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GASTROENTEROLOGY AND DIGESTIVE SYSTEM
Editorial

Are you wearing the right Genes? - From the Molecule to Public Health

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Greetings! As you open the inaugural issue of EC Gastroenterology and Digestive System journal, we plan to introduce a variety of articles covering from bench to bed side in the field of Gastroenterology & Hepatology. Our hope is that the Gastroenterology E- Cronican journal will be regarded nationally & internationally as one of the main journals for gastroenterology, endoscopy, and hepatology and the first choice of both clinicians and researchers in these fields around the globe.

My heart is in the prevention of colorectal cancer. Please allow me to share a portion from the blog written by one of my young patient with colon cancer.

"I am a 37 year old Caucasian male and at least forty lbs. overweight. I have high blood pressure, suffer from acid reflux and heartburn on a daily basis, and have sleep apnea I am cursed with bad genetics! My two sisters and I have all been diagnosed with colon cancer. We found that it is because we are "wearing the wrong the genes" but not by our choice. We have the genes for HNPCC (hereditary nonpolyposis colon cancer). Unfortunately, my middle sister passed away at the age of 29 after fighting the cancer for two years. Luckily, my other sister and I found our cancers in early stages, Thanks to Dr. Indrakrishnan, my Gastroenterologist and a Board member of Fight colorectal cancer organization. Until this time, however, I did nothing to prevent the onset of colon cancer. My journey began with a trip to Dr. Indrakrishnan's office. After discussing my family history, Dr. Indrakrishnan recommended an immediate colonoscopy. I woke up to the dreaded news that I have colon cancer. It took three weeks to completely recover from the surgery and during this period, I had plenty of time to reflect on my current and past lifestyle and my sisters 'lifestyles and how each of our lifestyle did not help that much with colon cancer in addition to wearing the wrong genes".

The treatment was successful and patient referenced above is doing well. Colorectal cancer is the second common leading cause of cancer deaths in the world. It is preventable, curable and easily treatable. This is relatively a unique disease for all the scientific journals as it presents multiple facets of management - Starting from genetics through pathogenesis & finally in the areas of medical and surgical management. As if these are not enough we encounter a plethora of studies on cost effectiveness and political aspects of this disease as well.

We can prevent much of the morbidity and mortality of colorectal cancer if we knew more about the risk of developing colorectal cancer and take effective preemptive action. Now, we know the existence of an established link between an inflammatory process and the genesis of colorectal cancer. In addition, there is evidence that intestinal microbiota may play a role between the initial steps of tumorigenesis and the initiation of an immune response that influences clinical outcome of the disease.

Up to five percent of cases of colorectal cancer occur in a variety of familial cancer syndromes. The commonest is the Lynch syndrome (aka hereditary nonpolyposis colorectal cancer), which is caused by a germ-line mutation in one of four DNA mismatch-repair genes. The discovery of the genetic basis of certain familial aggregations of colorectal cancer validated 90 years of clinical observation suggesting that such aggregations are hereditary. This has also promised the ability to detect asymptomatic carriers of the deleterious genes, with special attendant gains in the control of cancer. However, the two difficult questions are how common are the mutations of interest, and who should be tested for them!

As clinicians, we have been using genetic testing more frequently lately in the management of cancer. Cytogenetic and molecular genetic assays now play a part in the diagnosis and monitoring of a variety of solid tumors. It is fascinating to note that the identification of inherited mutations of genes that cause susceptibility to cancer provides new armamentarium to prevent and detect the cancer at an early stage. We are all aware that genomic instability commonly occurs in solid tumors and it has long been conjectured that this process may play a causal role in cancer. In the last decade, human molecular genetics has provided an opportunity to look deeper and hereditary cancer-predisposition syndromes are perfect guinea pigs for this hypothesis. Some of the first unequivocal support for the idea came from the discovery in the early 90s that hereditary nonpolyposis colon cancer is caused by germline mutations of mismatch-repair genes. Conditions such as familial adenomatous polyposis and the Lynch syndrome represent important models, and their contribution to the understanding of mechanisms of carcinogenesis is out of proportion to their frequency. Within a family with the Lynch syndrome, opportunities for genetic testing and enhanced surveillance do exist.

There is evidence that most tumors do arise from a single altered cell, the essence of clonal theory. With this, It is believed that a series of acquired genetic changes within the neoplastic clone may give rise to subpopulations of tumor cells with increasingly aggressive characteristics and this may result in the change in the aggression & progression of the tumor. This concept is quite conceivable as genetic apparatus of tumor cells is abnormally unstable. Over the last years, molecular studies through high-throughput technologies have led to the confirmation of critical alterations in colorectal cancer and the discovery of some new ones, ranging from mutations, DNA-methylations and structural chromosomal changes. The current theory is that specific genomic alterations may directly or indirect dysregulation of specific signaling pathways which usually exert their functions on critical cell phenotypes. These include but not limited to the regulation of cellular metabolism, proliferation, differentiation, and survival.

Advances in DNA sequencing and genomic profiling methods will play an important role in the cancer management. I hope that we will be able to identify the specific molecular defects in a person's cancer cells and this crucial information may permit the development of therapies that target or take advantage of those defects. This exciting information can help us to identify selected population with an increased risk of colorectal cancer. We may also extend this usefulness to develop effective therapeutic interventions to prevent the cancer.

Surgery remains the cornerstone for curative treatment of colorectal cancer and operative techniques have changed dramatically over the past decades. Laparoscopic approach with or without robotic- assisted surgery has become the norm for the surgical management of colorectal cancer. The emergence of targeted therapies is also playing an important role in prolonged life in metastatic disease in colorectal cancer. Furthermore, the advance of currently available diagnostic modalities and the experimental investigation of novel technologies such as the implementation of nanoparticles bring considerable promise for the detection, staging, and treatment of CRC and calls for improved stratification and prognostication to better allocate resources and justify associated costs while reducing morbidity and even mortality from the disease.

The promise of personalized medicine has become a clinical reality now with colorectal cancer genetics at the forefront of this next major advance in clinical medicine. This is no more evident than in the recent advances in testing of colorectal cancers for specific molecular alterations in order to guide treatment with the monoclonal antibody therapies which target the epidermal growth factor receptor. There are genetic mechanisms of colorectal cancer as to how these alterations relate to emerging biomarkers for early detection and risk stratification (diagnostic markers), prognosis (prognostic markers) and the prediction of treatment responses (predictive markers).

We hope that promising waves of trial data will come to us in the next decade or so and a new knowledge of relevant biomarkers may bring us closer to better & cost effective screening and surveillance strategies. To promote the basic and clinical research field in colorectal cancer, we invite investigators to contribute original research articles as well as review articles that will stimulate continuing efforts to expand the diagnosis and the treatment of colorectal cancer.

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