In sum, this project will result in a large and comprehensive dataset of comparable EGIs from many species, as well functional data such as scRNA-seq data, of multiple cell types and species. Analyses of such datasets will substantially improve our understanding of the evolution of enhancers and EGIs. In turn, these results will inform us as to how enhancers regulate gene expression and paralog generation. Taken together, these discoveries will be enormously useful for studying human health and disease. Particularly, EGIs that are conserved across mammals could represent potential targets for disease-causing mutations. Such conserved EGIs cannot be identified from sequence comparisons or non-comparative analyses. We have extensive experience with processing and analyzing Hi-C data (*1, 2*), identifying enhancers (*3*) and their target genes (*4, 5*). We are also experienced in conducting comparative analyses (*6, 7*), for which we have developed many pipelines that are readily available for this project (*6, 8*).

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