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Evaluation of a portable field colposcope in a non-cytology based cervical cancer screening program in rural India

Elisabeth Wikstrom Shemer
International Agency for Research on Cancer (WHO), France

Objectives: After the introduction of non cytological tests like visual inspection after acetic acid (VIA) or Human Papillomavirus (HPV) test, there is a paradigm shift in screening for cervical cancer. Though 'screen and treat' strategy is being recommended in low resource settings, the low positive predictive values of both the tests will lead to lot of overtreatment. GynocularTM is a battery-operated, portable device with three-step magnification and green-filter. Present study was conducted in a community setting to evaluate GynocularTM in detection of cervical neoplasias.

Methodology: Women between 30-60 years were screened using VIA and HPV test. Women positive on either test had evaluation by GynocularTM using IFCPC 2011 colposcopy classification and swede score. Punch biopsy was obtained from any lesion detected by GynocularTM. HPV positive women also had random punch biopsy from the cervix. The sensitivity, specificity and agreement between histology and gynocular diagnosis were estimated.

Results: Total 6884 women were screened from April, 2014 to March, 2015. Total 684 women were examined by GynocularTM. A total of 28 cases of CIN2+ were detected. The sensitivity and specificity of Gynocular (IFCPC Grade-2 threshold) to detect CIN 2+ were 92.9% and 96.1% respectively. The exact agreement between Gynocular examination and histology to classify the cervical lesions was 55.5% with kappa value of 0.29 (95% C.I. 0.22–0.36) indicated 'fair' agreement.

Conclusion: There is a great need for an inexpensive colposcope to be used for programs in LMICs. The agreement of GynocularTM with histology was same as that of colposcopy reported in our earlier study conducted in the same setting. The logistic advantage of the device and ability to capture images using mobile phone are beneficial to use Gynocular TM for cervical cancer screening program.

elisabeth@gynocular.com

OPCML, a systems regulator of receptor tyrosine kinases in ovarian and other cancers

Hani Gabra
Imperial College London, UK

OPCML, a GPI anchored tumor suppressor gene is inactivated by somatic methylation in multiple cancers. We demonstrated inactivation by LOH and somatic methylation in 80% of ovarian cancers. We showed that *OPCML* is a strong in-vivo tumor suppressor in SKOV-3 and PEO1 ovarian cancer cell lines with no expression of *OPCML*. We demonstrated that *OPCML* negatively regulates a specific repertoire of receptor tyrosine kinases (RTKs) including EPHA2, FGFR1, HER2 and AXL with no effect on other RTKs e.g., VEGFR1 and VEGFR3. shRNA knockdown of *OPCML* accelerates the growth of normal ovarian surface epithelial cells in vitro. Immunoprecipitation revealed that *OPCML* binds to EphA2, FGFR1, HER2 and AXL extracellular domains with no such interaction to EGFR, thus *OPCML* binds directly to RTKS that it negatively regulates. We demonstrated that *OPCML* is located exclusively in the raft membrane fraction and sequesters RTKs that it binds to the raft fraction. We demonstrate that *OPCML* abrogates EGF and Gas 6 mediated phosphorylation of FGFR1, HER2 and AXL and the downstream phosphosignaling of pErk and pAKT. A recombinant modified *OPCML*-like protein without a GPI anchor caused inhibition of wound healing assay and tumorigenicity in skov3. In summary, the *OPCML* tumor suppressor mediates its suppressor function on the external leaflet of the plasma membrane by systems level negative regulation of at least 5 RTKs, and a recombinant modified derivative biotherapy is a potent tumor suppressor protein therapeutic *in-vitro* and *in-vivo* that recapitulates the *in-vitro* mechanism.

h.gabra@imperial.ac.uk