

# HEEWON SEO, MS, PhD

3330 Hospital Drive NW, Calgary, AB T2N 4N1  
Heewon.Seo@ucalgary.ca

## SUMMARY

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Skilled bioinformatician in the field of pharmacogenomics with experience analyzing thousands of whole-genomes, exomes, (spatial) transcriptomes, and pharmacological profiles to discover molecular biomarkers for precision therapeutics and novel synergistic drug combinations for determining best treatment strategies in patients.

## AREAS OF EXPERTISE

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- Understanding the biomedical data life cycle in the era of constant data creation
- Development of new tools and methods for biomedical big data analysis
- Rapid construction of complex computational pipelines and their optimization
- Experience in working in high performance computing environments (on-premise and cloud)

## EDUCATION

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**PhD in Medical Science** (Biomedical Informatics) *Sep 2012 - Dec 2017*

Seoul National University College of Medicine, Seoul, Korea

*Thesis: **Methods for Variant- and Gene-based Analysis for Pharmacogenomics Research.***

**MS in Medicine** (Biomedical Informatics) *Sep 2010 - Aug 2012*

Seoul National University College of Medicine, Seoul, Korea

*Thesis: **Loss of Function Gene-set Analysis of Personal Genome using Pathway-disease Similarity.***

**BS in Computer Science** *Mar 2004 - Feb 2010*

Sejong University, Seoul, Korea

*GPA: 4.37/4.5, **Summa Cum Laude**, achieved the early graduation of excellent students within 3 years*

## RESEARCH/WORK EXPERIENCE

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**Lead Bioinformatician** *Jan 2024 - present*

Applied Spatial Omics Centre, Cumming School of Medicine, University of Calgary, Calgary, AB, Canada

- Developed a Web page to distribute project results (<https://ASOC.UCalgary.ca/>) and UofC-themed Web pages using Drupal (<https://cumming.ucalgary.ca/research/cat/spatial-omics/home>)
- Built a report tool that generates diagnostic plots for rigorous QC and basic analysis using the Nanostring GeoMx Digital Spatial Profiler data (<https://github.com/UC-ASOC/>)
- Established a Docker app to share the workflow of the spatial transcriptomics data for research reproducibility and replicability (<https://hub.docker.com/u/ucasoc>)
- Developed an ShinyApp that allows users to explore their GeoMx data and check the gene expression handy (<https://uc-asoc.shinyapps.io/geomxexpr/>)
- Established a QC process and analyzed spatial transcriptomics profiles from Nanostring GeoMx DSP/CosMx SMI and 10X Genomics Visium/Xenium in situ

## **RESEARCH/WORK EXPERIENCE (CONT'D)**

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### **Lead Bioinformatician**

*Nov 2020 - Dec 2023*

Arnie Charbonneau Cancer Institute, Cumming School of Medicine, University of Calgary, Calgary, AB, Canada

- Analyzed spatial transcriptomics to characterize interplays between tumour cells and tumour microenvironment (TME) which promote tumour progression, invasion, and resistance to therapy
- Leveraged immunofluorescence labelled tissue microarrays to understand tumour cell adaptation to the local TME using nearest neighbour analysis and identified micro-neighbourhoods that affect patients' prognosis
- Developed a correlation-based method, Solution Neighbour Space (SNS), to integrate multiomics datasets and SNS can be used to find the best rank(s) from non-negative matrix factorization driven by biological features
- Discovered CAR (chimeric antigen receptor)-T cell targets that are highly expressed in glioblastoma or sarcoma tumour cell surface using compendium RNA-seq datasets
- Mined and enumerated cell surface proteins (genes) from multiple data/knowledge-base and literature along with the level of evidence to prioritize CAR-T targets
- Identified genes that are highly enriched to the T-cell exposure compared to the non-exposure group in CRISPR screening
- Devised a pipeline to generate a consensus BAM using UMI (unique molecular identifiers) to rescue reads in shallow-depth/FFPE exome
- Developed an image analysis workflow for spatial neighborhood analysis that can be coupled with spatial transcriptomics to assess the correspondence between tumor-TME organization

### **Postdoctoral Fellow**

*Jan 2018 - Oct 2020*

Princess Margaret Cancer Centre, University Health Network, Toronto, Canada

- Developed the largest integrated database in high-throughput drug combination studies, SYNERGxDB (<http://SYNERGxDB.ca/>), and integrated molecular profiles of the corresponding preclinical models in order to discover effective combinations and predictive biomarkers of specific cancer types or a set of cell lines
- Discovered two synergistic drug combinations and four meaningful expression-based biomarkers for the combinations using SYNERGxDB
- Built a translational framework for precision oncology using a compendium of preclinical multimodal pharmacogenomics datasets and clinical patients cohorts
- Created a semi-automatic analysis tool on Microsoft Azure using Jupyter Notebook for exploring large pharmacogenomics datasets
- Devised an online tool to report significant biomarkers using a semi-automation system for better data representation and easier data investigation with multiple levels of granularity
- Performed meta-analysis of pancreatic cancer cell lines to discover expression-based biomarkers predictive of gemcitabine responses in order to improve current treatment strategies
- Analyzed multiple preclinical models including patient-derived cell lines and organoids in single or pairwise drug testing and their molecular profiles
- Identified two promising gemcitabine resistance biomarkers that may help patients overcome drug resistance in combination with inhibitors in pancreatic cancer

## RESEARCH/WORK EXPERIENCE (CONT'D)

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### Visiting Researcher

Jan 2018 - Oct 2020

Ontario Institute for Cancer Research (OICR), Toronto, Canada

- Analyzed large scale genomic and clinical data with appropriate statistical methods in order to identify gemcitabine resistance biomarkers in pancreatic cancer cohorts
- Discovered gemcitabine resistance biomarkers to select drugs (i.e. inhibitors) that sensitize gemcitabine resistance in pancreatic cancer and validated in survival analysis
- Conducted survival meta-analysis to validate the biomarkers in multiple pancreatic cancer cohorts to improve patient outcomes
- Participated in the molecular tumour board of the COMPASS (Changes and Characteristics of Genes in Patients With Pancreatic Cancer for Better Treatment Selection) trial

### Doctoral Researcher

Sep 2012 - Dec 2017

Seoul National University College of Medicine, Seoul, Korea

- Successfully found pharmaco-genes and -variants that have an association with mercaptopurine-induced neutropenia or busulfan-induced hepatotoxicity in paediatric cancer patients and ritodrine-induced pulmonary oedema in pregnant women
- Identified favourable prognostic markers of survival in allogeneic hematopoietic stem cell transplantation patients in donor exomes
- Solely developed a pharmacogenomics analysis platform for the analysis and interpretation of patient genomes and exomes in order to identify drug side effect associated genes and variants
- Built a computational gene-level approach to aggregate the impact of heterogeneous variants in sequencing data
- Analyzed whole-genome, whole-exome, targeted panels, whole-transcriptome, small RNAs, and microarray data with clinical information across platforms (i.e., Ion Proton, Complete Genomics, and Illumina)
- Closely inspected variant calls and read alignment statuses to improve caller algorithms and strategies
- Localized big open public omics datasets such TCGA (The Cancer Genome Atlas), 1KGP (1000 Genomes Project), ADSP (Alzheimer's Disease Sequencing Project), and SFARI (Simons Foundation Autism Research Initiative)
- Developed a diagnostic sequencing panel for pharmacotyping in childhood rare cancers (i.e. *acute myeloid leukemia*)
- Significantly involved in writing the grant proposal entitled, "Precision Medicine and Clinical Evaluation Technologies for Childhood Rare Cancers", and the application has been approved by the Korea Food & Drug Administration in 2016
- Doubled as a Server Administrator who was responsible for setting up and maintaining large-scale servers (472 cores, 4.25 TB RAM) and storage (756 TB) in Network/Lustre/Fraunhofer File Systems

## PUBLICATIONS

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- **CD73 inhibits cGAS-STING and cooperates with CD39 to promote pancreatic cancer.** Céilia Jacobberger-Foissac†, Isabelle Cousineau†, Yacine Bareche†, David Allard, Pavel Chrobak, Bertrand Allard, Sandra Pommey, Nouredin Messaoudi, Geneviève Soucy, Secil Koseoglu, Ricard Masia, Andrew C. Lake, [Heewon Seo](#), Christopher B. Eeles, Neha Rohatgi, Simon C. Robson, Simon Turcotte, Benjamin Haibe-Kains, John Stagg\* *Cancer Immunol Res* 2023;11(1):56-71
- **Orchestrating and sharing large multimodal data for transparent and reproducible research.** Anthony Mammoliti†, Petr Smirnov, Minoru Nakano, Zhaleh Safikhani, Christopher Eeles, [Heewon Seo](#), Sisira Kadambat Nair, Ian Smith, Chantal Ho, Gangesh Beri, Marc Hafner, Benjamin Haibe-Kains\* *Nat Commun* 2021;12(1):5797
- **CaReAI: Capturing Read Alignments in a BAM file Rapidly and Conveniently.** Yoomi Park†, [Heewon Seo](#)†, Kyunghun Yoo, and Ju Han Kim\* *J Big Data* 2021;8:23
- **Identifying Genetic Variants Associated with Ritodrine-induced Pulmonary Edema.** Seung Mi Lee†, Yoomi Park†, Young Ju Kim, Han-Sung Hwang, [Heewon Seo](#), Byung-Joo Min, Kye Hwa Lee, So Yeon Kim, Young Mi Jung, Suehyun Lee, Chan-Wook Park, Ju Han Kim\*, and Joong Shin Park\* *PLoS One* 2020;15(11):e0241215
- **Homozygote CRIM1 Variant is Associated with Thiopurine-induced Neutropenia in Leukemic Patients with both Wildtype NUDT15 and TPMT.** Yoomi Park†, Hyery Kim†, [Heewon Seo](#), Jung Yoon Choi, Youngeun Ma, Sunmin Yun, Byung-Joo Min, Myung-Eui Seo, Keon Hee Yoo, Hyoung Jin Kang, Ho Joon Im, and Ju Han Kim\* *J TRANSL MED* 2020;18(1):265
- **Gene-wise Variant Burden and Genomic Characterization of Nearly Every Gene.** Yoomi Park†, [Heewon Seo](#), Brian Ryu, and Ju Han Kim\* *Pharmacogenomics* 2020;21(12):827-840
- **SYNERGxDB: an Integrative Pharmacogenomic Portal to Identify Synergistic Drug Combinations for Precision Oncology.** [Heewon Seo](#)†, Denis Tkachuk, Chantal Ho, Anthony Mammoliti, Aria Rezaie, Seyed Ali Madani Tonekaboni, and Benjamin Haibe-Kains\* *Nucleic Acids Res* 2020;48(W1):W494-W501
- **ToxicoDB: an Integrated Database to Mine and Visualize Large-scale Toxicogenomic Datasets.** Sisira Kadambat Nair†, Christopher Eeles, Chantal Ho, Gangesh Beri, Esther Yoo, Denis Tkachuk, Amy Tang, Parwaiz Nijrabi, Petr Smirnov, [Heewon Seo](#), Danyel Jennen, and Benjamin Haibe-Kains\* *Nucleic Acids Res* 2020;48(W1):W455-W462
- **Discovery of Donor Genotype Associated with Long-term Survival of Patients with Hematopoietic Stem Cell Transplantation in Refractory Acute Myeloid Leukemia.** Chan-Young Ock†, [Heewon Seo](#)†, Dae-Yoon Kim, Byung Joo Min, Yoomi Park, Hyun Sub Cheong, Eun-Young Song, Inho Kim, Sung-Soo Yoon, Ju Han Kim\*, and Youngill Koh\* *Leuk Lymphoma* 2018;60(7):1775-1781
- **Deleterious Genetic Variants in Ciliopathy Genes Increase Risk of Ritodrine-induced Cardiac and Pulmonary Side Effects.** [Heewon Seo](#)†, Eun Jin Kwont, Young-Ah You, Yoomi Park, Byung Joo Min, Kyunghun Yoo, Han Sung Hwang, Ju Han Kim\*, and Young Ju Kim\* *BMC Med Genomics* 2018;11(1):4
- **APEX1 Polymorphism and Mercaptopurine-related Early Onset Neutropenia in Pediatric Acute Lymphoblastic Leukemia.** Hyery Kim†, [Heewon Seo](#)†, Yoomi Park, Byung Joo Min, Myung Eui Seo, Kyung Duk Park, Hee Young Shin, Ju Han Kim\*, and Hyoung Jin Kang\* *Cancer Res Treat* 2018;50(3):823-834

## PUBLICATIONS (CONT'D)

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- **Idiopathic Hypereosinophilia Is Clonal Disorder? Clonality Identified by Targeted Sequencing.** Jee-Soo Lee†, Heewon Seo, Kyongok Im, Si Nae Park, Sung-Min Kim, Jung-Ah Kim, Seon Young Kim, Joon-hee Lee, Sunghoon Kwon, Miyoung Kim, Insong Koh, Seungwoo Hwang, Heung-Woo Park, Ju Han Kim, and Dong Soon Lee\* *PLoS One* 2017;12(10):e0185602
- **Evaluation of Exome Variants using the Ion Proton Platform to Sequence Error-Prone Regions.** Heewon Seo†, Yoomi Park†, Byung Joo Min, Myung Eui Seo, and Ju Han Kim\* *PLoS One* 2017;12(7):e0181304
- **Posttranslational control of T-cell development by the ESCRT protein CHMP5.** Stanley Adorot, Kwang H Park, Sarah E Bettigole, Raphael Lis, Hee Rae Shin, Heewon Seo, Ju Han Kim, Klaus-Peter Knobloch, Jae-Hyuck Shim\*, Laurie H Glimcher\* *Nat Immunol* 2017;18(7):780-790
- **Disease Markers of Pediatric Idiopathic Nephrotic Syndrome and Markers of Steroid-responsiveness: Whole-transcriptome Sequencing of Peripheral Mononuclear Cells.** Hee Gyung Kang†, Heewon Seo†, Jae Hyun Lim, Jong Il Kim, Kyoung Hee Han, Hey Won Park, Ja Wook Koo, Kee Hyuck Kim, Ju Han Kim\*, Hae Il Cheong, and Il-Soo Ha\* *J Int Med Res* 2017;45(3):948-963
- **Gastrointestinal Tuberculosis is not Associated with Proton Pump Inhibitors: A Retrospective Cohort Study.** Kyoung Sup Hong†, Seung Joo Kang, Jong Kyoung Choi, Ju Han Kim, Heewon Seo, Suehyun Lee, Jae-Woo Jung, Hye-Ryun Kang, Sang-Heon Cho, and Joo Sung Kim\* *World J Gastroenterol* 2013;19(2):258-264
- **Development of Korean Rare Disease Knowledge Base.** Heewon Seo†, Dokyoon Kim, Jong-Hee Chae, Hee Gyung Kang, Buyng Chan Lim, Hae Il Cheong, and Ju Han Kim\* *Healthc Inform Res* 2012;18(04):272-278

## SOFTWARE

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- **SYNERGxDB** (<https://SYNERGxDB.ca/>) is a web-based database that provides the largest integrated database in drug combination screenings and molecular profiles to discover effective combinations and predictive biomarkers.
- **CaReAI** [kæri:əl] (Capturing Read Alignments, <https://github.com/lootpiz/CaReAI>) is a high-performance alignment capturing tool for visualizing the read-alignment status of nucleotide sequences and obtaining read-level data for evaluating variant calls and detecting technical biases.
- **VVA** (Variant Visualization and Annotation, <https://github.com/lootpiz/VVA>) is a gene- and variant-centred visualization tool to be used for exome sequencing data analysis and is optimized for displaying the overall distribution of variants in a gene at a glance.
- **KRDK** (Korean Rare Disease Knowledge base, <http://www.snubi.org/software/raredisease/>) is a web-based, research oriented data repository that provides comprehensive information for rare disease research: disease review, clinics, directory, mutation database, patient registry, and biobank.

## PROGRAMMING LANGUAGE SKILLS

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- High-level languages: C/C++
- Scripting languages: R, Python, javascript, PHP, and HTML
- Structured query languages (SQL): MySQL, MariaDB, and NoSQL (MongoDB)
- Operating system: Good working knowledge of Linux and MacOS
- Adobe products: Illustrator, Photoshop, and Premiere Pro

## REFERENCES

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- **A. Sorana Morrissy, PhD**, Sorana.Morrissy@ucalgary.ca  
Assistant Professor,  
Department of Biochemistry and Molecular Biology, University of Calgary, Calgary, AB, Canada
- **Benjamin Haibe-Kains, PhD**, Benjamin.Haibe-Kains@uhnresearch.ca  
Senior Scientist,  
Princess Margaret Cancer Centre, University Health Network, Toronto, ON, Canada
- **Ju Han Kim, MD, PhD, MS**, juhan@snu.ac.kr  
Chair and Professor,  
Div. of Biomedical Informatics, Seoul National University College of Medicine, Seoul, Korea