The adrenal glands are small but vital organs located above the kidneys that produce hormones essential for life. These hormones enable the body to respond to stress, regulate blood pressure, control inflammatory processes, and maintain proper metabolism. Disorders in adrenal hormone production lead to serious diseases: excess causes Cushing's syndrome with weight gain and hypertension, while deficiency triggers Addison's disease characterized by dangerous weight loss and chronic fatigue. Despite the crucial importance of these organs, the mechanisms of their growth and adaptation remain incompletely understood.

The architecture of the adrenal glands is complex and multi-layered. The outer layers (cortex) produce steroid hormones, while the inner medulla produces adrenaline. The entire structure is surrounded by a connective tissue capsule covered with adipose tissue. This complex structure makes studying the adrenal glands challenging because traditional molecular biology methods based on mechanical homogenization lose information about the specific localization and function of individual layers.

Recent technological advances in spatial transcriptomics now enable analysis of the activity of all 20,000 genes while preserving the precise location of each cell within organs. This revolutionary approach allows observation of how different adrenal cell types communicate with each other and respond to various stimuli, providing information unavailable using conventional methods.

Our project aims to create the first comprehensive atlas of gene activity in the mouse adrenal gland across five major growth types. We will investigate natural age-related adrenal growth, analyzing the molecular reasons for the significantly larger size of female adrenal glands compared to males in mice. We will analyze mechanisms of rapid gland enlargement under the influence of stress hormones like ACTH, regeneration processes following surgical removal of the medulla, and compensatory adrenal growth after unilateral adrenalectomy. We will also examine the influence of sex hormones—testosterone and estradiol—on adrenal development.

Using advanced Visium HD technology with 2-micrometer resolution, we will map gene expression patterns in 156 mice under precisely controlled experimental conditions. We will validate the obtained data using complementary technologies: Xenium for even higher resolution analysis of key genes and immunohistochemistry to verify the activity of selected genes at the protein level.

Our preliminary studies have already yielded interesting discoveries published in scientific journals, including identification of novel markers distinguishing individual adrenal layers and unexpected interactions between the adrenal glands and surrounding adipose tissue. We discovered that the female-specific X-zone utilizes unique signaling pathways absent in males, providing the first spatial map of sexual dimorphism in the adrenal gland.

A key element of the project will be the "Spatial Atlas of Mouse Adrenal Growth"—a publicly accessible interactive website where scientists worldwide can explore our complete dataset. Researchers will be able to search for any genes, visualize where and when they are active across all growth conditions, and download data for their own analyses. A prototype atlas is already available at https://adrenaldash.duckdns.org.

Why is this important? Mouse adrenal physiology closely mirrors human adrenal function, making our findings directly relevant to human health. By identifying molecular pathways controlling adrenal growth, we may discover new therapeutic targets for serious diseases such as adrenocortical carcinoma (a rare but aggressive cancer), Cushing's syndrome, and adrenal insufficiency. Understanding compensatory growth mechanisms may improve treatment outcomes for patients requiring adrenal surgery. Revealing how stress hormones trigger gland enlargement has implications for disorders associated with chronic stress, metabolic syndrome, and hypertension affecting millions of people worldwide.

Beyond immediate medical applications, the atlas will serve as a fundamental reference resource for the endocrinology research community, enabling discoveries we cannot currently anticipate. Our molecular atlas will chart new territories in adrenal biology, potentially transforming how we understand and treat adrenal diseases.