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Introduction of a national HPV vaccination program into Bhutan

Sangay Phuntsho
University of California, USA

Background: Cervical cancer is the most common cancer in Bhutanese women. To help prevent the disease, the Ministry of Health (MoH) developed a national human papillomavirus (HPV) vaccine program.

Methods: MoH considerations included disease incidence, the limited reach of cervical screening, poor outcomes associated with late diagnosis of the disease and Bhutan's ability to conduct the program. For national introduction, it was decided to implement routine immunization for 12 year-old girls with the quadrivalent HPV6/11/16/18 (QHPV) vaccine and a one-time catch-up campaign for 13-18 year-old girls in the first year of the program (2010). Health workers would administer the vaccine in schools without-of-school girls to receive the vaccine at health facilities. From 2011, HPV vaccination would enter into the routine immunization schedule using health-center delivery.

Results: During the initial campaign in 2010, over 130,000 doses of QHPV were administered and QHPV3-dose vaccination coverage was estimated to be around 99% among 12 year-olds and 89% among 13-18year-olds. QHPV vaccine was well tolerated and no severe adverse events were reported. In the three following years, QHPV vaccine was administered routinely to 12 year-olds primarily through health centers instead of schools during which time the population-level 3-dose coverage decreased to 67-69%, an estimate which was confirmed by individual-level survey data in 2012 (73%). In 2014, when HPV delivery was switched back to schools, 3-dose coverage rose again above 90%.

Discussion: The rapid implementation and high coverage of the national HPV vaccine program in Bhutan were largely attributable to the strength of political commitment, primary healthcare and support from the education system. School-based delivery appeared clearly superior to health centers in achieving high-coverage among 12 year-olds.

Conclusions: Bhutan's lessons for other low/middle-income countries include the superiority of school-based vaccination and the feasibility of a broad catch-up campaign in the first year.

sangayp2014@gmail.com

New candidates to discriminate among thyroid carcinomas, benign lesions and normal tissues based on transcriptome and genome-wide methylation analysis

Silvia Regina Rogatto
Sao Paulo State University, Brazil

The majority of thyroid lesions diagnosed is proven to be benign after surgery. High accuracy in pre-operative diagnosing of thyroid tumors particularly follicular subtypes is still a challenge. Expression profiling (8x60K, Agilent Technologies) was carried out in 61 papillary carcinomas (PTC) and 13 adjacent non-neoplastic tissues (NT). A panel of 28 transcripts was further evaluated by RT-qPCR in benign thyroid lesions (BTL) and a diagnostic algorithm was trained (86 PTC, 23 NT and 8 BTL) and validated (120 PTC, 10 NT and 140 BTL). Methylation profiling (450 K, Illumina) was performed in 50 NT, 17 BTL, 60 PTC, 10 follicular, 1 poorly differentiated and 3 anaplastic carcinomas. Combined expression of CLDN10, HMGA2 and LAMB3 achieved 94% of sensitivity and 96% of specificity in the validation set of samples. Cases with higher algorithm scores were associated with lymph nodes involvement. Aberrant methylation in nine loci showed sensitivity of 92% and specificity of 77% to discriminate between benign lesions from thyroid carcinomas. Three of 9 loci were able to stratify patients with PTC according to the risk of developing lymph node metastasis. We also developed a prognostic classifier based on five hypomethylated probes which was able to predict poor outcome in patients with malignant tumors (Sensitivity: 77%; Specificity: 90%). In overall, transcritpome and methylome analysis revealed genes with potential to differentiate PTC and BTL/NL tissues as well as cases with lymph nodes involvement. In addition, methylome analysis allowed the identification of a classifier useful to predict outcome in patients with thyroid carcinoma.

silvia.rogatto2@gmail.com