Methods: As part of a CRN pilot project, focus groups were conducted with Kaiser Permanente Colorado members in 2009 to determine individual perspectives and public opinion about the importance and value of family history, DTC genetic testing, and DTC advertising and other media representations of DTC genetic tests. Focus groups were conducted by concordant population groups: General population KPCO members, members who self-identify as African American, members who self-identify as Hispanic/Latino, women with a recent referral for BRCA1/2 testing, KPCO primary care providers, and KPCO specialty care providers. **Results:** Results on focus group demographics, media use, trust in information, and most trusted information sources are presented. Additional results include coding focus group transcripts for value and polarity (positive/negative) of opinion on family history and genetic testing. Additional coding for how different population groups frame opinion on the issue (progressive, deterministic, caution) include results on whether frames are similar or different across population groups. Finally, information on the impact of media presentations on member opinion and decision-making were assessed. **Conclusions:** Individual opinions about the value of family history and genetic testing for disease risk vary greatly. Salience of themes related to genetic testing and DTC genetic tests specifically may vary across concordant population groups.

Keywords: Direct-to-consumer genetic testing, Health and family history, CRN pilot project

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PS1-10:

Response to Metformin and Genetic Variants of Organic Cation and Multidrug and Toxin Extrusion Transporters

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Background and Aims: Metformin is the most widely-used anti-diabetic drug in the United States. However, medication management fails to achieve therapeutic goals in ~20% of patients. This study attempted to identify genetic polymorphisms associated with metformin treatment failure. We studied the associations between polymorphisms in two liver and kidney organic cation transporter genes (OCT1 & OCT2) and two kidney multidrug and toxin extrusion transporter genes, (MATE1 & MATE2K) and response to metformin monotherapy. **Methods:** At Kaiser Permanente Southeast and Marshfield Clinic Research Foundation we identified 304 type 2 diabetes (T2DM) patients on metformin monotherapy who: were enrolled for ≥6 months prior to initiation; remained on metformin ≥90 days following initiation; and had a HbA1c measured prior to first metformin prescription and then after initiation. From this group we selected 171 patients who had not received metformin or other anti-diabetics previously, and had baseline HbA1c levels >7.0% prior to metformin initiation. We genotyped 10 SNPs, and assessed response by measuring absolute and relative change in HbA1c after metformin initiation. **Results:** Three SNPs were identified that were significantly associated with reduced response to metformin, after adjustment for baseline HbA1c, dose, and ethnicity. In a dominant model, heterozygosity or homozygosity for minor A allele in the MATE1 intronic SNP, rs2289669, resulted in a smaller absolute change in HbA1c (mean of 0.45% less reduction in absolute change in HbA1c; 95% CI 0.17 to 0.74%) compared to individuals homozygous for major G allele. In a recessive model, homozygosity for minor A allele in MATE2K 5'-UTR SNP, rs12943590, resulted in smaller absolute change in HbA1c (mean of 0.43% less reduction in absolute change in HbA1c, 95% CI 0.053 to 0.86%). The reduced function SNPs in OCT1 & OCT2 were not associated with metformin response, except for rs34059508 (G465R). This SNP showed a positive (but not statistically significant) association with smaller absolute change in HbA1c (mean of 0.49%; 95% CI -0.06354 to 1.045%). **Conclusions:** These three variants of metformin transporter genes may be important for

personalizing treatment for patients with T2DM. A replication study in a larger population is currently being planned.

Keywords: Genetic polymorphisms, Metformin transporter genes, Metformin treatment

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PS1-11:

Specimen Collection Within the Cancer Research Network: A Critical Appraisal

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Background and Aims: The Genomics Working Group (of the Cancer Research Network (CRN) Pharmacovigilance Project) explored single-site experiences with genomic studies to understand challenges and opportunities for collecting and using biological specimens. Its specific aims were to: (i) describe the availability of existing biospecimens; (ii) document successful past specimen collection strategies; (iii) identify potential barriers to selected recruitment strategies; and (iv) develop standardized study documents for future genomic research. **Methods:** We distributed a survey on existing biospecimen availability to principal investigators at all CRN Pharmacovigilance sites. Information collected included the number of specimens, storage methods, and type of specimens available. Investigators were also asked to identify past and current studies at their institutions in order to collect information on successful specimen collection strategies. A literature review was conducted both to identify potential barriers to participation and to understand the feasibility of various recruitment procedures. Benefits and limitations of 'opt-out' and 'opt-in' specimen collection methods were examined. Lastly, we developed study documents, including recruitment letters and informed consent forms, for future saliva and blood specimen collection efforts. **Results:** Two of the CRN HMOs currently have large-scale banked blood or saliva specimens (>20,000) within existing repositories. One site has two large-scale studies (>20,000 participants each) with banked specimens able to provide DNA for future research. Whole blood or blood components are the most commonly collected specimen types, and multiple CRN sites have access to banked tumor blocks. There were 33 past or current studies that included biospecimen collection. There was a trade-off between intensive data collection requirements and recruitment yield, cost, and participation burden. **Conclusions:** There is great potential for collection, storage, and use of biospecimen samples for research within the CRN. For future collection efforts, 'opt-out' models allow fast sample accrual, but impact data de-identification requirements. 'Opt-in' models allow for broad data collection, but are resource and time intensive. Pathology time and support may be a barrier to future use of stored samples.

Keywords: Genomics Working Group, Specimen collection strategies, Genomic research

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PS1-12:

Use of Tumor Registry to Obtain Family History Information

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Background: The Human Genome project has revolutionized the field of medicine to move toward personalized medicine. The family history is a screening tool to identify families at risk for common conditions allowing for personalized care. For breast cancer syndromes, genetic testing, counseling and prophylactic treatment are available. While there are data about the efficacy and clinical utility of the family history, there are areas that still need investigation. Does obtaining the family history lead to patient

recommendations? Do patients act on recommendations? Are there barriers to action and are there improved outcomes? One established barrier is the time to obtain a pedigree and knowledge basis for interpretation. Options for obtaining and interpreting a family history are necessary due to these barriers. We examined the use of tumor registry data as a cost effective option for providing family history, and age information. **Methods:** The tumor registry data were examined to identify women that were diagnosed with breast cancer between 2004-2008. These data were then substratified for age and family history. A family history was considered positive if it met the US Preventative Health Task Force criteria for breast cancer. The EMRX allowed identification of patients who had genetic counseling and or testing recommended and how many patients followed up on those recommendations. **Results:** Between 2004-2008 there were 1,594 patients with a newly diagnosed breast cancer. Of these, 113 had no information (7%). There were 1,112 (75%) that had at least one 1st or 2nd family member with a significant malignancy. There were 61 patients that met criteria for a positive family history. Fourteen patients were at or below age 50, and 47 over age 50. Of the 61 patients, 37 (60.7%) were offered genetic counseling and/or testing. **Conclusions:** The tumor registry data did identify individuals with a positive family history of breast cancer and was cost effective. In conjunction with the EMRX, it is possible to see if the appropriate recommendations were made and whether individuals followed the recommendations. These individuals present opportunities for future research in barriers to care, and biomarker research in individuals with a familial risk.

Keywords: Tumor Registry, Personalized medicine, Family history screening

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PS1-13:

Using the PMRP Cohort to Develop a Model for Incorporating Genetic and Environmental Factors into Prostate Cancer Screening Decisions

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Background: Prostate cancer screening with PSA has decreased the average age of prostate cancer detection and increased the number of men who undergo prostate biopsies. Currently two thirds of the prostate biopsies performed due to a high PSA test are negative for prostate cancer leading to unnecessary expense and distress for the individual. One way to decrease the unnecessary procedures associated with PSA screening would be to identify individuals who are either at increased or reduced risk of prostate cancer using newly discovered genetic and environmental risk factors. **Aims:** Using the males in the Personalized Medicine Research Project (PMRP) population that have had a PSA test, determine if genetic and environmental factors can be incorporated into the PSA screening model to better discriminate individuals who will have a diagnosis of prostate cancer from those with negative biopsies. **Methods:** Individuals in PMRP who were diagnosed with prostate cancer (N=466) were compared with the entire Marshfield Clinic population to determine cancer screening characteristics such as rate of PSA screening and average age at cancer diagnosis. All men in PMRP who have had a PSA test (N=4659) were genotyped for at least 12 polymorphisms that have been associated with prostate cancer in GWAS studies and dietary history was collected if available. **Results:** Individuals diagnosed with prostate cancer in the PMRP population tend to have more PSA tests prior to diagnosis than the general population (an average of 7) with 69% (N=320) having at least one PSA test prior to a prostate biopsy. A total of 935 of the 4659 men in the study have had a prostate biopsy with a positive biopsy rate of 34%. Using a panel of 12 previously identified polymorphisms; seven were significantly associated with prostate cancer in our population. Individuals with 1 or fewer risk alleles (15.6% of the population 146 of 935) were less likely to have a diagnosis of prostate cancer on biopsy (OR 1.6). **Conclusions:** The PMRP population that has experienced at least one PSA screen is a viable population for testing new screening algorithms that incorporate genetic and environmental factors for better identification of prostate cancer risk.

Keywords: Prostate cancer screening, PSA screening, Genetic and environmental risk factors

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PS1-14:

Utilization and Effectiveness of KRAS Testing for Colorectal Cancer

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Background: New genomic and personalized medicine (GPM) applications have the potential to enhance our ability to screen for disease predisposition and treatment responsiveness. Surveying colorectal cancer (CRC) tissue for mutations in the KRAS gene is one such test that can help decide how to treat patients with metastatic colorectal cancer (mCRC). KRAS testing provides an opportunity for oncologists to tailor the use of anti-EGFR therapy to increase treatment effectiveness and potentially minimize adverse events. The FDA has recently changed the labeling of anti-EGFR therapies to indicate that it is not effective for the treatment of patients with KRAS mutations. KRAS testing has already become standard clinical practice in many settings. In this study, we will assess the patterns of diffusion and utilization of KRAS testing and evaluate the characteristics of patients, providers, and health systems as they relate to the uptake of KRAS testing. We will also conduct a comparative analysis of KRAS testing for mCRC patients treated in community practices to evaluate its effectiveness in terms of both progression-free survival and overall survival. **Methods:** This study will include a total of 800 mCRC cases diagnosed between January 1, 2005 and July 31, 2010 from 7 HMORN sites. Using electronic records at each site, we will capture information on relevant patient characteristics including disease characteristics, comorbidities, history of all cancer-directed therapies, acute complications, receipt of palliative care and contextual socioeconomic variables. We will use chart review to supplement, or in some cases verify, the electronic data. **Conclusion:** The study will serve as a model for evaluating the potential impact of GPM applications to improve health outcomes, reduce costs, and influence patient and physician decision-making in the area of personalized therapies.

Keywords: KRAS testing, Patient treatment, Genomic and personalized medicine applications

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Cancer

C-B2-01:

A Panel of Markers with Potential Clinical Diagnostic Application

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Background and Aims: Distinguishing low/intermediate grade neuroendocrine carcinoma (carcinoid and atypical carcinoid) from a high grade neuroendocrine carcinoma [small cell carcinoma and large cell neuroendocrine carcinoma (LCNEC)] of the lung can be difficult, especially in small biopsy specimens. Patients diagnosed with a low/intermediate grade carcinoma would be treated surgically while patients diagnosed with small cell carcinoma with chemotherapy. Biomarkers may increase the diagnostic accuracy. **Methods:** We studied 42 consecutive cases of neuroendocrine tumors of the lung (20 small cell carcinomas, 7 large cell neuroendocrine carcinomas, 12 carcinoids and 3 atypical carcinoids) with the objective of comparing the expression of the panel of biomarkers (CD117, KOC, Ki-67, pVHL and p16) between the low and high grade neuroendocrine tumors of the lung. Tissue microarrays were constructed and expression of each biomarker was evaluated using immunohistochemistry. Staining was standardized and scored as "0" = Negative, "1+" = Focal, "2+" = 30 -49% cells staining and "3+" = 50-100% cells staining positively. For the purpose of the present study, a specimen scored as "0" or "1+" was classified as negative, while a specimen scored as "2+" or "3+" was considered positive. In estimating the likelihood of expression of the biomarkers, specimens were