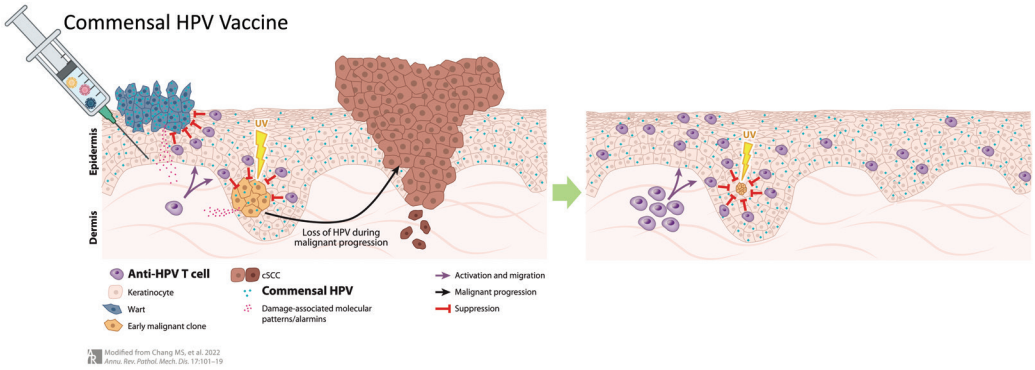

Fig. 1: T Cell Immunity to Commensal Human Papillomaviruses (HPVs) Cross-Protects Tissues Against Cancer. HPV broadly colonizes human skin cells. In the immunocompetent setting, skin cells colonized with HPV trigger T cell responses that prevent warts and block skin cancer development from malignant cells. In immunocompromised and elderly patients, the immune response to HPV is diminished, which leads to a marked increase in skin cancer risk. Thus, commensal HPV immunotherapy to boost T cell immunity in the skin can control malignant clones and prevent/treat skin cancer in the at-risk population.

Leveraging the human virome to combat cancer, autoimmunity, and other age-associated diseases

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To date, several immunotherapies have proven efficacious against late-stage cancers; however, the immune system's role in controlling the early development of cancer remains uncertain. The Demehri laboratory studies the immune system's role in maintaining tissue homeostasis and regulating the early stages of cancer development. In particular, the objective is to harness the beneficial functions of the human virome and immune system. Our research has elucidated the mechanisms that drive immune activation sufficient to prevent cancer formation from pre-cancerous lesions. This approach raises an excellent opportunity to discover novel immune pathways that can be leveraged in cancer prevention and therapy.

To realize the immune system's potential in maintaining tissue homeostasis, we study the pathways that lead to immune system activation against early phases of abnormal cellular differentiation and malignant transformation. These efforts have led us to discovering the critical role that commensal virome plays in our body. Commensals are microbes that ubiquitously reside in the body without harming human health.

Our innovative discovery posits that commensal eukaryotic viruses (e.g., HPVs and HPyVs) can play a beneficial role in maintaining healthy immune (antigen-driven) responses. Further, their absence underlies the emergence of cancer as well as aging and autoimmune diseases. With the goal of harnessing this potential, we have conducted pioneering studies on the impact of commensal virus–immune system interplay on organs exposed to environmental carcinogens and aging. We aim to determine how the immune system's control of the commensal virome regulates the homeostasis of virus-colonized tissues. The beneficial functions of the commensal virome revealed through this effort could ultimately be applied to prevent and treat cancer and other age-associated diseases.

We have generated robust proof-of-concept data showing the efficacy of commensal virome immunotherapies to combat epithelial cancers, eliminate aging cells, and protect against autoimmunity. Based on our paradigm-shifting concept, we have also developed a Discovery Engine that will feed a product pipeline of virome-directed therapeutics.