

Cover Letter: Postdoctoral Fellow – Metabolic Homeostasis

Dear Selection Committee,

I am interested in the Postdoctoral Fellow position in Metabolic Homeostasis at Roche's Institute of Human Biology. With my background in gut microbial biotechnology and a passion for understanding complex biological systems, I am excited about the opportunity to contribute to your innovative research at the intersection of adipose tissue biology and metabolic homeostasis.

Research Background and Transition

My fascination with complex biological systems has been a driving force throughout my academic career. My doctoral research at ETH Zurich focused on understanding how dietary and gut microbially produced micronutrients affect the growth and metabolism of microbes residing in the human adult gut. This work has resulted in four research publications, demonstrating my ability to conduct high-quality research and effectively communicate scientific findings.

While my expertise lies in gut microbial biotechnology, I see a compelling opportunity to apply my skills and knowledge to the field of adipose tissue biology and metabolic homeostasis. The complex interplay between gut microbiota and host metabolism, including adipose tissue function, represents an exciting bridge between my current expertise and the research focus of this position. This transition would allow me to expand my understanding of systemic metabolic regulation while leveraging my existing skillset.

I believe that many of the techniques and approaches I've mastered are directly transferable to studying adipose tissue:

- 1) Experience with *in vitro* models: My experience with anaerobic batch fermentations and *in vitro* models of the human colon has provided me with strong foundation techniques. I am eager to apply these skills to learn, develop, and work with cellular and organoid models of adipose tissue.
- 2) Analytical Techniques: During my doctoral research, I developed and utilized various analytical methods, including UHPLC-UV/MS, HPLC-RI, and GC-MS. These skills will be valuable in analyzing metabolites and signaling molecules involved in adipose tissue function and its interactions with other tissues.
- 3) Molecular Biology and Omics Approaches: My work involved both 16S rRNA marker-gene sequencing and metagenomic analysis. I am confident that these skills, along with my recent training in RNA-seq analysis, will be applicable to studying gene expression and signaling pathways in adipose tissue.

Motivation and Research Vision

The focus of your project on understanding the mechanisms by which adipose tissue interacts with other tissues to mediate whole-body energy homeostasis is fascinating. I am particularly intrigued by the potential to explore the sensory innervation of adipose tissue and its functional consequences. Building on my experience and your research goals, I propose the following research aims:

- 1) Developing Multicellular *in vitro* Systems: Utilize my expertise *in vitro* modeling to develop multicellular *in vitro* systems that accurately represent the interactions between adipose

tissue and sensory neurons. This would involve adapting my skills in anaerobic culture to the specific requirements of adipose and neuronal cell types.

- 2) Characterizing Adipose-Neuron Interactions: Apply my analytical skills (e.g., UHPLC-MS/MS) to identify and quantify signaling molecules and metabolites involved in adipose-neuron communication. This would build upon my experience in metabolite profiling and method development.
- 3) Transcriptomic and Functional Analysis: Utilize RNA-seq and other omics approaches to characterize the transcriptional changes in both adipose tissue and sensory neurons under various conditions, such as different metabolic states or in response to specific stimuli.

Scientific Mission and Personal Development

My broad scientific goal is to use advanced molecular and computational techniques to understand complex biological systems and their impact on human health. While my previous work focused on the gut microbiome, I see this postdoctoral position as an exciting opportunity to expand my research scope to translational research and drug development. I am particularly motivated by the translational aspect of this research and its potential to contribute to our understanding of diabetes and other metabolic disorders. The opportunity to work in an interdisciplinary environment at Roche, collaborating with biologists, engineers, and data scientists, and mentoring junior scientists fits with my desire to tackle complex scientific questions from multiple angles and sharing knowledge.

Moreover, I am excited about the prospect of learning new techniques specific to adipose tissue research, such as adipocyte differentiation protocols and methods for studying neuronal function. I believe that my strong foundation in molecular biology, analytical techniques, and data analysis, combined with my eagerness to learn, will allow me to quickly adapt to this new field and make meaningful contributions to your research goals.

Throughout my academic career, I have demonstrated the ability to prioritize tasks effectively and focus on critical details while maintaining a broader perspective on research objectives. This skill will be invaluable in managing the complex projects and collaborations involved in this position.

If selected, I would be available to start in November 2024 or earlier, depending on the project requirements.

Thank you for considering my application. I look forward to the possibility of discussing how my background, skills, and motivation align with your team's goals in advancing our understanding of metabolic homeostasis.

Sincerely,

A handwritten signature in black ink, appearing to read 'Palni Kundra', with a horizontal line drawn underneath it.

Palni Kundra