Understanding the lactating breast at the single-cell level

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In order for lactation to occur, the adult mammary gland must undergo dramatic changes to transform the normal resting breast into a functional organ able to fulfill its purpose of milk production. Human milk provides distinctive benefits for the suckling infant and contains a uniquely formulated set of components that contribute to human development. Given that lactation is such an important evolutionary adaptation, it is surprising that the cell signals driving breast maturation and essential for milk production remain unknown. Cells contained in human milk are one of the most dynamic and heterogeneous components which offer a unique non-invasive insight into the cells of the lactating mammary gland. To understand the mechanisms governing breast maturation and milk production, we sought to comprehensively characterize human milk cells and compare them with resting mammary epithelial cells (isolated from esthetic breast mammoplasties). Using single-cell RNA-sequencing and fluorescence-activated cell sorting, we find that single human milk cells display different gene expression profiles and cell surface markers compared to resting breast cells. Interestingly, when human milk cells are cultured under floating collagen gel conditions they generate mammary gland organoids similar to those derived from resting breast cells, albeit at a lower frequency. Preliminary findings from this study suggest that human milk cells are different to those isolated from the resting breast, however they do share some similar functional characteristics such as organoid generation in culture. Further analysis will enable us to determine the cell types and signaling pathways leading to breast maturation and milk production. This will provide comparative data for future studies on abnormal mammary gland growth such as in case of low milk production or breast cancer. For the future, we aim to render the milk cell organoids functional to dissect mechanisms of normal human mammary gland plasticity and lactation.