Genomic HPV profiling at CIN2 and subsequent risk of progression

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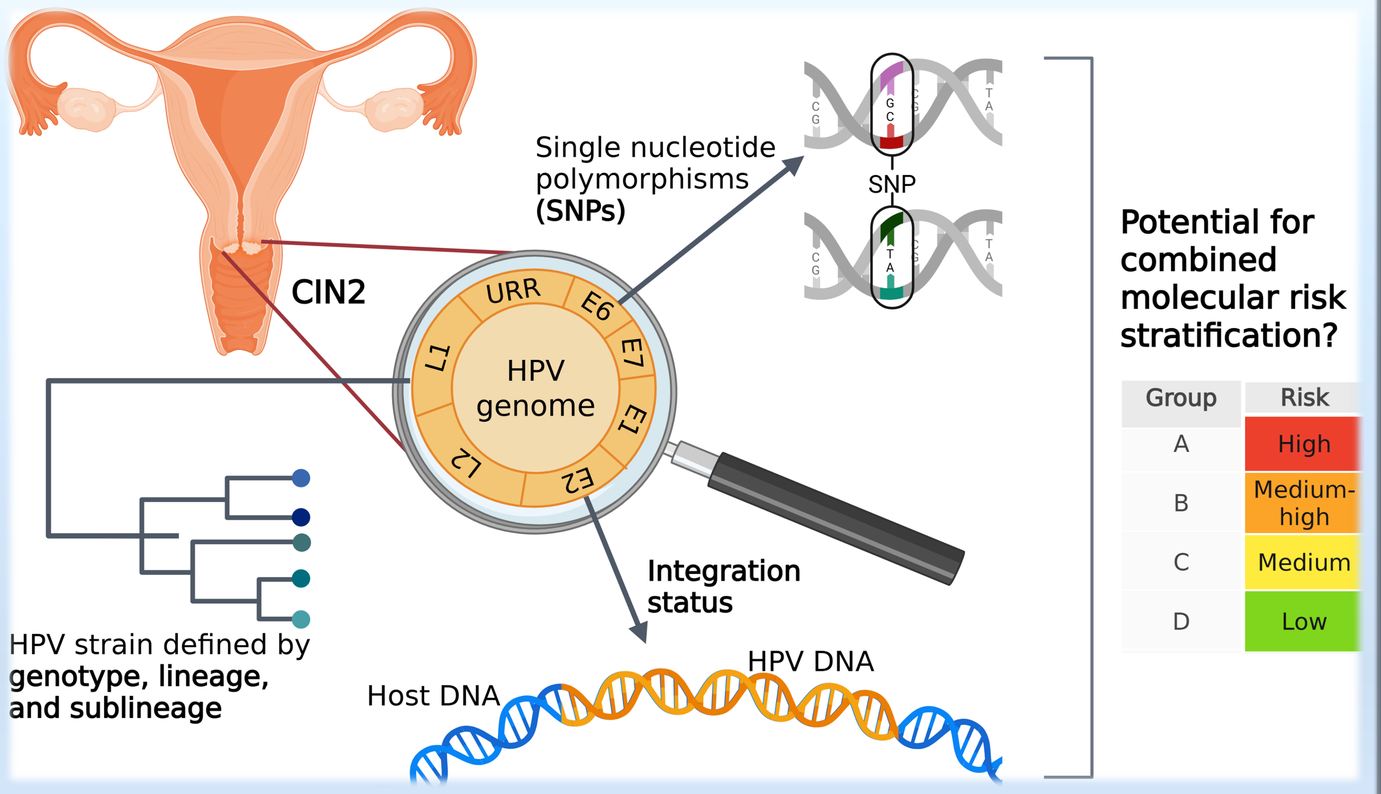
INTRODUCTION

- Most HPV infections clear spontaneously within 1-2 years, but some persist and progress to premalignant lesions (CIN2 and CIN3) or cervical cancer[1]
- Biomarkers to identify lesions at risk of progression are lacking
- HPV genomic characteristics (lineages, sublineages, SNPs, and integration status) have been linked to cancer prognosis, but their role in premalignant lesions remains unclear. [2-7]

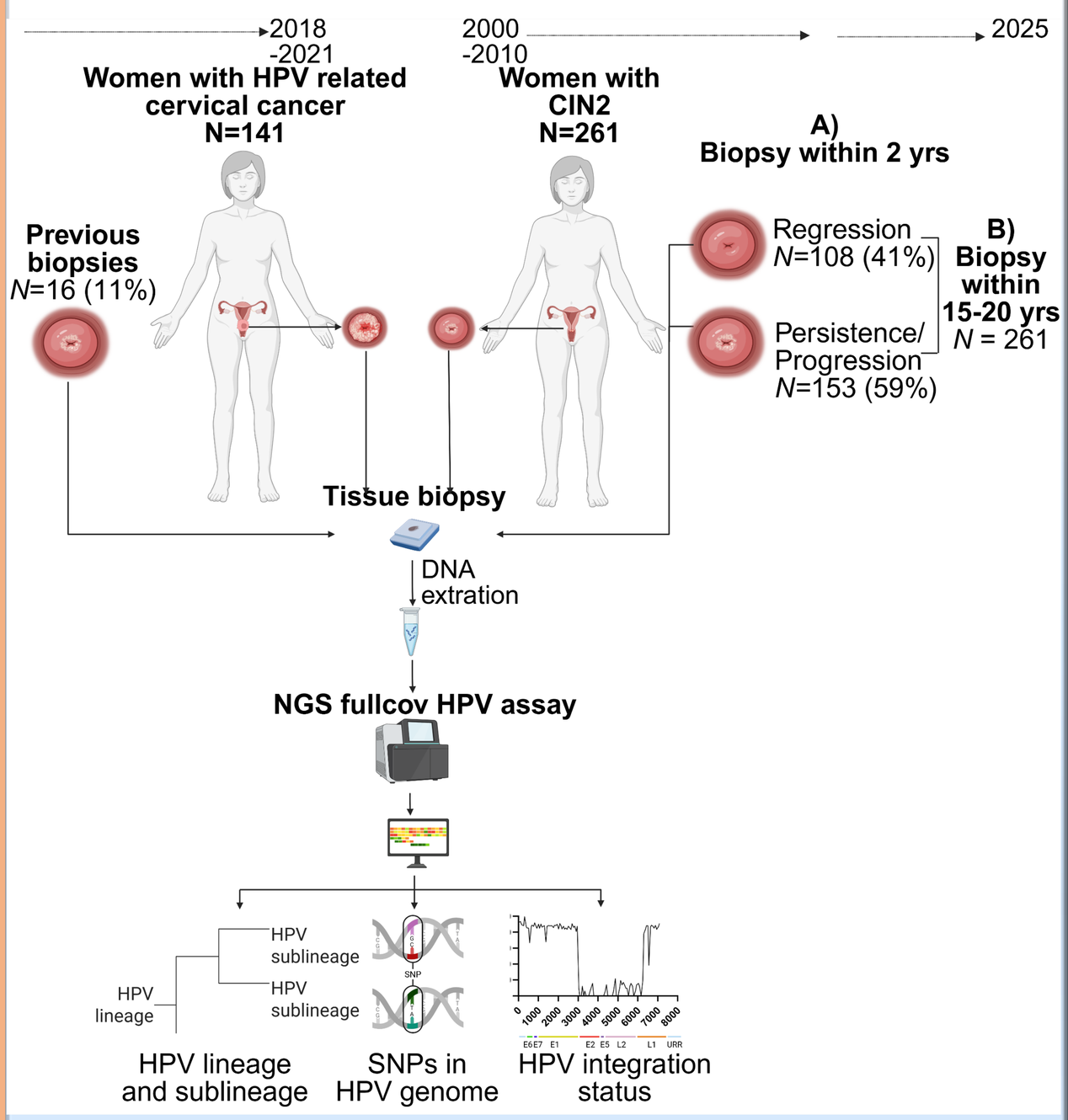
1: Stanley M. et al., Infect Agent Cancer. 2010, 2: Clifford et al., Papillomavirus Res. 2019, 3: Mirabello et al., Cell. 2017, 4: Vinokurova et al., Cancer research. 2008, 5: Lang Kuhs et al., Ann Oncol. 2022, 6: Oumeslakht et al., Gene. 2021, 7: Bonlokke et al. Mol Oncol. 2023



Hypothesis

Specific HPV variants and integration patterns are associated with progression risk of premalignant cervical lesions.

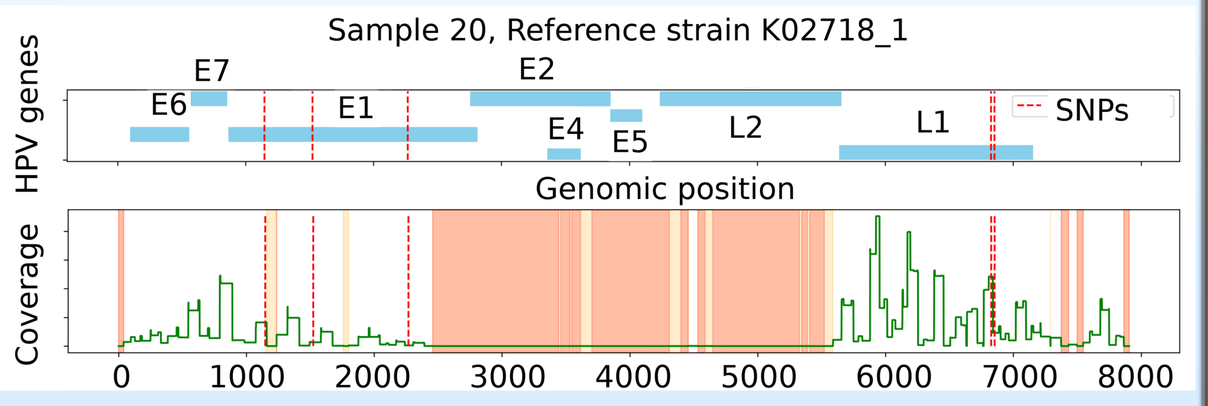
METHODS



PRELIMINARY RESULTS

Cancer cohort: The NGS pipeline for detecting HPV genotype, lineage, sublineage, SNPs, and integration has been successfully completed for 88 of the 141 patient samples.

Figure 1. Example of genomic tree for an HPV16+ cancer patient.

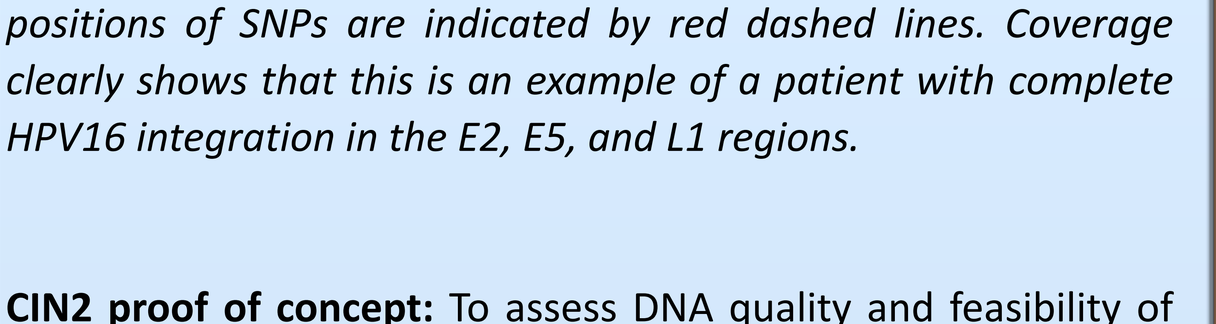


The strain is mentioned in the title (K02718_1_, which refers to HPV genotype 16, lineage A, sublineage A1). The genomic positions of SNPs are indicated by red dashed lines. Coverage clearly shows that this is an example of a patient with complete HPV16 integration in the E2, E5, and L1 regions.

CIN2 proof of concept: To assess DNA quality and feasibility of detecting HPV lineage, sublineage, SNPs, and integration in premalignant lesions, 9 random CIN2 patients has been analysed_

- HPV genotype, lineage, sublineage, SNPs and integration status successfully determined for all 9 CIN2 samples

Figure 2. Example of genomic tree for an HPV31+ CIN2 patient with later lesion regression



Strain HQ537685.1 belongs to HPV genotype 31, lineage A, sublineage A1. Coverage show that this patient has non-integrated (i.e., episomal) HPV31.

PERSPECTIVES

- A combined molecular risk profile could supplement histopathology and ***improve risk stratification*** in cervical cancer screening.
- Potential to ***reduce overmanagement and overtreatment*** of women with low-risk CIN2 lesions.
- Longitudinal assessment of HPV molecular profiles may elucidate ***viral stability*** and potential latency mechanisms.
- Understanding HPV genomic evolution over time could refine follow-up intervals and management strategies.

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