2. VEGF-A and Cox-2 SNPs may be useful markers of aggressiveness in these patients; 3. Molecular data may orientate the appropriate target therapy in novel clinical trials.

Su2128

Age, Gender, and Folate Metabolism Polymorphisms Influence on Gene Promoter Methylation in CRC Patients

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Colorectal cancer (CRC) is the third most common cancer in men and the second in women worldwide. Almost 60% of the cases occur in developed regions. CRC arises from a multistep process that involves an accumulation of mutations /epimutations in tumor suppressor genes and protooncogenes. DNA methylation is an important control program that modulates gene expression in the organism. Genome-wide hypomethylation and promoter-specific hypermethylation are thought to contribute to age-related pathologies. Moreover female sex hormones have been implicated in the etiology of several women's cancers and may participate in different pathways associated with distinct DNA methylation signatures. Folates are essential nutrients whose metabolism is required for the production of S-adenosylmethionine (SAM), the major intracellular methylating agent, and for the synthesis of DNA and RNA precursors. Impairments in folate metabolism might result in increased frequency of point mutations as well as altered methylation of tumor suppressor genes, thereby contributing to cancer initiation and progression. Reduced folate levels have been associated with increased CRC risk in healthy people, whilst increased folate availability is believed to enhance CRC progression in individuals harbouring preneoplastic lesions. There is increasing interest in understanding the correlation among folate availability, its metabolism, and the methylation levels of tumor suppressor genes in CRC tissues. For this purpose we collected 104 CRC patients and searched for correlation among clinico-pathological characteristics, common polymorphisms of genes participating in folate metabolism (MTHFR 677C >T, MTHFR 1298A>C, MTR 2756A>G, MTRR 66A>G, TYMS 28bp repeats, TYMS 1494 6bp del, RFC1 80A>G, DNMT3B -149 C>T, and DNMT -579 G>T) and promoter methylation of APC, MGMT, hMLH1, RASSF1A, CDKN2A, tumor suppressor genes. Genotyping was performed by means of PCR/RFLP technique and DNA methylation analyses by means of methylation-sensitive high resolution melting (MS-HRM). A precise value of gene promoter methylation was obtained by means of an algorithm recently developed by us. MGMT and hMLH1 methylation levels showed a significant positive correlation with aging and female gender. Moreover, some interesting correlation among folate metabolism polymorphisms and promoter methylation levels were found. No significant association among promoter methylation and CRC location, stage and tumor size was found. Only a borderline association between TNM stage IV and increased hMLH1 methylation and TNM stage III and a higher RASSF1A methylation (with respect to the other stages) have been observed. The study of epigenetic marks to better understand colorectal carcinogenesis and to identify new tools for diagnosis and prognosis as well as for therapeutic interventions is then extremely promising.

Su2129

Whole Exome Sequencing Revealed Putative Driver Mutations in Esophageal Cancer

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Esophageal cancer is one of the most common malignancies in the Western world with increasing incidence of esophageal adenocarcinoma (EAC). Despite improvements in staging, surgical procedures, and post-operative treatments, the overall survival of patients with esophageal cancer remains low. In order to evaluate the mutation status of EAC and squamous cell cancer of the esophagus (SCC) we performed next generation sequencing (NGS) approaches on a wide set of tumor-derived DNA from histological classified EAC and SCC biopsies. Whole exome analysis was performed on 16 DNA samples from histological characterised esophageal cancer (n=8) and the corresponding non-tumor biopsies (n=8). Extracted DNA was applied to NimbleGen capture exon hybridisation, adapter ligation and subsequent deep sequencing on an Illumina HiSeq platform. After tumor macrodissection, DNA from additional 147 formalin-fixed and paraffin-embedded (FFPE) EAC and SEC biopsies was extracted using the Qiagen M48 robotic system. After DNA quality control, multiplex PCR libraries, representing tumor-relevant genetic loci, were prepared from 50 quality controlled EAC and SCC DNA samples. Multiplex libraries were analyzed for more than 2000 putative driver mutations by next generation sequencing on the MiSeq Illumina platform. 745 putative driver mutations in 657 genetic loci were found in a first whole exome screening step. p53 hot spot mutations occurred in two third of the esophageal cancers. In addition to the p53 mutations, whole exome analysis identified more than two mutation hits in genes for the regulatory phosphatase unit, an adhesion P-cadherin and cycline kinase 12. These mutations were also addressed by conventional Sanger sequencing. Subsequently, DNA samples from 147 SCC and EAC were studied. Analyses of a hot spot cancer panel in 50 samples, that had passed the quality control, confirmed high frequency of p53 mutations, but a lack of K-Ras mutations. In addition, a set of further mutations such as in PIC3CA, PP2R1B, and PPP1R1B were shown, whose clinical relevance has to be addressed in future studies. NGS is a sensitive method in evaluation of the mutation status of esophageal cancer, providing the opportunity to detect a wide range of genetic alterations, which have to be linked to cancer progression, therapeutic outcome and personalized treatment options in future studies.

Su2130

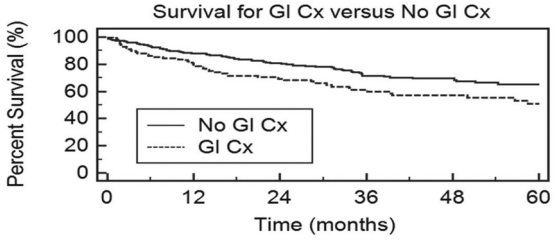
Outcomes of Lung Transplant Patients With Severe GI Complications

Loretta Erhunmwunsee, Jennifer M. Hanna, Anthony Castleberry, Matthew Hartwig, Christopher R. Mantyh

Purpose: The incidence of gastrointestinal (GI) complications after Lung Transplantation (LTx) is not well described. This study attempts to identify the incidence of GI complications after LTx, characterize the risk factors that lead to GI complications, and then determine the impact of GI complications on post-transplant outcomes. Methods: A prospective database of patients who underwent LTx between 2005 and 2011 was queried. Generalized linear regression was used to determine risk factors for developing GI complications. A multivariable Cox regression model was developed to predict the impact of GI complications and other factors on the survival of these patients. Results: During the study period 543 patients underwent LTx. 137 GI complications (Table 1) occurred in 124 of these patients. 62 of these patients subsequently underwent operative management of their GI complication. Patients who had a GI complication had a statistically significant worse 5 year survival (51% vs 65%) when compared to those who did not have a GI complication (p=0.006) (Figure 1). On univariable analysis, having a diagnosis of cystic fibrosis (p=0.03), ischemic time (p=.05), total length of stay (LOS) (p=0.0008), total ICU days (p=0.0004) and an elevated FK level (p=.005) were associated with having a GI complication after transplantation. On multivariable analysis, total ICU days (OR= 1.005, 95% CI 1.003-1.007) was an independent factor associated with having a GI complication. Conclusions: There is a high incidence of GI complications in patients who undergo LTx. Recipients who suffer a GI complication after LTx have diminished overall survival. Total ICU days was an independent factor associated with having a GI complication.

GI Complication Incidence

N=124 patients	Total Number	Number that went to OR
C diff colitis	26 (19%)	0
Biliary	22 (16%)	20 (91%)
Perforation/Leak	13 (9.5%)	10 (76.9%)
Diverticulitis	11 (8%)	9 (81.8%)
GI Bleed	10 (7.3%)	0
Gastroduodenal ulcer	9 (6.6%)	0
Esophageal candidiasis	9 (6.6%)	0
Slipped Nissen	6 (4.4%)	6 (100%)
SBO	5 (3.6%)	4 (80%)
Bleed -Non-GI	5(3.6%)	3 (50%)
Ischemic Colitis	4 (3%)	2 (50%)
Retroperitoneal abscess	2 (1.5%)	2 (100%)
Eneterocutaneous Fistula	2 (1.5%)	1 (50%)
Miscellaneous	13 (9.5%)	5 (38.5%)
Total	137	62 (46%)



Su2131

Per-Umbilical Laparoscopic Access

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Introduction: The advent of laparoscopic surgery is one of the most important advances in modern surgical technique. In order to perform laparoscopic procedures it is necessary to access the peritoneal cavity and establish a pneumoperitoneum. Placement of the first port remains a critical and unavoidable step in laparoscopic surgery. In order to minimize complications associated with placement of the first trocar, several techniques have been reported. Herein we describe the per-umbilical technique (PUT) approach developed by our surgical group that takes advantage of the anatomical defect left by the umbilical vessels at the umbilicus after birth. PUT provides a quick, safe, and reliable initial surgical access to the peritoneal cavity that has produced excellent functional and cosmetic results. Methods: Retrospective cohort of patients who underwent various laparoscopic procedures by our surgical group using PUT for access to the peritoneum from January 2000 to September 2012 at the ABC Medical Center, in Mexico City. Patients with prior midline laparotomy