US and Australian universities and have developed a strong interdisciplinary academic background. I believe these experiences have allowed me to acquire a diverse set of knowledge and skills that make me a suitable candidate for a bioinformatics research position.

I am currently working on my PhD dissertation, entitled Dissecting RNA Silencing Pathways in the White Mold Fungus, *Sclerotinia sclerotiorum* with Dr. Shinyi Marzano at South Dakota State University. Specifically, I have been using gene disruption mutants to identify the roles of dicers (dcl-1 and dcl-2) and argonaute enzymes (agl-2 and agl-4) in the small RNA (sRNA) metabolism of the plant pathogenic fungus, *Sclerotinia sclerotiorum*. I have also confirmed the effectiveness of ds-RNA based pesticides that target the *S. sclerotiorum* RNA silencing pathway and have analyzed the diversity and evolution of mycoviruses identified from the whole root metatranscriptomes of various plant host species infected by arbuscular mycorrhizal fungi. Several articles on this research have already been published in peer-reviewed journals.

Prior to my PhD, I earned a BS in Biological Science from University of DC (Washington DC, USA) in 2009 and an MS degree in Biology (Bioinformatics) from South Dakota State University in 2013. Following the completion of my master's degree, I worked on several projects focused on bioinformatics and statistical genetics. In 2015, I accepted an opportunity to work in Australia at the University of Queensland-Translational Research Institute (TRI), where I worked as a bioinformatics researcher in Dr. Matthew Brown's group. The goals of this group were to characterize the genetic origins of disease and translate these findings into clinical practice. I was primarily involved in the characterization of the genetic landscape of Acute Myeloid Leukemia (AML), and, to that end, I analyzed sequence genotyped SNP data from a cohort of 150 clinically characterized AML samples sequenced with whole exome and whole genome sequencing. I also analyzed a cohort of 900 control exomes and 600 whole genomes to validate and compare genotyping algorithms and sequencing technologies and to perform gene discovery for both somatic and germline risk variants. For this latter work, I used statistical genetics algorithms that identified both protective and deleterious variants. I then compared pathology, cytogenetic, and Sequenom genotyping data to refine and calibrate these algorithms. I also used several variant calling methods to characterize germline, copy number, and structural variants in AML.

While working at TRI, I also developed an algorithm to quality control Next Generation Sequencing (NGS) data in order to estimate pair-wise identity by descent (IBD) probabilities from high-density single nucleotide polymorphism (SNP) data. I demonstrated that the estimated IBD probabilities effectively identified contaminated, related, and distantly-related samples. This method could be used to quality control NGS genotype data, including sequences produced by

targeted sequencing panels. I have developed several algorithms for these purposes, and the R codes are available for free on my Github account.

I spent the initial years of my career studying human cancer cells, as well as diseases affecting plants, insects, and fungi, by analyzing NGS data (whole genome, whole exome, RNA-seq, SNPs, microbiome, etc.). Since the beginning my PhD program, I have taken several “data-heavy” graduate level courses from Statistics and Computer Science departments in order to develop my skills for big-data analysis, algorithm development, and scientific computing, including analysis of biological data. Additionally, I have been writing computer programs in R, python, Perl, JavaScript, and also have been working on Linux/Unix system with extensive use of shell (bash) and PBS scripts for over 10 years of my research career. Therefore, for my post-doctoral research, I would be interested in joining a research lab where I could use various statistical analyses, including machine learning, and artificial neural networks to study the genomics of various diseases.

This cover letter provides only a brief synopsis of my background and experiences. I would be glad to meet and further discuss my qualifications. I have enclosed my CV along with this letter.

Thank you very much for your time and consideration, and I look forward to hearing from you.

Sincerely,

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Curriculum Vitae

Achal Neupane

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Education

- PhD (Bioinformatics), August 2017-May 2020
South Dakota State University, Brookings, South Dakota, USA,
- Master of Science (Bioinformatics), August 2011-May 2013
South Dakota State University, Brookings, South Dakota, USA.
- Bachelor of Science (Biological Science), August 2005-December 2009
University of the District of Columbia (UDC), Washington, DC, USA.

Research Experience

- **Research Assistant (PhD candidate)**
Department of Biology and Microbiology, South Dakota State University, USA (Aug 2017- present)
 - Studying the effects of hypovirulence-associated DNA virus 1 (SsHADV-1) and Sclerotinia sclerotiorum hypovirus 2 Lactuca (SsHV2L) on white mold fungus pathogen *Sclerotinia sclerotiorum* using small RNAseq and RNAseq data
 - Studying the evidence/effect of RNAi by induction of virus in *Sclerotinia sclerotiorum* using bioinformatics approaches.
 - Studying the roles of dicers and argonautes on *Sclerotinia sclerotiorum* antiviral Small RNA Processing
 - Analyzing metatranscriptomic data to study novel mycoviruses infecting arbuscular mycorrhizal fungus *Rhizophagus* spp and other pathogenic fungi.
 - Studying the effect of crop rotation in soil microbiome diversity affecting the overall yield from Illinois-Urbana sites.
 - Studying the effects of soil salinity in microbiome diversity by analyzing 16S and ITS data from South Dakota.
- **Research Scholar**
University of Queensland, Translational Research Institute, Brisbane, Australia (Jan 2015- Jun 2016)
 - Studied and characterized the genetic landscape of Acute Myeloid Leukemia (AML) by analyzing sequence genotyped SNP data from 480 exomes and 150 whole genomes from AML samples.
 - Analyzed a cohort of 900 control exomes and 600 whole genomes to perform gene discovery for both somatic and germline risk variants using sophisticated statistical genetics algorithms that identify both protective and deleterious variants.

- Validated and compared genotyping algorithms and sequencing technologies using pathology, cytogenetic and Sequenom genotyping data to refine and calibrate these algorithms.
 - Discovered AML related genes using SKAT and burden like statistical genetics tools. Used several variant calling methods to characterize germline, copy number and structural variants in AML and control samples in whole exome sequenced samples.
 - Developed algorithms to identify sample contamination, identity and ethnicity for quality control of Next Generation Sequencing (NGS) data.
- **Research Assistant**
 School of Biological Sciences, University of Nebraska-Lincoln, Nebraska, USA (Aug 2013- May 2014)
 - Studied the modes of pathogenesis and impacts of western corn rootworm (WCR) in corn roots by analyzing gene expression of gustatory receptors using larval/egg transcriptome data.
 - Identified several gamma-aminobutyric acid type A (GABAA) receptor and gustatory receptors from the WCR transcriptome.
 - Performed bioinformatics analysis to study the conservation of gene structure and function of chemoreceptor protein family across insect genome.
- **Teaching Assistant**
 Department of Biology and Microbiology, South Dakota State University, USA (Aug 2011- May 2013)
 - Taught undergraduate level biology/genetics laboratory courses
 - Graded weekly assignments, quizzes and exams.
 - Courses taught:
 - General Biology I (BIOL 151) lab, Fall 2011
 - General Biology II (BIOL153) lab, Spring 2012
 - General Biology I (BIOL 151) lab, Fall 2012
 - General Biology I (BIOL 153) lab, Spring 2013
- **Research Assistant**
 Department of Biology and Microbiology, South Dakota State University, USA (Aug 2011- Jul 2013)
 - Identified all three families of mitogen-activated protein kinases (MAPKs), and characterized the legume specific MAPK genes involved in *Rhizobium*-legume interaction.
 - Identified MAPK and MAPKK gene members in soybean, *Lotus*, *Medicago* and *Phaseolous* and studied their evolutionary relationships with respect to their counterparts in different non-legume species.
 - Used approaches in bioinformatics and comparative genomics to study functional and evolutionary divergence of MAPK genes in legumes.
 - Performed MAPK silencing and hairy root transformation using RNAi constructs in soybean.
 - Performed time-course expression analysis of MAPKs in root nodulation of mock and *Rhizobium* inoculated soybean seedlings using RT-PCR and Microarray analysis.

- Mentored undergraduate researchers.
- **Research Fellow**
MERCK Pharmaceuticals-University of the District of Columbia Cancer Research, DC, USA Project (Apr 2009-Dec 2009)
 - Studied molecular mechanisms involved in apoptosis (programmed cell death) induced by organotin drugs in various cancer cell lines.
 - Provided research support in chemical and cellular studies designed to determine the carcinogenic effects on humans.
 - Performed various biological techniques: cell culture, gel electrophoresis/SDS-PAGE, immunofluorescence, western blot and various biological assays.
- **Undergraduate Teaching Assistant**
Department of Biology, University of the District of Columbia, DC, USA (Aug 2007 – Apr 2009)
 - Assisted professors and students in performing experiments, prepared biological samples and chemical reagents for general biology classes.
 - Performed laboratory inventory, ordered and maintained laboratory chemicals and supplies.
 - Handled biological specimens and worked under GLP guidelines.

Publications

Peer- reviewed journal articles

- **Neupane, A.**, Feng, C., Mochama, PK., Saleem H., and Lee Marzano SY. (2019). Roles of Argonautes and Dicers on *Sclerotinia sclerotiorum* Antiviral RNA Silencing. *Frontiers in Plant Science*; 10:976.
- SY., Marzano, **Neupane, A.**, Domier, L. (2018). Transcriptional and Small RNA Responses of the White Mold Fungus *Sclerotinia sclerotiorum* to Infection by a Virulence-Attenuating Hypovirus. *Viruses*; 10 (12), 713.
- **Neupane, A.**, Feng, C., Feng, J., Kafle, A., Bücking, H., and Marzano, SY. (2018) Metatranscriptomic Analysis and In Silico Approach Identified Mycoviruses in the Arbuscular Mycorrhizal Fungus *Rhizophagus* spp. *Viruses* 10 (12), 707.
- Neupane, S., Schweitzer, SE., **Neupane, A.**, Andersen, EJ., Fennell, A., Zhou and Nepal, MP. (2019). Identification and Characterization of Mitogen-Activated Protein Kinase (MAPK) Genes in Sunflower (*Helianthus annuus* L.). *Plants (Basel)* 8.
- Neupane, S., Andersen, E., **Neupane, A.**, and Nepal, M. (2018) Genome-Wide Identification of NBS-Encoding Resistance Genes in Sunflower (*Helianthus annuus* L.). *Genes* 9 (8), 384.
- Mochama, P., Jadhav, P., **Neupane, A.**, Marzano, SY. (2018) Mycoviruses as Triggers and Targets of RNA Silencing in White Mold Fungus *Sclerotinia sclerotiorum*. *Viruses* 10 (4).
- S. Piya, **Neupane, A.**, Butler, J., Larson, GE., and Nepal, MP. (2014) Genetic Diversity and Population Structure of Sickleweed (*Falcaria vulgaris* L.) in the Upper Midwest USA Midwest USA. *Biological Invasions* 2014:1-11.
- **Neupane, A.**, Nepal, MP., Benson, BV., MacArthur, KJ., and Piya, S. (2013). Mitogen-Activated Protein Kinase Genes and their Evolutionary History in *Lotus*, *Medicago* and *Phaseolus*. *Plant Signaling & Behavior*; 8:e27189.

- **Neupane, A.**, Piya, S., Subramanian, S., Rohila, JS., Reese, N., and Nepal, MP. (2013). Identification, Nomenclature, and Evolutionary Relationships of Mitogen-Activated Protein Kinase (MAPK) Genes in Soybean. *Evolutionary Bioinformatics*; 9:363-86.
- Piya, S., **Neupane, A.**, Butler, J., Larson, GE., and Nepal, MP. (2012). Inferring the introduction history of sickleweed (*Falcaria vulgaris* L.) in the United States. *Proceedings of the South Dakota Academy of Science*; 91:113-129.

Presentations

- **Neupane, A.**, and Marzano, S. Profiling the Classes of the RNA Editing in Virus-derived small RNAs in White Mold *Sclerotinia sclerotiorum*. *American Society for Virology*, 2019, 20-24 July, Minneapolis, USA (Oral).
- **Neupane, A.**, Mochama, P., Saleem, H., Marzano, S. Roles of Dicers and Argonautes on *Sclerotinia sclerotiorum* Antiviral Small RNA Processing. *Plant and Animal Genome Conference XXVII*, 2019, 12-16 January, San Diego, CA, USA (Poster).
- Smith, A., **Neupane, A.**, Ellis, J., Afrin, S., Burow, R., Stinson, C., Leo, P., Cristino, A., Moore, A. MEK inhibitor resistance in acute myeloid leukaemia. *New Direction in Leukaemia Research*, 2016, 16-19 March, Peppers Noosa, Australia (Poster)
- Leo, P., **Neupane, A.**, Bassal, M., Maung, Z., Newell, F., Ellis, M., Boxall, G., Smith, A., Marlton, P., D'Andrea, R., Gonda, T., Brown, M., Saal, R., Moore, A. Gene Discovery in Acute Myeloid Leukaemia: somatic and germline mutations. *International Congress of Immunology*, 2016, 21-26 August, Melbourne, Australia (Oral).
- Moore, A., Leo, P., **Neupane, A.**, Bassal, M., Newell, F., Ellis, M., Boxall, G., Smith, A., Marlton, P., D'Andrea, R., Gonda, T., Brown, M., Saal, R., Anderson, L. Sensitivity of Whole Exome Sequencing for the Detection of FLT3-ITD and NPM1 Mutations in Acute Myeloid Leukaemia. *European School of Hematology (ESH)*. 2015, 10-12 September, Budapest, Hungary (Oral).
- **Neupane, A.**, Eyun, S., Wang, H., Siegfried, BD., and Moriyama, EN. Transcriptome analysis of western corn rootworm larvae and eggs. *IWGO & International Conference of Diabrotica Genetics*. 2014, 14-17 April. Chicago, IL, USA (Poster).
- **Neupane, A.**, Piya, S., Reese, N., Rohila, JS., Subramanian, S., and Nepal, MP. Identification of Mitogen Activated Protein Kinase Family members in Soybean. *Botanical Society of America Conference 2012*, 7-11 July. Columbus, OH, USA (Poster).
- Piya, S., **Neupane, A.**, Butler, J., Larson, GE., and Nepal, MP. Population Genetics of *Falcaria vulgaris* (Sickleweed) in North America. *Botanical Society of America Conference 2012*, 7 -11 July. Columbus, OH, USA (Poster).
- Piya, S., **Neupane, A.**, Butler, J., Larson, GE., and Nepal, MP. Introduction history and spread of *Falcaria vulgaris* Bernh. (Apiaceae) in the United States based on herbarium records. *South Dakota Academy of Science 2012*, 13-14 April. Vermillion, SD, USA (Oral).
- **Neupane, A.**, Piya, S., Subramanian, S., Rohila, JS., Reese, N., and Nepal, MP. A Nomenclatural Conundrum: Applying Existing Nomenclature to the Identification of Soybean (*Glycine max*) MAP Kinase Genes. *ASPB Midwestern Sectional Society 2012*, 24-25 March. Lincoln, NE, USA (Poster).
- **Neupane, A.**, Anjorin, C., Song, X., and Kumar, D. Anticancer Activity of Novel Ionic Triorganotin Derivatives against MDA-MB 231 Breast Cancer Cells. *HBCU-UP*

National Research Conference 2009, October 29-November 1. Washington, DC, USA (Poster).

Research Grants

- University of Nebraska-Lincoln travel grants (\$1500, FY 2014)
- Center for Excellence in Drought Tolerance Research (CEDTR)-USDA/NIFA (#SA1100029): Identification and characterization of mitogen-activated protein kinases (MAPKs) involved in root nodulation in *Glycine max*. (\$4000, FY 2012/2013).
- MERCK/ AAAS: Anticancer activity of novel ionic triorganotin derivatives against MDA-MB 231 breast cancer cells. (\$5000, FY2009).

Computer Skills

- Programming languages: R, Python, JavaScript, Perl, PHP, ASP.NET, MySQL
- Operating systems: Linux/Unix, Linux based high performance computing (HPC) cluster
- Genome analysis tools: GATK, Picard, Samtools, bcftools
- Microbiome analysis: Qiime2, Vegan, Phyloseq
- *De novo* alignment/assembly tools (Trinity, MIRA2, Velvet, Bowtie, etc.)
- Sequence search tools (BLAST, HHblits, HMMER and various standalone programs)
- Phylogenetics software (RAxML, Mega, PhyML, Phylip, MrBayes, PAUP and Network)
- DNA assembly and analysis software (Sequencher and Geneious)
- GitHub/Bitbucket: achalneupane

Graduate level courses in Computer Science and Statistics

- Data Structures and Algorithms (Python; 3 credits)
- Perl Programming for Biological Applications (3 credits)
- Statistical Methods II
- Statistical Programming (R and SAS)
- Modern Applied Statistics I
- Modern Applied Statistics II

Membership in Professional Organizations

- Associate member, Sigma XI
- Member, American Association for the Advancement of Science (AAAS)

Awards and Achievements

- Sigma Xi Masters Research Paper, South Dakota State University, (2012)
- Dean's List Honoree, University of the District of Columbia, Washington DC (2006-2009)
- United Nations Mission in Nepal (UNMIN) Scholarship (2002)

References

- Dr. Shinyi Marzano
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