Thank you for the Informatics Scientist position interview on March 01 2019

Dear Dr. Brilliant:

I appreciate you taking the time to speak to me about the Informatics Scientist position available at Marshfield Clinic Research Institute (MCRI). I am excited about the opportunity to join Center for Precision Medicine Research (CPMR) with such a well-regarded organization and colleagues.

I am really interest in the Informatics Scientist position in CPMR and it is exact what I planned for my future research which I want to integrate multi-omics and make deep-learning analysis to high dimension data composed by genomics, epi-genomics, transcript-omics, proteomics, metabolomics and electrical health records (EHR). In my previous research I have tried different approaches with now concept or new statistics to combine these multi-omics data including “methylation haplotype and methylation haplotype load” in Nature Genetics, 2017 and miRNA-SNP and CpG-SNPs in Clinical Epigenetics 2015 and 2017. I am quite familiar with these different dataset and the data-processing procedures from the raw data (fastq or fluorescence signal) to advance statistic inference.

With this position, I will apply my computational skill to connect all these multi-omics information within MRCI and public data from Epigenome Roadmap Project, Blueprint Project, UK-biobank Project, TCGA-Cancer Genome Project, GTEx Project. I am confident to the long time programing experience to deal with and analyze these data in Stand-alone or PBS system and make all possible support to my colleagues in MCRI. Meanwhile, I hope to apply my DNA methylation data generation skills to generate DNA methylation information to PMRP dataset which I think will be helpful to build more reputation for PMRP data. I have quite strong enthusiasm to the research in MRCI and my current works have been acknowledged by many collaborators. Several collaboration study working together with Massachusetts General Hospital and School of Public Health in University of Texas have received interesting preliminary results. I think it will be a great start point for me to prepare some external grant application based on my previous publication and research as well as the research in MRCI and collaborations.

I appreciate the time you took to interview me. I am very interested in working with you and look forward to hearing from you. Please don’t hesitate to let me know if you any further questions.

Yours sincerely,

Shicheng Guo

Thank you for the Informatics Scientist position interview on March 01 2019

Dear Dr. Hebbring:

I appreciate you taking the time to speak to me about the Informatics Scientist position available at Marshfield Clinic Research Institute (MCRI). I am excited about the opportunity to join Center for Precision Medicine Research (CPMR) with such a well-regarded organization and colleagues.

I am really interest in the Informatics Scientist position in CPMR and it is exact what I planned for my future research which I want to integrate multi-omics and make deep-learning analysis to high dimension data composed by genomics, epi-genomics, transcript-omics, proteomics, metabolomics and electrical health records (EHR). In my previous research I have tried different approaches with now concept or new statistics to combine these multi-omics data including “methylation haplotype and methylation haplotype load” in Nature Genetics, 2017 and miRNA-SNP and CpG-SNPs in Clinical Epigenetics 2015 and 2017. I am quite familiar with these different dataset and the data-processing procedures from the raw data (fastq or fluorescence signal) to advance statistic inference.

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In terms of DNA methylation detection to PMRP samples, I think it will be quite helpful for our research. I am preparing apply multiplex sequencing with MCRI MiSeq Sequencing Machine (TG MiSeq Reagent Kit v3, 2x25 million paired-end 300bp reads: 1,869$) with Nextera XT DNA Library Preparation Kit (96 indexes, 384 samples, 4x1020$=4080$). As pharmacoepigenetics (PeGx), we can have several different hypothesis: 1) DNA methylation status polymorphism in the population provide drug response and side-effect variation. 2) DNA methylation related drug resistance. 3) Additive effect from DNA methylation and genetic polymorphism to gene expression which associated with drug response and outcome. All these hypothesis can be validated with PMRP cohort and the result should be quite interesting. There are still very limited publication in the field of PeGx and more conclusion should be validated by detail study design.

Finally, I appreciate the time you took to interview me. I am very interested in working with you and look forward to hearing from you. Please don’t hesitate to let me know if you any further questions.

Yours sincerely,

Shicheng Guo

Thank you for the Informatics Scientist position interview on March 01 2019

Dear Dr. Shukla:

I appreciate you taking the time to speak to me about the Informatics Scientist position available at Marshfield Clinic Research Institute (MCRI). I am excited about the opportunity to join Center for Precision Medicine Research (CPMR) with such a well-regarded organization and colleagues.

I am really interest in the Informatics Scientist position in CPMR and it is exact what I planned for my future research which I want to integrate multi-omics and make deep-learning analysis to high dimension data composed by genomics, epi-genomics, transcript-omics, proteomics, metabolomics and electrical health records (EHR). In my previous research I have tried different approaches with now concept or new statistics to combine these multi-omics data including “methylation haplotype and methylation haplotype load” in Nature Genetics, 2017 and miRNA-SNP and CpG-SNPs in Clinical Epigenetics 2015 and 2017. I am quite familiar with these different dataset and the data-processing procedures from the raw data (fastq or fluorescence signal) to advance statistic inference.

With this position, I will apply my computational skill to connect all these multi-omics information within MRCI and public data from Epigenome Roadmap Project, Blueprint Project, UK-biobank Project, TCGA-Cancer Genome Project, GTEx Project. I am confident to the long time programing experience to deal with and analyze these data in Stand-alone or PBS system and make all possible support to my colleagues in MCRI. Meanwhile, I hope to apply my DNA methylation data generation skills to generate DNA methylation information to PMRP dataset which I think will be helpful to build more reputation for PMRP data. I have quite strong enthusiasm to the research in MRCI and my current works have been acknowledged by many collaborators. Several collaboration study working together with Massachusetts General Hospital and School of Public Health in University of Texas have received interesting preliminary results. I think it will be a great start point for me to prepare some external grant application based on my previous publication and research as well as the research in MRCI and collaborations.

I am quite interested in fecal-seq assay since there is very limited DNA methylation data from fecal-DNA and which might be very informative for colon cancer or some other digestive diseases. This low-cost fecal-DNA methylation detection method was based on the difference of CpG density in human and bacterial. In human genome, there is a group of methylation binding protein, such as MBD2, MBD5. These protein could bind methylated DNA fragment with high CpG density. In this method, bait protein created by genetically fusing the human methyl-CpG binding domain protein 2 (MBD2) to the Fc tail of human IgG1. MBD2-Fc protein is then bound by a paramagnetic Protein A immunoprecipitation bead to create a complex that selectively binds double-stranded DNA with 5-methyl CpG dinucleotides. Because vertebrate DNA contains a high frequency of methylated CpGs while bacterial DNA does not, this MBD bait complex selectively binds host DNA. This method is quite easy to be implemented in Marshfield Clinic PMRP cohort with low-cost to identify fecal-DNA methylation based biomarkers. We can have more discussion if you are interested in it and we can try to build this pipeline in CPMR.

Finally, I appreciate the time you took to interview me. I am very interested in working with you and look forward to hearing from you. Please don’t hesitate to let me know if you any further questions.

Yours sincerely,

Shicheng Guo