Epithelial apical actin protrusions: using zebrafish to understand them in development and disease

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Epithelia have apical surface structures that aid in their function. These include intestinal microvilli that are important for absorption and actin microridges that likely play a role in glycocalyx organization and abrasion resistance in non-keratinizing stratified squamous epithelia. Actin microridges are actin protrusions that have a maze-like organization. How such laterally-long actin protrusions are built remains unclear, with seemingly contradictory evidence indicating that either multiple bundles or a network of actin form this structure and a hypothesis suggesting that it is formed from multiple microvilli fused side to side. Using light and electron microscopy in the zebrafish periderm we show that microridges exhibit molecular and structural similarities to the leading edge of migrating cells, such as the localization of the Arp2/3 complex, WASp-like protein, filamin, cofilin and alpha-actinin and the organization of actin in a network of filaments with no obvious bundles present. We also find that the underlying terminal web cytoskeleton is arranged parallel to the membrane resembling the lamella of motile cells. Consequently, we propose that microridges can be thought of as multiple leading edge-like protrusions on the apical surface of a polarized epithelial sheet. In another part of my talk, I will present evidence that the function of myosin Vb is essential for the maintenance of normal peridermal microridges as well as that of microvilli in enterocytes. Furthermore, I will show that in the absence of myosin Vb function zebrafish enterocytes exhibit cellular attributes of microvillus inclusion disease, a fatal enteropathy in human infants. Overall, my work reveals how cells form laterally-long actin-based protrusions and establishes a zebrafish model to study the pathophysiology of microvillus inclusion disease.