DNA METHYLATION MARKERS IN HPV-INDEPENDENT PRECURSORS OF VULVAR SQUAMOUS CELL CARCINOMA

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**Methodology** A series of 220 HPV-independent vulvar samples were collected, including healthy controls, LS, dVIN, LS adjacent to VSCC, dVIN adjacent to VSCC and VSCC. Samples were tested for 12 DNA methylation markers with quantitative multiplex methylation-specific PCR (qMSP), including genes ASCL1, CADM1, FAM19A4, GHSR, LHX8, MAL, miR124–4, PHACTR3, PRDM14, PRF1, SST, ZIC1 and ZNF582.

**Results** Across all twelve markers, significantly higher methylation levels were shown with increasing severity of disease ($p<0.001$, Kruskal-Wallis test) (figure 1). Comparable low methylation levels were found in healthy vulvar controls and LS samples. Interestingly, LS adjacent to VSCC showed significantly higher methylation levels compared to LS of patients without cancer, whereas none of the markers showed a significant difference in methylation levels between dVIN and dVIN adjacent to VSCC. In fact, methylation levels in dVIN, dVIN adjacent to VSCC and VSCC were consistently high across almost all markers.

**Conclusion** Our findings indicate the potential of DNA methylation biomarkers to detect HPV-independent precursor lesions with a high cancer risk. As a next step, we aim to further explore these markers in vulvar lesions of patients with a known cancer outcome. Timely identification and treatment of vulvar lesions with a high cancer risk can substantially reduce the risk of malignant progression.