Full molecular screening for cervical cancer on cervical (self-)samples

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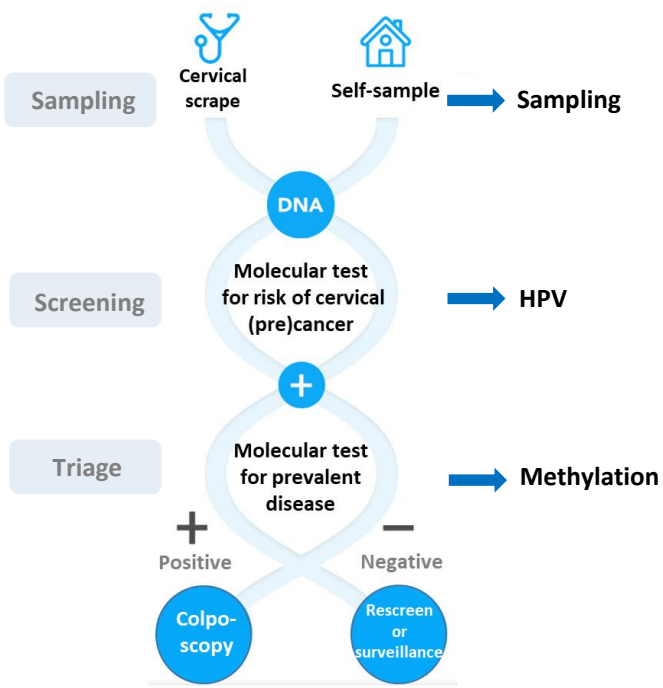
INTRODUCTION

- Cervical cancer is caused by a persistent infection with a high-risk human papillomavirus type (hrHPV). Primary HPV screening is being implemented globally.
- Only small subset (<10%) of hrHPV infections persist and eventually cause transformation of the epithelium, which can result in premalignant lesions and cervical cancer (CIN2/3+).
- To prevent over referral and overtreatment HPV-positive screened women must be triaged with additional test to select only those at high risk for CIN2/3+.
- Host cell DNA hypermethylation analysis of *FAM19A4* and *hsa-miR124-2* is a proxy for HPV-induced malignant transformation. Only subset of CIN3 have this cancer-like methylation profile and require direct treatment.
  Commercially available as PreCursor-M+/QIAsure Methylation Test.
- Cervical self-sampling for PCR-based HPV testing:
  - increases coverage of cervical screening
  - has similar clinical accuracy for CIN2/3+ compared to clinician-collected samples
  - provides combined with *FAM19A4/miR124-2* methylation a validated full molecular workflow for screening and triage.

FULL MOLECULAR SCREENING WORKFLOW



Turn around time: within 1 day

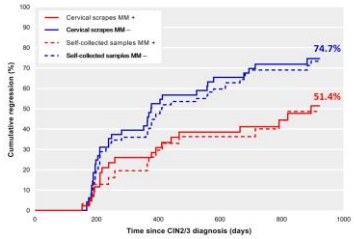
HPV SCREENING WITH NEUMODX HPV ASSAY

- NeuMoDx HPV assay (QIAGEN) is a fully automated high-throughput, random-access platform that integrates nucleic acid extraction, target amplification, detection and reporting. Sample-to-result is around 1 hour.

- NeuMoDx HPV Assay has been clinically validated for primary cervical cancer screening on clinician-taken samples according to the international guidelines for primary HPV screening assays (Heideman, Poljak *et al.,* Viruses, 2022)
- Compatible with different collection media
- Validation on self-samples – *coming soon*.

TRIAGE BY *FAM19A4/miR124-2* METHYLATION

- *FAM19A4/miR124-2 methylation* assay is clinically validated for triage of HPV+ women in different European screening settings. Overall CIN3+ sensitivity and specificity in HPV+ women: 77% and 78%, respectively (Bonde *et al.*, Int.J.Cancer. 2021).
- *FAM19A4/miR124-2* methylation-negative women show more regression of CIN3 compared with methylation positive women in both clinician- and self-collected samples (Kremer *et al.*, 2022, J.Clin.Oncol)



- A negative *FAM19A4/miR124-2* methylation test in pregnant women with CIN3 rules out progressive disease and cervical cancer (Hampl *et al.*, 2022, Int.J.Cancer)
- Intra- and inter-lab reproducibility >90%
- Automated workflow on QIAsymphony

SUMMARY

➢Automated fulll molecular cervical screening is clinically validated.
  - ➢ HPV test to identify risk population
  - ➢ PreCursorM+/ QIAsure methylation to prevent overreferral, overtreatment and unneccessary harm to women