[Indian J Chest Dis Allied Sci 2017;59:103-105]

Abstracts' Service

Second Malignancy Risk Among Pediatric, Adolescent, and Young Adult Survivors of Fusion-Positive and Fusion-Negative Sarcomas: Results From the SEER Database, 1992 Through 2012

Philip J. Lupo, Austin L. Brown and Simone Hettmer

Cancer 2016;122:3492–500

Background. The current study builds on the hypothesis that cancer-predisposing germline mutations are less common among patients with fusion-positive (F+) sarcomas compared to those with fusion-negative (F-) sarcomas, resulting in a lower risk of developing second malignant neoplasms (SMNs) in those with F+ sarcomas.

Methods. Standardized incidence ratios (SIRs) for developing SMNs were evaluated in 4822 survivors of F + and 3963 survivors of F- sarcomas that were diagnosed between 1992 and 2012 in pediatric, adolescent, and young adult patients (aged birth-39 years) and reported in the Surveillance, Epidemiology, and End Results (SEER) database. Cox proportional hazards models (adjusted hazard ratio [aHR]) and competing risk methods (subhazard ratio [sHR]) were used to evaluate SMN risk in those with F- versus F+ sarcomas while controlling for demographic and clinical variables.

Results. SMN risk was found to be nearly 2-fold greater among survivors of F+ sarcomas (SIR, 1.86; 95% confidence interval [95% CI], 1.48-2.30) and nearly 3-fold greater among survivors of F- sarcomas (SIR, 2.89; 95% CI, 2.30-3.59) compared with the reference population. Although SMN types were noted to be similar between the fusion groups, the rate of any SMN was noted to be greater among survivors of F- sarcomas (aHR, 1.38 [95% CI, 1.01-1.89] and sHR, 1.27 [95% CI, 0.94-1.73]) when compared with survivors of F + sarcomas. The difference was most notable for solid tumor SMNs after index sarcomas were diagnosed between 2002 and 2012, for which rates of SMN were >2-fold greater among survivors of F- sarcomas (aHR, 2.31 [95% CI, 1.20-4.48] and sHR, 2.24 [95% CI, 1.13-4.43]).

Conclusions. The findings of the current study highlight the increased SMN risk experienced by survivors of sarcoma and demonstrate higher SMN rates in survivors of F- sarcomas compared to those with a history of F + sarcomas. Cancer 2016. © 2016 American Cancer Society.

An Essential Pathology Package for Low- and Middle-Income Countries

Kenneth A. Fleming, Mahendra Naidoo, Michael Wilson, John Flanigan, Susan Horton, Modupe Kuti, Lai Meng Looi, Chris Price, Kun Ru, Abdul Ghafur, Jianxiang Wang and Nestor Lago

American Journal of Clinical Pathology 2017;147:15–32

Objectives. We review the current status of pathology services in low- and middle-income countries and propose an "essential pathology package" along with estimated costs. The purpose is to provide guidance to policy makers as countries move toward universal health care systems.

Methods. Five key themes were reviewed using existing literature (role of leadership; education, training, and continuing professional development; technology; accreditation, management, and quality standards; and reimbursement systems). A tiered system is described, building on existing proposals. The economic analysis draws on the very limited published studies, combined with expert opinion.

Results. Countries have underinvested in pathology services, with detrimental effects on health care. The equipment needs for a tier 1 laboratory in a primary health facility are modest ($2-$5,000), compared with $150,000 to $200,000 in a district hospital, and higher in a referral hospital (depending on tests undertaken). Access to a national (or regional) specialized laboratory undertaking disease surveillance and registry is important. Recurrent costs of appropriate laboratories in district and referral hospitals are around 6% of the hospital budget in midsized hospitals and likely decline in the largest hospitals. Primary health facilities rely largely on single-use tests.

Conclusions. Pathology is an essential component of good universal health care.

SOX2 Drives Bronchial Dysplasia in a Novel Organotypic Model of Early Human Squamous Lung Cancer

Lúcia L. Correia, Jo-Anne Johnson, Peter McErlean, Julien Bauer, Hassan Farah, Doris M. Rassl, Robert C. Rintoul, Tariq Sethi, Paul Lavender, Emma L. Rawlins, Trevor D. Littlewood, Gerard I. Evan and Frank M. McCaughan

American Journal of Respiratory and Critical Care Medicine 2017;195:1494–1508

Rationale. Improving the early detection and chemoprevention of lung cancer are key to improving outcomes. The pathobiology of early squamous lung cancer is poorly understood. We have shown that amplification of sex-determining region Y-box 2 (SOX2) is an early and consistent event in the pathogenesis of this disease, but its functional oncogenic potential remains uncertain. We tested the impact of deregulated SOX2 expression in a novel organotypic system that recreates the molecular and microenvironmental context in which squamous carcinogenesis occurs.

Objectives. (1) To develop an *in vitro* model of bronchial dysplasia that recapitulates key molecular and phenotypic characteristics of the human disease; (2) to test the hypothesis that SOX2 deregulation is a key early event in the pathogenesis of bronchial dysplasia; and (3) to use the model for studies on pathogenesis and chemoprevention.

Methods. We engineered the inducible activation of oncogenes in immortalized bronchial epithelial cells. We used three-dimensional tissue culture to build an organotypic model of bronchial dysplasia.

Measurements and Main Results. We recapitulated human bronchial dysplasia *in vitro*. SOX2 deregulation drives dysplasia, and loss of tumor promoter 53 is a cooperating genetic event that potentiates the dysplastic phenotype. Deregulated SOX2 alters critical genes implicated in hallmarks of cancer progression. Targeted inhibition of AKT prevents the initiation of the dysplastic phenotype.

Conclusions. In the appropriate genetic and microenvironmental context, acute deregulation of SOX2 drives bronchial dysplasia. This confirms its oncogenic potential in human cells and affords novel insights into the impact of SOX2 deregulation. This model can be used to test therapeutic agents aimed at chemoprevention.

Variations in Cancer Centers' Use of Cytology for the Diagnosis of Small Cell Lung Carcinoma in the National Cancer Data Base

Ted Gansler, Stacey A. Fedewa, Chun Chieh Lin, Ahmedin Jemal and Elizabeth M. Ward

Cancer (Cancer Cytopathol) 2016;124:44–52

Background. Cytology is an accurate, safe, cost-effective, and guideline-recommended method for the diagnosis of small cell lung carcinoma (SCLC), but little is known about whether its use varies by treatment facility and patient characteristics.

Methods. Methods of diagnosis (cytology vs histology) for 86,830 patients with SCLC from 1314 facilities that contributed data to a nationwide registry and associations of diagnostic methods with patient and facility characteristics were studied in bivariate and multivariate analyses.

Results. The percentages of SCLC cases diagnosed by cytology in community cancer programs, comprehensive community cancer programs, academic cancer programs, and National Cancer Institute-designated cancer centers were 13.2%, 15.4%, 23.3%, and 31.3%, respectively ($P < .0001$). The corresponding prevalence ratios (and 95% confidence intervals [CIs]) of cytologic diagnosis using multivariate marginal logistic regression models and National Cancer Institute-designated cancer centers as the referent category were 0.45 (95% CI, 0.36-0.57), 0.52 (95% CI, 0.42-0.64), and 0.78 95% CI, (0.62-0.96), respectively. In contrast, the use of cytology varied little by patient demographic and clinical factors.

Conclusions. The substantial variation among different types of cancer centers in their use of cytology for the diagnosis of SCLC suggests a need for additional research to study reasons for these differences as well as quality-improvement interventions to encourage adherence to guidelines for SCLC diagnosis.

The Association between Chronic Airflow Obstruction and Poverty in 12 Sites of the Multinational BOLD Study

John Townend, Cosetta Minelli, Kevin Mortimer, Daniel O. Obaseki, Mohammed Al Ghobain, Hamid Cherkaski, Myriam Denguezli, Kirthi Gunesekera, Hasan Hafizi, Parvaiz A. Koul, Li C. Loh, Chakib Nejjari, Jaymini Patel, Talant Sooronbayev, Sonia A. Buist and Peter G.J. Burney

European Respiratory Journal 2017 Jun 1;49(6). pii: 1601880.

Poverty is strongly associated with mortality from COPD, but little is known of its relation to airflow obstruction.

In a cross-sectional study of adults aged ≥ 40 years from 12 sites (N=9255), participating in the Burden of Obstructive Lung Disease (BOLD) study, poverty was evaluated using a wealth score (0-10) based on household assets. Obstruction, measured as forced expiratory volume in 1 s (FEV_1)/forced vital capacity (FVC) (%) after administration of 200 µg salbutamol, and prevalence of FEV_1/FVC<lower limit of normal were tested for association with poverty for each site, and the results were combined by meta-analysis.

Mean wealth scores ranged from 4 in Blantyre (Malawi) and Kashmir (India) to 10 in Riyadh (Saudi Arabia), and the prevalence of obstruction, from 16% in Kashmir to 3% in Riyadh and Penang (Malaysia). Following adjustments for age and sex, FEV_1/FVC increased by 0.36% (absolute change) (95%CI: 0.22, 0.49; p<0.001) per unit increase in wealth score. Adjustments for other confounders reduced this effect to 0.23% (0.11, 0.34), but even this value remained highly significant (p<0.001). Results were consistent across sites (I^2=1%; P_{het}=0.44). Mean wealth scores explained 38% of the variation in mean FEV_1/FVC between sites (r^2=0.385, p=0.031).

Airflow obstruction is consistently associated with poverty at individual and community levels across several countries.

Immunohistochemistry Is Rarely Justified for the Diagnosis of Viral Infections

Isaac H. Solomon · Jason L. Hornick and Alvaro C. Laga

American Journal of Clinical Pathology 2017;147:96–104

Objectives. To determine the utility of immunohistochemistry (IHC) for the diagnosis of viral infections in surgical pathology specimens lacking characteristic viral cytopathic effects.

Methods. Five years of cases at an academic medical center were reviewed for the use of IHC to detect cytomegalovirus (CMV), herpes simplex virus 1 and 2 (HSV-1 and HSV-2), varicella zoster virus (VZV), adenovirus, or polyomavirus (ie, BK or JC).

Results. In total, 1,636 viral IHC stains were ordered on 1,099 specimens from 957 cases. Altogether, 134 (8.2%) stains were positive, including 59 (7.9%) of 749 for CMV, 34 (8.9%) of 384 for HSV-1 and HSV-2, 16 (11.5%) of 139 for VZV, three (1.4%) of 210 for adenovirus, and 22 (14.3%) of 154 for polyomavirus. In 101 (75.4%) of 134 cases, viral cytopathic effect (VCPE) was readily identifiable on H&E slides. No significant changes in clinical care occurred in any of the cases without definitive VCPE that had positive staining cells on IHC.

Conclusions. These findings suggest that IHC for viral infections without a high degree of clinical or histologic suspicion is unnecessary in most cases.