Alterations in host protein trafficking during Human papillomavirus infection and oncogenesis

Human papillomaviruses (HPV) cause nearly 5% of all human tumours, including cervical cancer and head and neck cancers. Two major viral oncoproteins, E6 and E7, are responsible for cell transformation and cancer development. Recent studies have identified a novel function of HPV proteins in regulating host endocytic transport pathways. Our preliminary data show that HPV E6 and L2 proteins interact with the sorting nexins SNX27 and SNX17 and alter the transport of host cargo proteins. **This supports our hypothesis that HPV infection could directly interfere with host cell protein localisation and transport, thus having broader implications for cell physiology and pathophysiology.** This topic is highly interesting as the importance of these processes has only recently been highlighted and is still largely unknown.

The aim of the presented project is to elucidate how HPV proteins modulate endocytic cargo trafficking and to define the biological consequences thereof. This will be done by detailed biochemical characterisation of HPV-protein interactions with the host trafficking machinery and by linking the contribution of these interactions to HPV-driven tumorigenesis. We will apply standard biochemical and cell biology methods, which will be augmented by modern approaches like in vivo imaging, 3D organotypic raft cultures and clinical sample analysis.

The results of this study will define whether targeting interactions between HPV proteins and the host trafficking machinery could have **prophylactic** or **therapeutic** value in HPV-related pathologies. Furthermore, these studies will provide a list of potential **diagnostic and prognostic biomarkers** - cellular proteins whose expression patterns are altered during HPV infections and malignancies. This is particularly important for head and neck HPV cancers, where the disease burden resulting from HPV infections is likely to increase while reliable diagnostic and prognostic markers are still missing.