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Dear Drs. Fertig, Greene, Hampton, Hicks, Love, and Patro,

      I am thrilled to collaborate with each of you as part of our proposed work for the *Chan Zuckerberg Initiative Seed Networks for the Human Cell Atlas* RFA. In addition to the outstanding collaborations I have had with most of you to date, I am excited that we will be combining our expertise to develop and extend methods and resources for rapid search, annotation, and exploration of the single cell datasets provided as part of the Human Cell Atlas project using reduced-dimensional representations. I am honored to serve as coordinating PI for this group of talented investigators, and I am certain that we will provide a suite of invaluable assets as we integrate with the broader HCA network. Our proposal to adapt low-dimensional representations will provide the building blocks for search approaches that can be practically applied across very large datasets such as the HCA.

      I am committed to evaluating, developing, adapting a variety of dimensionality reduction methods for single cell RNA-Seq to establish a versioned catalog of latent space representations across the Human Cell Atlas (Aim 2). We will annotate these low-dimensional representations using both cellular metadata derived directly from the HCA, as well as with biological processes gleaned from analysis of gene networks and pathways with enriched representation in specific latent spaces. My lab will be responsible for coordinating spot-check experimental validations of latent spaces as required, by leveraging resources in our existing wet laboratory, and in conjunction with other investigators in the HCA network with available and appropriate model systems. Furthermore, my group will continue to develop and extend efficient and accurate transfer learning approaches, both within our network and in conjunction with Chan Zuckerberg Initiative and Human Cell atlas investigators more broadly, to increase the adoption and utility of the latent space representations. Finally, I am eager to contribute to the development of educational materials around the topics of single cell RNA-Seq analysis and the use of latent space representations of cell types, cell states, and biological processes. I plan to incorporate these training materials into a workshop to be held as part of the annual McKusick Short Course on Human and Mammalian Genetics at Jackson Laboratories, at which I have been an instructor on single cell biology for the past few years.

      I am enthusiastic about our collaborative efforts to increase the adoption and utility of low-dimensional representations of the Human Cell Atlas, and I look forward to working with each of you to achieve the aims proposed in this study.

Sincerely,

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