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Hello Sir/Ma'am,

I am writing this letter with great enthusiasm as I am interested in the Computational or Bioinformatics Research/Staff Scientist position in your group. I have a broad background in computational and quantitative biology with specific training and expertise in genomics, chromatin biology and machine learning. I am currently completing my postdoctoral studies with **Prof. Martin Aryee and Prof. Alexander Meissner**, where my focus is to understand the dynamics of gene regulation using single-cell genomics.

My long-term research interests are understanding the dynamics of gene regulation and how alterations in gene expression contribute to different diseases using high throughput sequencing datasets, including RNA-seq (bulk and single-cell), ChIP-seq, ATAC-seq (bulk and single-cell) and CRISPR based assays (CRISPRi, CRISPRa and dual assays), long read sequencing data and integration of these datasets. In addition, I develop tools & approaches for genomic data analysis and apply machine learning algorithms to understand inter and intra-sample variations in the datasets. My academic training and research experience have given me an excellent background in multiple disciplines, including computational biology, molecular biology, and genetics. I have extensive experience generating and testing hypotheses by modeling publicly available datasets, including TCGA, CCLE, GTex, Gene Expression Omnibus and DepMap.

Following my master's studies in Computational Biology at the Carnegie Mellon University, Pittsburgh PA, I pursued my interest in computational biology and began my research focusing on two major themes for my doctoral thesis under the mentorship of **Prof. Zhandong Liu, Prof. Huda Zoghbi and Prof. Kunal Rai** at Baylor College of Medicine and MD Anderson Cancer Center, Houston, Texas. First, I used **integrative genomics and systems biology methods to analyze large-scale multi-omics sequencing data**. These approaches were applied to identify novel gene regulatory networks (Litvak et al. 2012, Pohodich et al. 2018, Kochat*, Raman* et al. 2021), novel epigenomic enhancer subtypes in colorectal cancer (Orouji*, Raman*, Singh* et al. 2021) and decode the role of TRIM28/KRAB repressors modulating heterochromatin and CpG methylation in pluripotent stem cells (Oleksiewicz*, Gładych *, Raman* et al. 2017). Second, I have **contributed to developing statistical methods/approaches in identifying the latent variables**, also known as batch effects (Yi*, Raman* et al. 2018) and sources of spurious results such as failure to measure baseline variability in RNA-seq datasets (Raman*, Pohodich* et al. 2018, Raman et al. 2021). For my postdoctoral training, I continue to build on my previous training in transcriptional regulation by moving into multi-omic single-cell assays (Gu*, Raman* et al. 2021; Shareef et al. 2021) and further understand the role of DNA methylation in the development

and diseases.

I have strong written and verbal communication skills and have collaborated with scientists and non-scientists of diverse backgrounds. In addition, I am a strong team player, which is evident through various academic projects I have worked on and successfully published. I have attached my two-page resume, academic curriculum vitae and anticipate an opportunity to meet and discuss the position.

Sincerely,
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References:

- 1) Litvak V, Ratushny AV, Lampano AE, Schmitz F, Huang AC, **Raman A**, Rust AG, Bergthaler A, Aitchison JD, Aderem A. A FOXO3-IRF7 gene regulatory circuit limits inflammatory sequelae of antiviral responses. *Nature*. 2012 Oct 18;490(7420):421-5. doi: 10.1038/nature11428. Epub 2012 Sep 16. PMID: 22982991; PMCID: PMC3556990.
- 2) Pohodich AE, Yalamanchili H, **Raman AT**, Wan YW, Gundry M, Hao S, Jin H, Tang J, Liu Z, Zoghbi HY. Forniceal deep brain stimulation induces gene expression and splicing changes that promote neurogenesis and plasticity. *Elife*. 2018 Mar 23;7:e34031. doi: 10.7554/eLife.34031. PMID: 29570050; PMCID: PMC5906096.
- 3) Kochat V*, **Raman AT***, Landers SM, Tang M, Schulz J, Terranova C, Landry JP, Bhalla AD, Beird HC, Wu CC, Jiang Y, Mao X, Lazcano R, Gite S, Ingram DR, Yi M, Zhang J, Keung EZ, Scally CP, Roland CL, Hunt KK, Feig BW, Futreal PA, Hwu P, Wang WL, Lazar AJ, Slopis JM, Wilson-Robles H, Wiener DJ, McCutcheon IE, Wustefeld-Janssens B, Rai K, Torres KE. Enhancer reprogramming in PRC2-deficient malignant peripheral nerve sheath tumors induces a targetable de-differentiated state. *Acta Neuropathol*. 2021 Sep;142(3):565-590. doi: 10.1007/s00401-021-02341-z. Epub 2021 Jul 20. PubMed PMID: 34283254.
- 4) Orouji E*, **Raman AT***, Singh AK*, Sorokin A, Arslan E, Ghosh AK, Schulz J, Terranova C, Jiang S, Tang M, Maitituoheti M, Callahan SC, Barrodia P, Tomczak K, Jiang Y, Jiang Z, Davis JS, Ghosh S, Lee HM, Reyes-Uribe L, Chang K, Liu Y, Chen H, Azhdarinia A, Morris J, Vilar E, Carmon KS, Kopetz SE, Rai K. Chromatin state dynamics confers specific therapeutic strategies in enhancer

subtypes of colorectal cancer. *Gut*. 2021 May 31. doi: 10.1136/gutjnl-2020-322835. PubMed PMID: 34059508.

5) Oleksiewicz U*, Gładych M*, **Raman AT***, Heyn H, Mereu E, Chlebanowska P, Andrzejewska A, Sozańska B, Samant N, Fąk K, Auguścik P, Kosiński M, Wróblewska JP, Tomczak K, Kulcenty K, Płoski R, Biecek P, Esteller M, Shah PK, Rai K, Wiznerowicz M. TRIM28 and Interacting KRAB-ZNFs Control Self-Renewal of Human Pluripotent Stem Cells through Epigenetic Repression of Pro-differentiation genes. *Stem Cell Reports*. 2017 Dec 12;9(6):2065-2080. doi: 10.1016/j.stemcr.2017.10.031. Epub 2017 Nov 30. PMID: 29198826; PMCID: PMC5785758.

6) Yi H*, **Raman AT***, Zhang H, Allen GI, Liu Z. Detecting hidden batch factors through data-adaptive adjustment for biological effects. *Bioinformatics*. 2018 Apr 1;34(7):1141-1147. doi: 10.1093/bioinformatics/btx635. PMID: 29617963; PMCID: PMC6454417.

7) **Raman AT***, Pohodich AE*, Wan YW, Yalamanchili HK, Lowry WE, Zoghbi HY, Liu Z. Apparent bias toward long gene misregulation in MeCP2 syndromes disappears after controlling for baseline variations. *Nat Commun*. 2018 Aug 13;9(1):3225. doi: 10.1038/s41467-018-05627-1. PMID: 30104565; PMCID: PMC6089998.

8) **Raman AT**. A research parasite's perspective on establishing a baseline to avoid errors in secondary analyses. *Gigascience*. 2021 Mar 12;10(3):giab015. doi: 10.1093/gigascience/giab015. PMID: 33710326; PMCID: PMC7953484.

9) Gu H*, **Raman AT***, Wang X, Gaiti F, Chaligne R, Mohammad AW, Arczewska A, Smith ZD, Landau DA, Aryee MJ, Meissner A, Gnirke A. Smart-RRBS for single-cell methylome and transcriptome analysis. *Nat Protoc*. 2021 Aug;16(8):4004-4030. doi: 10.1038/s41596-021-00571-9. Epub 2021 Jul 9. Review. PubMed PMID: 34244697.

10) Shareef SJ, Bevill SM, **Raman AT**, Aryee MJ, van Galen P, Hovestadt V, Bernstein BE. Extended-representation bisulfite sequencing of gene regulatory elements in multiplexed samples and single cells. *Nat Biotechnol*. 2021 May 6. doi: 10.1038/s41587-021-00910-x. Epub ahead of print. PMID: 33958785.

* denotes for co-first authorship or authors contributed equally to the manuscript.