Differential analysis of multi-modal omics data from IBD mouse models

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L-arginine is a semi-essential amino acid and central intestinal metabolite. Our collaborators from the University Hospital Erlangen (Jochen Mattner and team) have observed that an enhanced availability of L-arginine promotes the resolution of experimental colitis while a reduced availability of L-arginine aggravates disease in IBD mouse models[1,2]. To decipher the mechanisms underlying these observations, our collaborators generated datasets of (sc)RNA-seq from intestinal tissues, intestinal immune cells and of 16S rRNA analyses of fecal samples from animal models with and without decreased availability of L-arginine. They have also obtained untargeted metabolomics data from fecal samples. The task of the project is to carry out differential analyses for these data and to thereby identify potential molecular pathways and mechanisms that could explain the observed phenotypic differences.

Specifically, the proposed project should proceed in the following steps:

1. Run a standard scRNA-seq analysis pipeline (quality control, dimensionality reduction, clustering, cell type assignment) on the available scRNA-seq data.
2. Identify differentially expressed genes within a specific cell population or identify differentially abundant cell states, again using standard tools and pipelines.
3. Interpret the signatures obtained in step 2 to the other data modalities in the context of additional mechanistic information, e.g., by integrating protein-protein interaction networks or metabolic pathway databases.

Requirements

- Programming skills in Python or R.
- Willingness to independently dive into cellular biology (reading textbooks, etc.)
- Willingness to engage in continuous interdisciplinary exchange with our collaborators at the University Hospital Erlangen.

Depending on the results, continuation of the project in the context of a MSc thesis is possible.

References

1. Baier, J., Gänsbauer, M., Giessler, C., Arnold, H., Muske, M., Schleicher, U., Lukassen, S., Ekici, A., Rauh, M., Daniel, C., et al. (2020). Arginase impedes the resolution of colitis by altering the microbiome and metabolome. J. Clin. Invest. *130*, 5703–5720. https://doi.org/10.1172/JCI126923.

2. Nüse, B., Holland, T., Rauh, M., Gerlach, R.G., and Mattner, J. (2023). L-arginine metabolism as pivotal interface of mutual host-microbe interactions in the gut. Gut Microbes *15*, 2222961. https://doi.org/10.1080/19490976.2023.2222961.