123

***HRAS* MUTATIONS IN COSTELLO SYNDROME: DETECTION OF ACTIVATING MUTATIONS IN CODON 12 AND CODON 13 AND LOSS OF HETEROZYGOSITY IN RHABDOMYOSARCOMA.** K.A. Rauen,[1] A.L. Estep,[1] W.E. Tidyman,[1] M.A. Teitell,[2] P.D. Cotter,[1,3] [1]University of California, San Francisco, San Francisco, CA; [2]University of California, Los Angeles, Los Angeles, CA; [3]Children's Hospital Oakland, Oakland, CA.

Costello syndrome (CS; MIM 214080) is a rare multiple congenital anomaly disorder in which individuals have characteristic dysmorphic craniofacial features, cardiac abnormalities, ectodermal and musculoskeletal anomalies, endocrinopathy, developmental delay, and a predisposition to neoplasia both benign and malignant. In this study, we examined a large, well-characterized cohort of patients with the clinical diagnosis of CS. We sequenced *HRAS* in 36 unrelated individuals with the clinical diagnosis of CS and three sets of parents and 10 normal controls. We screened for *HRAS* coding region mutations in an effort to define *HRAS* mutations in CS and attempt to establish a possible genotype-phenotype correlation. In addition, we sequenced *HRAS* to establish loss of heterozygosity in a rhabdomyosarcoma and fibrosarcoma from a CS patient. *HRAS* mutations were identified in 33 out of 36 (92%) patients with the clinical diagnosis of CS. Mutations were found in codon 12 or 13. Two different missense point mutations were identified in codon 12: 34G→A and 35G→C, predicting an amino acid substitution of gly12ser and gly12ala, respectively. The 34G→A transition mutation, the most common mutation observed in this cohort of patients, was found in 30 of 33 patients. Two patients were found to have a codon 12 35G→C transversion. One patient in the cohort had a codon 13 mutation: 37G→T transversion, predicting an amino acid substitution of gly13cys. Parental DNA samples from three CS patients with the 34G→A mutation did not harbor a mutation. *HRAS* was sequenced from DNA isolated from a rhabdomyosarcoma and fibrosarcoma from a patient who had the germline activating mutation 34GA. Sequence analysis demonstrated LOH of the wild-type allele of *HRAS* as demonstrated by detection of only 34A in exon 1. Our data show that the majority of Costello syndrome patients have de novo heterogeneous *HRAS* mutations. Furthermore, tumorigenesis in Costello syndrome patients is accompanied by additional somatic changes affecting the *HRAS* gene.

124

ARRAY COMPARATIVE GENOME HYBRIDIZATION IDENTIFIES CHROMOSOMAL ORIGINS OF TWO MARKER CHROMOSOMES FROM 11q AND 17p: THE FIRST REPORT OF A PATIENT WITH TWO DIFFERENT MARKER CHROMOSOMES. R.D. Clark,[1] D.S. Demos,[1] L.G. Shaffer,[2] [1]Department of Pediatrics, Loma Linda University School of Medicine, Loma Linda, CA; [2]Signature Genomic Laboratories, Spokane, WA.

This unique case with two supernumerary marker chromosomes of different origins demonstrates the value of using array comparative genome hybridization (array-CGH) with pericentric clones for the identification of marker chromosomes. A 27-month-old hypotonic male was found, by conventional cytogenetics, to be mosaic for a marker chromosome. Analysis of a blood specimen revealed 47,XY,+mar[31]/48,XY,+2mar[1]/46,XY[3]. Microarray CGH (SignatureChip™) utilizing 230 genetic loci on 41 chromosome arms, including all pericentric regions, detected single copy gains at 11q12 and 17p11.2 pericentromeric regions. The area of gain on 17p did not include the Smith Magenis syndrome region. Fluorescence in situ hybridization using BAC clones from 11q12 (RP11–872D17+) and 17p11.2 (RP11–846F4+) identified two marker chromosomes: one marker of chromosome 11 origin in 4/11 cells, one marker of chromosome 17 origin in 3/11 cells and two markers, one of each chromosomal origin, in 4/11 cells. After a normal pregnancy and delivery, hypotonia and poor head control were apparent at 6 months. He responded well to physical therapy and walked at 23 months. He now imitates housework, helps with dressing, has a 30-word vocabulary, and uses 2-word phrases. There are no behavior or sleep problems. Growth is normal, but head circumference is at the 98th%ile. Physical exam shows a socially appropriate, playful toddler with dysmorphic features. There is dolichocephaly, prominent glabella, short upturned nose, long philtrum and thin upper lip, diastasis recti, tapered fingers, joint hypermobility, pes planus, hypotonia, and normal reflexes. Lab studies are normal, as are MRI of the brain and ophthalmologic examination. Among large published studies of supernumerary marker chromosomes, the finding of two markers from two different chromosomal origins is rare and, to our knowledge, no cases have been reported with two markers derived from chromosomes 11 and 17 in the same patient. We conclude that array-CGH is a powerful adjunct to cytogenetic investigations, and with pericentric clones, it is particularly useful in the identification of marker chromosomes. In this case, it not only identified the origin and size of the duplicated regions but also revealed a previously unsuspected level of complexity. The characterization of additional marker chromosomes by array-CGH will identify their chromosomal origins and the extent of euchromatin content and allow for phenotype-genotype correlations among similar cases.

Health Care Research I
Concurrent Session
8:30 AM

Friday, February 3, 2006

125

LIFE AT THE MARGINS: UNDERSTANDING THE SOCIAL DETERMINANTS OF HIV/AIDS IN WOMEN'S HEALTH THROUGH MULTIDISCIPLINARY TRANSLATIONAL RESEARCH. S.G. Berkhout,[1,2] K. Shannon,[2] C. Lai,[2] T. Kerr,[2] M. Tyndall,[2] [1]MD/PhD Program, University of British Columbia, Vancouver, BC, Canada; [2]The Centre for Excellence in HIV/AIDS, Vancouver, BC, Canada.

Purpose: Although numerous factors associated with increased risk of HIV infection have been identified among injection drug users in Vancouver's downtown east side (DTES), few studies have systematically compared the intersection of gender on such variables. This study provides a preliminary assessment of the underlying context of social, economic, and health-related factors thought to play a role in the observation that women living in the DTES are at an increased risk of HIV infection and have had limited success with antiretroviral treatment. **Methods:** Data were acquired through the Community Health and Safety Evaluation (CHASE) project database, a large (n = 3,530) prospective open cohort study assessing priority health issues in the DTES. Data were stratified by gender and HIV status and analyzed using descriptive and univariate statistics. Variables included frequency of drug use, housing stability, food security, and access to health services. **Summary:** HIV-positive women have a significantly lower health rating compared to HIV-negative women in the same community (OR 1.567; 95% CI: 1.043–2.354). HIV infection among women was also associated with more frequent injection cocaine and crystal methamphetamine use as well as the use of non-injection crack. In contrast to HIV-positive men, women with HIV were more likely to report limited clinic hours (OR 1.591; 95% CI: 1.035–2.446), difficulty keeping appointments (OR 1.792; 95% CI: 1.206–2.665), and poor treatment by health care professionals (OR 1.689; 95% CI: 1.128–2.291) as barriers to care. **Conclusions:** Despite knowledge of health care service and high levels of self-reported service use, barriers to accessing consistent and appropriate health care continue to exist. Even with frequent use of needle exchange services, injection drug use continues to be associated with HIV infection. More detailed analyses of the patterns of women's drug use and the interpersonal relationships associated with this use are clearly needed. The context within which HIV risk exists for women living in the DTES is unique and involves among other things issues of stigma, violence, and limited power and agency. We suggest that the structure of current prevention and treatment services may not be well suited to the reality of life for women in the DTES.

126

DOES WEST LOS ANGELES HAVE SUFFICIENT PRIMARY CARE RESOURCES FOR ITS LOW-INCOME RESIDENTS? S. Revels,[1] M. Horejs,[3] T. Hughes,[2] C. Archie,[1,2] [1]UCLA David Geffen School of Medicine, [2]Venice Family Clinic, [3]Westside Family Health Center.

Objective: The purpose of this study is to assess the Health Professional Shortage Area (HPSA) designation of the Venice Family Clinic Medical Service Study Area (MSSA) 78.2z, a state-defined 14.8 square mile region composed of Santa Monica South, Mar Vista, Ocean Park, and Culver City, with a population of 78,796. It is proposed that there is an overall lack of primary care resources for the area's impoverished residents. **Background:** The west side of Los Angeles is home to over 58,000 low-income uninsured men, women and children. Venice Family Clinic offers primary care to over 19,000 patients; 77% are uninsured, and 3,400 are homeless. **Methods:** A cross-sectional study of physicians in MSSA 78.2z, and contiguous areas, was employed to quantify the number of physicians serving the low-income population. All primary care providers in 78.2z, and surrounding regions, were identified and mailed surveys, regarding hours of direct patient contact with low-income clients. Doctors who failed to return surveys are being phoned. Statistical information regarding the demographics of MSSA 78.2z was obtained from the US Census Bureau. **Results:** The sample size was 439, with 23 physicians practicing in 78.2z. In 78.2z, the prevalence of primary care physicians treating poor patients is low, with an equivalent of only 2.0 doctors. The population provider ratio is 14,585:1. The study is in progress, with 43% of surveys completed. **Conclusion:** There are inadequate primary care resources available for the low-income population of 78.2z, and extreme barriers to care exist in contiguous areas. According to these preliminary data, MSSA 78.2z meets most criteria for HPSA designation by the California Office of Statewide Health Planning and Development (OSHPD).

127

COMPUTER-BASED SCREENING OF VETERANS FOR METABOLIC SYNDROME. J. Keane,[1,2] J.L. Meier,[3] R.H. Noth,[1,2] A.L.M. Swislocki,[1,2] [1]Medicine Service, VA Northern California Health Care System (VANCHCS), Martinez and Mather, CA; [2]Department of Internal Medicine, UC Davis School of Medicine, Davis, CA; [3]Pharmacy Service, VANCHCS, Martinez, CA.

In part as a result of an obesity epidemic, the prevalence of the "metabolic syndrome" is greater than previously believed. However, despite growing public and professional attention to the condition, estimates of its overall prevalence vary widely. Because of the potential impact of this syndrome on VA health care, we wished to ascertain the prevalence in the VANCHCS using the VA computerized clinical database. To do so, we modified the ATPIII criteria, keeping fasting blood glucose (FBS), blood pressure, triglyceride, and HDL cholesterol criteria but substituting BMI ≥ 30 for waist:hip ratio. We also accepted current pharmacotherapy for diabetes as qualifying for elevated FBS; current therapy with niacin, gemfibrozil, or fenofibrate for elevated triglyceride; and recent use of multiple ICD-9 codes for hypertension for elevated blood pressure. We examined all clinical records between July 1, 2004 and June 30, 2005 for veterans registered in VANCHCS who filled any prescription during this interval (n = 51,026). Their average age was 63 years; 93% were male. Twenty-five percent (n = 13,010) were diagnosed as having metabolic syndrome by meeting at least three of the above 5 criteria. Since only 60% (n = 30,727) of the population had data for 3 or more criteria, the actual percent with metabolic syndrome is probably substantially higher. We conclude that over one-quarter of our veterans in the VANCHCS may have metabolic syndrome based on our modified ATPIII criteria. We need to be screening more of our veterans with fasting laboratory testing. This computerized screening of a large clinical database can then provide an effective strategy to aid clinicians in identifying more patients at risk for cardiovascular disease.

128

AN EVALUATION OF THE CLINICAL APPROPRIATENESS AND ECONOMIC COSTS OF ROUTINE MAGNESIUM TESTING. J.R. Rylander, S.R. Stoltz, Department of Medicine, UCSF-Fresno, Fresno, CA.

Purpose: Abnormal serum magnesium values are commonly encountered in a wide spectrum of patients. However, except in unique circumstances, it is unclear whether or not minor magnesium abnormalities even require treatment or whether correction of the magnesium level to normal has any bearing on patient morbidity and mortality. During the past few years, there seems to have been a substantial increase in routine serum magnesium testing on patients admitted to hospitals. The primary objective of this study is to document the changes in the quantity of routine magnesium testing done on patients within a large community hospital setting. A second objective of the study is to measure the excess costs of unnecessary magnesium testing. **Methods:** To test the hypothesis that there has been an increase in magnesium testing, two time periods were chosen for comparison: July 1, 1999 to June 30, 2000 and July 1, 2003 to June 30, 2004. Total magnesium lab tests were obtained from laboratory services and hospital administration at three hospitals in Fresno, California-Clovis Community Hospital (CCH), Fresno Community Hospital (FCH), and University Medical Center (UMC). For each time frame, 100 random patient charts were reviewed by the authors to determine whether or not magnesium testing was necessary. **Results:** The current patient charge for magnesium testing is $98.00 for inpatient and $54.00 for outpa-