3q26 Amplification is Rarely Present in Women Whose LSIL Cytology does not Represent CIN 2+ Disease

Harper DM[1,2], Lankachandra KM[3], Wall J[2], Jalali GR[4], Kershnar E[4,] Harris G[1]

University of Missouri-Kansas City School of Medicine, Departments of Community and Family Medicine[1], Obstetrics and Gynecology[2], Pathology[3], Kansas City, MO USA. [4]Ikonisys, Inc, New Haven, CT.

Objective: 10-17% of women with LSIL cytology truly have CIN 2+ disease at colposcopically directed biopsy and 20% of the CIN 2+ lesions derive from women with LSIL cytology. No molecular marker has yet been able to triage LSIL cytology effectively. If possible, the triage would spare women the referral to colposcopy. Irreversible chromosomal damage occurs during oncogenesis. Increasing cervical dysplastic severity occurs with increasing amplification of the 3q26 chromosomal region. The purpose of this study is to evaluate the test characteristics of 3q26 amplification in women whose routine cytology is reported as LSIL with emphasis on the negative predictive value for reassurance. **Methods**: We conducted a retrospective study using the available SurePath™ liquid cytology LSIL archival samples from women 17-59 years old which were linked to colposcopically directed biopsy samples taken on average 36 days after cytology sampling (3-90 day range). Nuclei from the LSIL samples were hybridized with a single-copy probe for the chromosome 3q26 region and a control probe for the centromeric alpha repeat sequence of chromosome 7, using standard FISH methods. Amplification was defined as five or more signals present in at least 2 cells. **Results:** Of the 68 paired cytology/biopsy samples, 3q26 amplification occurred in 40% of the women with CIN 2+ disease (sensitivity 95% CI: 12, 74). There was no amplification in 91% of women with less than CIN 2 disease (specificity 95% CI: 81, 97); and the negative predictive value was 90% (79, 96).
Conclusions: The lack of 3q26 amplification in women with screening cytology LSIL results offers reassurance that CIN 2+ disease has not developed. Future prospective studies are ongoing.