Validation of a non-invasive low-volume transcriptomic analysis to predict cervical cancer progression in HPV positive patients

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HPV promotes its own DNA integration and persistence through oncoproteins E6 and E7, by influencing the host immune system through immune evasion mechanisms, leading to the so-called PIM. PIM supports viral persistence, propagation, and promoting CIN parthenogenesis first and invasive carcinoma then. Our aim is to describe, by non-invasive samples low-volume transcriptomics analysis, the HPV infection immunologic signatures at different stages of CC progression from dysplasia to full-blown cancer, with the intent to evaluate their functional role in immune escape and potentially identifying their correlation with CC prognosis.

A preliminary analysis has seen the comparisons of samples conserved at different temperatures and the benchmarking of low-input samples with their respective bulk counterpart. Tissue expression validation has been performed through the TIGER resource. Variant calling has been performed with nf-core/sarek and nf-core/hlatyping on both thin-prep and bulk sample to validate thin-prep RNA quality. Finally CibersortX has been used for TIME deconvolution and results have been compared to TCGA-CESC. A trajectory analysis of immune cell populations abundances from healthy to cancer condition passing through dysplasia has been performed to highlight the populations that play a major role in the host response to HPV and will be explored in further analysis. Upon the achievement of a reasonable number of samples, a predictive model will be developed to identify high-risk dysplasia patients.

Enriched genes of all thin-prep samples have been found to be characteristics of cervical-like tissues, moreover dysplasia and cancer samples exhibited an intense inflammatory activity. Further validation for RNA quality has showed a high level of agreement. Finally, CibersortX estimates of immune cell abundances observed in our cancer cohort have been compared to the TCGA cervical cancer one, obtaining comparable results.

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