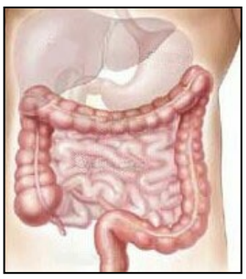
COLORECTAL CANCER RESEARCH UPDATES

Month Ending November 22nd, 2013



The following colorectal cancer research update extends from October 19th – November 22nd, 2013 inclusive and is intended for informational purposes only.

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DRUGS / SYSTEMIC THERAPIES

1. IMPACT and COMPACT Studies Running Out of Princess Margaret Hospital (Oct. 19/13)

IMPACT (Integrated Molecular Profiling in Advanced Cancer Trial) and **COMPACT** (Community Oncology Molecular Profiling in Advanced Cancer Trial) are two clinical trials being run by the Princess Margaret Cancer Centre in Toronto that will help advance Personalized Cancer Medicine by basing treatment on the molecular profile of each patient's tumour. Launched on March 1, 2012, IMPACT is the first Canadian comprehensive molecular profiling program that seeks to provide doctors with specific cancer gene information so that each patient's treatment can be tailored to his/her specific form of the disease. Cancer was once thought of as a single disease that affected many different parts of the body. Researchers now know that the genetic abnormalities that initiate each patient's cancer are different, even if cancers from the same part of the body may look the same under a microscope. **IMPACT** is providing molecular information which enables doctors to determine the right treatment for the right patient at the right time. Led by **Drs. Phillipe Bedard and Lillian Siu**, the first stage of IMPACT involves patients who are being treated at the Princess Margaret Cancer Centre for advanced breast cancer, **colorectal cancer**, ovarian cancer and non-small cell lung cancer, as well as those referred for early phase (Phase I) clinical trials. Molecular testing for IMPACT is conducted under the direction of Dr. Suzanne Kamel-Reid and results from the testing are included in the patient's electronic health record (this permanent record is important as future treatment options become available). The genetic profile for each patient's tumour is then discussed at multi-disciplinary IMPACT Tumour Board Meetings. Here doctors and researchers gather to provide input from their particular specialties and propose a personalized treatment plan that is tailored to each patient. The original goal of the study was to profile 500 patients. The response to date has been so positive and overwhelming (close to 400 patients already participating) that the target has now been increased to 1,000 patients. Additional disease sites such as head and neck, pancreatic and biliary are also being considered. The lessons learned in this trial, including new systems, protocols and standards, will be pivotal to the development and expansion of Personalized Cancer Medicine. Each patient enrolled in IMPACT will have their cancer specimens (which were previously obtained for diagnosis) tested for specific cancer biomarkers, focusing on 24 genes and 281 mutations. It is the hope that this information will enable doctors at PMH to prescribe treatments for patients that target their tumours more effectively. Here is the link to the study description:

http://clinicaltrials.gov/show/NCT01505400

COMPACT is the next stage in the evolution of Personalized Cancer Medicine – taking the model out to community partners beyond The Princess Margaret. Like IMPACT, COMPACT will focus on breast, **colorectal**, ovarian and non-small cell lung cancer, but will involve 500 patients per year being treated at other centres within a 200km radius, including the following Centres:

- St. Michael's Hospital
- Mount Sinai Hospital
- Credit Valley Hospital
- Durham Regional Cancer Centre
- St. Joseph's Hospital
- William Osler Health Centre
- Trillium Health Centre
- Royal Victoria Hospital
- Grand River Regional Hospital
- Sunnybrook Odette Cancer Centre
- North York General Hospital
- Southlake Regional Health Centre
- Markham Stouffville Hospital
- Toronto East General Hospital

Patients will be referred to COMPACT by their oncologists and come to The Princess Margaret for testing and to consent to the trial. A report (along with suggested treatment options) will be sent back to their primary physician to be reviewed with the patient. Treatment may take place elsewhere.

http://thepmcf.ca/Pages/NewsAndMedia/NewsStory.aspx?s=736

2. Avastin + Xeloda Benefits in Elderly mCRC (Oct.19/13)

Adding bevacizumab (*Avastin*) to capecitabine (*Xeloda*) significantly improves progression-free survival (time before the cancer gets worse) in elderly patients with metastatic colorectal cancer, with no unexpected safety concerns, according to results from the first phase 3 study of bevacizumab in an exclusively elderly population. The data suggest that bevacizumab plus capecitabine is an effective and tolerable treatment regimen for patients with metastatic colorectal cancer aged 70 years and older who are deemed unsuitable for irinotecan-based or oxaliplatin-based treatments. The AVEX study has shown a clinically meaningful benefit. For most elderly patients with advanced colorectal cancer the combination

of bevacizumab with capecitabine seems to be a good option for the initiation of systemic treatment. The study authors emphasize that this study is an "essential" addition to the evidence base because patients with colorectal cancer older than 70 years have been highly underrepresented in clinical trials, despite the fact that this age group accounts for about half of all patients with metastatic colorectal cancer. The study was conducted in 280 patients 70 to 87 years of age. About two thirds of the patients were older than 75 years, and the majority had comorbidities and received concomitant medications. These patients had previously untreated and unresectable metastatic colorectal cancer, and were not deemed to be candidates for oxaliplatin-based or irinotecan-based chemotherapy regimens. They were randomized to 1 of 2 treatments:

- twice-daily oral capecitabine 1000 mg/m² on days 1 to 14, or
- the same regimen of capecitabine plus intravenous bevacizumab 7.5 mg/kg on day 1 every 3 weeks until disease progression, unacceptable toxic effects, or withdrawal of consent.

The results show a significant improvement in median progression-free survival with the combination, compared with monotherapy (9.1 vs 5.1 months). Median overall survival did not differ significantly in the combination and monotherapy groups (20.7 vs 16.8 months), but the study was not sufficiently powered to detect an overall survival difference, the researchers note. The proportion of patients who used any subsequent treatment was the same in the 2 groups.

Cunningham, David, et al., Bevacizumab plus capecitabine versus capecitabine alone in elderly patients with previously untreated metastatic colorectal cancer (AVEX): an open-label, randomized phase 3 trial. The Lancet Oncology. Vol. 14, Issue 11: pp. 1077-1085

3. **Possible Resistance Mechanisms of Colorectal Cancer to Avastin** (Oct.24/13)

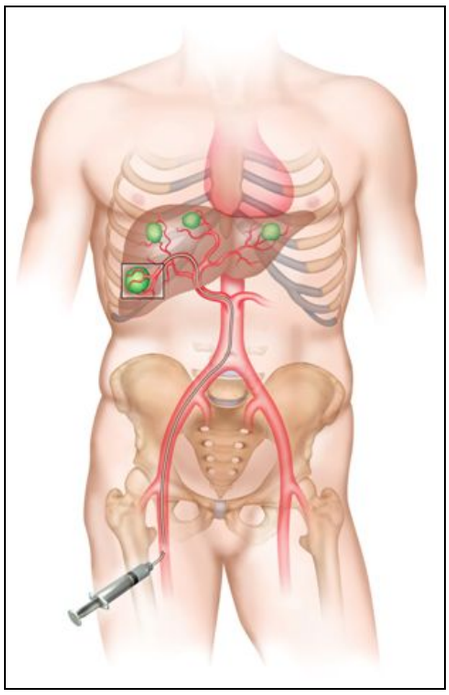
The results of this study suggest that when colorectal cancer is targeted by the drug bevacizumab (Avastin), tumors may switch dependence from VEGF-A, which is targeted by the drug, to related growth factors including VEGF-C, VEGF-D and placental growth factor. This change to new growth-factor dependence may allow colorectal cancer to push past bevacizumab's blockage of VEGF-A to continue to drive tumor growth. Think of it like damming a river. Bevacizumab can block the main flow, but then once a tumor's need builds up behind this dam, water starts to flow around the blockage in the form of streams and tributaries. That's like these other growth factors -- eventually a tumor becomes able to use these tributaries of VEGF-C, VEGF-D and placental growth factor to supply itself with the 'water' it needs. The analogy of liquid is an apt one -- bevacizumab slows cancer's growth by limiting a tumor's ability to grow the new blood vessels it needs to supply itself with nutrients. Especially in combination with chemotherapy, bevacizumab has proven an effective treatment for colorectal cancer. But then there frequently comes a point at which bevacizumab stops working and the tumor restarts its growth. This study asked why. Specifically, investigators serially tested the levels of other VEGF-related growth factors in 42 patients treated with bevacizumab and chemotherapy, at many points during the course of their treatment. "What we saw is that levels of VEGF-C and placental growth factor went **up** just before tumors progressed and then stayed high during the periods of tumor growth. Interestingly, VEGF-D was only elevated during progression. But it seems that tumors may be using these growth factors as ways to create blood vessel growth in the absence of VEGF-A, blocked by bevacizumab," says lead investigator Lieu. Then the researchers also took a snapshot of levels in 403 colorectal cancer patients, at one time during treatment. Because this group included patients who were and were not being treated with chemotherapy along with bevacizumab, they could show that the rise in VEGF levels was, in fact, due to bevacizumab and not to some interaction with the chemotherapy. "It's too early to say with certainty that VEGF-C, VEGF-D, and placental growth factor are the cause of colorectal cancer resistance to bevacizumab, but the correlation we saw in this study is compelling," Lieu says. Current studies are exploring the use of drugs that block more blood-vessel-growth-promoting factors than VEGF-A. For example, Lieu points to the example of aflibercept (Zaltrap), which was given FDA approval in August, 2013 for the treatment of metastatic colorectal cancer, along with the chemotherapy regimen known as FOLFIRI. The drug inhibits placental growth factor along with VEGF-A. "It's an attractive strategy, and also proof of concept that by targeting not only the primary mechanism of tumor growth but also one or more of these 'workarounds,' this drug or other future drugs could stall growth longer than blocking any one of these growth factors, individually," Lieu says. Lieu points out that in addition to targeting these additional growth factors, the fact that spikes in VEGF-C and placental growth factor presage tumor progression could give doctors and researchers a clue that bevacizumab has lost its efficacy. Though more work is needed, Lieu can imagine using spikes in VEGF-C or prenatal growth factor to recommend evaluating new treatment options.

Lieu, Christopher H, et al., The association of alternate vegf ligands with resistance to anti-vegf therapy in metastatic colorectal cancer. PLoS ONE 8(10): e77117. DOI: 10.1371/journal.pone.0077117

RADIATION THERAPY/INTERVENTIONAL RADIOLOGY

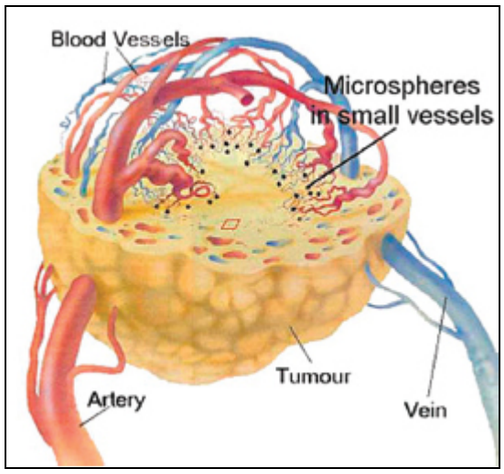
4. **Nuclear Medicine Therapy Increases Survival for Patients with Colorectal Cancer Liver Mets** (Oct.30/13)

For patients who fail to respond to current first-line and second-line treatments for colorectal cancer liver metastases (also known as salvage patients), radioembolization with Y-90 microspheres could extend survival according to new research. A systematic review conducted by researchers showed that approximately 50% of salvage patients have an overall survival of more than 12 months after this nuclear medicine therapy. A structured review was performed by researchers to gather all available evidence on radioembolization for the specific group of patients with colorectal cancer liver metastases.



Microspheres are microscopic polymer beads that contain the radioactive element yttrium-90 (Y90) and emit beta radiation to kill cancer cells. Due to their small size, they travel easily through the bloodstream directly to the liver. The microspheres become lodged in the small blood vessels supplying the tumor and kill the cancer cells.

Source: http://www.skyridgemedcenter.com/conditions_we_treat/cancer_care/liver_cancer/sir-spheres-microspheres-qa.htm



Source: http://www.altabatessummit.org/technology/sirspheres.html

"Although quite some reviews are printed on the subject of radioembolization, we felt that a structured and comprehensive review on survival and response data for these patients was lacking," said Charlotte E.N.M. Rosenbaum, PhD, lead author of the study "Radioembolization for Treatment of Salvage Patients with Colorectal Cancer Liver Metastases: A Systemic Review." Researchers reviewed a total of 13 articles on Y-90 radioembolization as a monotherapy and 13 articles on Y-90 radioembolization as a combined with chemotherapy. Among the studies, disease control rates (i.e., complete response, partial response and stable disease) ranged from 29-90% in the monotherapy studies, which involved 901 patients. In the studies in which Y-90 radioembolization was combined with chemotherapy, involving 472 patients, disease control rates ranged from 59-100%. "From the studies included in this systematic review, survival proportions of approximately 50% were found. Therefore, in this group of salvage colorectal cancer liver metastases patients who otherwise have no regular treatment options and a life expectancy of less than six months, Y-90 radioembolization seems to be a hopeful treatment option," noted Rosenbaum. She continued, "Our paper shows all published data on this subject from the first randomized trial onwards. Furthermore, we have determined 12-month survival proportions for all included articles to provide a better overview and to better allow for comparisons. Finally, this overview of the literature shows which topics have not been the focus of much research and may thus be interesting for further work."

Rosenbaum, H. M.. Radioembolization for Treatment of Salvage Patients with Colorectal Cancer Liver Metastases: A Systematic Review. **Journal of Nuclear Medicine*, 2013; 54 (11): 1890 DOI: 10.2967/jnumed.113.119545***

SCREENING

5. U.S. Screening Guidelines May Miss 10% of Colon Cancers (Oct.22/13)

For people with a family history of adenomas (colon polyps that lead to colon cancer), up to 10% of colorectal cancers could be missed when current U.S. national screening guidelines are followed. In the largest population-based study to date, researchers from Huntsman Cancer Institute (HCI) at the University of Utah made this finding based on nearly 127,000 individuals who underwent colonoscopy in Utah between 1995 and 2009. Family history of colon cancer is widely accepted as a factor that increases risk for the disease. This study quantified the increased risk to first-degree relatives (parents, siblings, children) of patients with adenomas or advanced adenomas at 35 to 70 percent higher than in relatives of patients without these conditions. The study also detected smaller percentages of elevated risk in more distant second- (aunts and uncles, grandparents) and third-degree relatives (cousins, nieces and nephews, great-grandparents). "We expected to see increased risk in first-degree relatives, but we weren't sure the risk would also be higher for more distant relatives in multiple generations," said N. Jewel Samadder, MD, MSc, principal investigator. "The biggest surprise was the percentage of missed cancers under the current guidelines. We figured there would be a few percent, but 10 percent is a large number," he added. For the general population, current national colon cancer screening guidelines recommend colonoscopy every 10 years starting at age 50. For first-degree relatives of people diagnosed with colorectal cancer or advanced adenomas before they were 60 years old, increased screening is recommended—colonoscopies every five years starting at age 40. The screening recommendations for more distant relatives of people diagnosed before 60 and for all relatives of people diagnosed at or after age 60 are the same as for the general public. "Our results support the current screening guidelines, but they also raise the issue of whether some level of more aggressive screening should be considered, not only for first-degree relatives of patients with polyps diagnosed at or below age 60, but also for those first-degree relatives of patients diagnosed above age 60," said Samadder. "To validate other components of the current screening guidelines, we need to continue with a more in-depth examination of the risk of colorectal cancer in relatives of patients diagnosed with colorectal cancer or advanced adenomas, looking at factors such as the size of the polyp, the degree of cell abnormality and location of the tumor in the bowel." The study examined colonoscopy results from Utah residents between 50 and 80 years of age, linking them with cancer and pedigree information from the Utah Population Database (UPDB). "The records came from both Intermountain Healthcare and University of Utah Health Care, which represents 85 percent of all patient care in Utah and includes facilities from academic medical centers to small rural clinics," said Samadder. "No other study has combined genealogical and cancer data with records from two major health care organizations which have integrated electronic patient data."

Samadder, Jewel N.,et al. Risk of colorectal cancer and adenomas in the families of patients with adenomas.* Cancer*, 2013; DOI: 10.1002/cncr.28227

6. Older Adults Still Benefit from Colonoscopy (Oct.24/13)

There is no upper age limit to the usefulness of colon cancer screening, say doctors at the Cleveland Clinic in the US. Colorectal cancer screening tests are valuable for detecting bowel cancer and polyps before any symptoms develop. In the US, it's recommended that screening – either with a faecal occult blood test (FOBT), sigmoidoscopy or colonoscopy – should start at age 50 and earlier in those with a family history of colon cancer. But it's not been clear at what age the screening should stop. Researchers at the Cleveland Clinic Foundation have analyzed records from 981 colonoscopies. Just over half were screens and the rest were to evaluate symptoms. More than a third were performed on patients in their fifties, 28 per cent on those in their sixties and the rest on the over seventies. The prevalence of overall bowel cancer peaked at 70 – but the number of cases of certain forms of cancer and numerous polyps continued to rise with age. The researchers conclude that screening should continue throughout life. But many patients seem unaware that they are eligible for a free screen under U.S. Medicare arrangements – a telephone poll revealed that 16% did not know if the FOBT was covered, and a further 12% thought it was not covered.

http://www.newsfix.ca/2013/10/26/older-adults-still-benefit-from-colonoscopy/

OTHER

7. Risk for Treatment Failure is Higher in Younger Patients (Oct.18/13)

Younger patients with metastatic colorectal cancer represent a high-risk group that is less likely to respond to treatment. Colorectal cancer in patients younger than 40 years is more likely to grow despite treatment. Further, younger patients are at greater risk of death compared with people in other age groups. This research was presented at the 2013 European Cancer Congress in Amsterdam, The Netherlands. An analysis of 20,034 patients in 24 phase III clinical trials showed that the youngest and oldest patients had the highest risk of disease progression and death, compared with middle-age patients. Compared with 57-year-old patients, people younger than 40 years had a 30% increased risk of dying from the disease, and they had a 28% increased risk of their disease spreading during the first year of follow-up compared with 61-year-old patients. Colorectal cancer occurs in 4.6% of patients who are younger than 50 years, and the incidence of the disease in this age group increased at a rate of 1.5% per

year from 1992 to 2005. The most dramatic increases were observed in the 20-to-29-years group, with an increase in cases of 5.2% annually in men and 5.6% annually in women. Among those 30-to-39-years, the annual increase in cases was 3% in men and 2% in women. “The reasons why the incidence of colorectal cancer is increasing in younger patients remain unknown; although genetic predisposition, environmental factors, fewer early cancer detections in this population, or a combination of these factors are thought to play a role,” said investigator Christopher Lieu, MD, of Colorado University (CU) Cancer Center and CU's School of Medicine in Aurora. “We carried out this study to see whether age was associated with time until cancer progresses or the patient dies. We also wanted to get a better picture of the age-response relationship and identify how risk changes as people age, rather than simply comparing one group (patients younger than 40 [years]) with another group (patients older than 40 [years]),” Lieu said. Previous studies in this field split the population into two mutually exclusive groups, establishing rigid limits between those patients younger than 40 or 50 years and those older. The new research, however, did not use such a cut-off approach and includes data spanning all ages. “The reason we did this is we believe a 49-year-old patient with colorectal cancer may be different than a 20-year-old. By including them in the same group of people younger than 50 years old, we might be mistakenly considering them the same,” said Lieu. “Analysis of this incredibly large population of patients has allowed us to answer meaningful questions, such as the outcomes of young versus older patients. Our results show young age is associated with worse overall survival and progression-free survival,” said Lieu. “Young patients with metastatic colorectal cancer represent a group who are at high risk for treatment failure.”

http://www.oncologynurseadvisor.com/risk-for-treatment-failure-is-higher-in-younger-patients-with-metastatic-colorectal-cancer/article/316683/

8. Internet Users More Likely to Engage in Cancer-Preventive Behaviours (Oct.22/13)

Older men and women who used the internet were more likely to participate in screening for colorectal cancer, participate in physical activities, eat healthily, and smoke less, compared with those who did not use the internet, according to this study. A large, population-based, cohort study of older adults in England, called the English Longitudinal Study of Aging, collected data from men and women aged 50 or older, and found that men and women who were consistent internet users were twice as likely to participate in colorectal screening than nonusers. Both men and women who used the internet consistently were also 50% more likely to take part in regular physical activity, 24% more likely to eat at least five servings of fruits and vegetables daily, and 44% less likely to be current smokers. There was, however, no association between internet use and participation in breast cancer screening among women. "We accounted for sociodemographic factors that influence internet use and various measures of physical capabilities and cognitive function that decline with age, and still found an association between internet use and cancer-preventive behaviors," said Christian von Wagner, Ph.D., senior lecturer in behavioral research in early diagnosis of cancer at the University College London, United Kingdom. "The interesting aspect here is a dose-response relationship between internet use and cancer preventive-behaviors: Intermittent users were more likely to have cancer-preventive behaviors than never-users, and consistent users were more likely to have cancer-preventive behaviors than intermittent users." Von Wagner and colleagues, however, identified a "digital divide." Internet use was higher in younger, male, white, wealthier, and more educated participants and lower in older, less wealthy, and nonwhite individuals with physical disabilities. "It is important that policymakers recognize the role internet use plays in influencing inequalities in cancer outcomes, and help increase access to the internet among this demographic," he said. The researchers used data from 5,943 respondents who answered questions collected in wave one in 2002, and were followed up with questions every two years in waves two to five, until 2011. Questions included internet/email use, self-reported colorectal and breast cancer screening, physical activity, eating habits, physical and cognitive abilities, and demographics. Among the study participants, 41.4% reported not using the internet, 38.3% reported using the internet in waves one to three (intermittent users), and 20.3% reported using the internet in all five waves (consistent users).

Von Wagner, Christian, et al., . Internet Use and Cancer-Preventive Behaviors in Older Adults: Findings from a Longitudinal Cohort Study. **Cancer Epidemiology, Biomarkers & Prevention*, October 2013***

9. **The Role Played by Estrogen in Colon Cancer Prevention/Treatment** (Oct.22/13)

Estrogen has been shown to reduce incidence of colon cancer. Williams, an assistant professor with the UH Center for Nuclear Receptors and Cell Signaling (CNRCS), plans to provide a detailed understanding of the role and potential of the nuclear receptor estrogen receptor beta (ERbeta) in colon cancer prevention and treatment. A large body of work has suggested that signals conveyed by estrogen can prevent or delay colon cancer development, but little is understood of the underlying mechanisms. Williams' lab offers unique models and data that can clarify how estrogen influences colon cancer development. Through this five-year project, the lab will investigate the mechanistic basis for novel colon cancer prevention and therapy using ERbeta to validate biomarkers and develop future therapy and prevention strategies. "Our preliminary studies, performed with the help of graduate students Karin Edvardsson, Trang Vu and Philip Jonsson, have yielded positive results, and we look forward to expanding upon our research with this NCI grant," Williams said. "Our goal is to increase opportunities for improved colon cancer prevention and therapies."

http://www.eurekalert.org/pub_releases/2013-10/uoh-roe102113.php

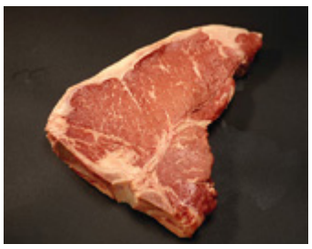
10. Lycopene May Reduce the Risk of Colorectal Cancer (Oct.18/13)

Many health organizations recommend eating more produce for colorectal cancer protection, but the mechanism for its disease-fighting ability is less well understood. Fruits and vegetables are rich in fiber and antioxidants – compounds that protect cells – and scientists have suspected that both play a role. Researchers from Stuttgart, Germany looked the relationship of three antioxidants – **lycopene**, **beta-carotene**, and **alpha-tocopherol** – and their association with colorectal adenomas, growths that are possibly precancerous. The 165 volunteers were part of a larger study of lifestyle habits and colorectal adenomas. All had a recent colonoscopy to evaluate hidden blood in the stool, but were otherwise healthy, with no prior personal or family history of colorectal cancer or polyps. Polyps discovered during the colonoscopy exam were removed and classified as adenomatous – growths that might turn cancerous if not removed – or hyperplastic, which tend to be smaller and are thought to be unlikely to ever develop into cancer. A nutritionist questioned the volunteers about their diets, including consumption of alcoholic beverages, and other habits. Blood samples were measured for levels of lycopene, beta-carotene, and alpha-tocopherol. The investigators looked for relationships between blood levels of the antioxidants and colorectal growths. Low blood levels of lycopene and smoking were both associated with an increased risk for adenomas, after other factors were ruled out that can influence colorectal cancer risk, such as age, body fat, and gender. There was no relationship between the presence of adenomas and levels of beta-carotene and alpha-tocopherol. Lycopene is concentrated in tomatoes and tomato products. The researchers concluded that ***lycopene is in part responsible for the protective effect high tomato intake has against the risk of colorectal adenomas***. Other studies have shown that beta-carotene and alpha-tocopherol have a healthful influence too, but this study does not substantiate that. Lycopene appears to protect cells from the damage caused by free radicals, which are by-products from the body's oxygen use and also a result of exposure to cigarette smoke and excessive sunlight. Besides tomatoes and tomato products, other lycopene-rich foods include watermelon, pink grapefruit, pink guava, and papaya.

http://www.newsfix.ca/2013/07/08/lycopene-may-reduce-the-risk-of-colorectal-cancer/

11. Gene May Explain Link Between Meat and Colon Cancer Risk (Oct. 24/13)

A specific genetic variant might help explain why eating red and processed meat is associated with an increased risk of colon cancer, a small, new study contends. The study also found that another genetic variant might play a role in the lower risk of colorectal cancer associated with eating vegetables, fruits and fiber. The findings could have public health significance since diet is a modifiable risk factor for this type of cancer, the researchers said. The study included more than 9,000 people with colorectal cancer and a similar-sized group of people without cancer. The investigators said they found a significant interaction between the genetic variant known as **rs4143094** and **processed meat consumption**. This variant is located in a chromosome region that includes GATA3, a gene previously linked to several forms of cancer.



Another significant diet-gene link was found in the genetic variant **rs1269486**, which was associated with a **reduced risk of colorectal cancer**, according to the study. The study results were presented at the annual meeting of the American Society of Human Genetics, in Boston. How specific foods affect genes and colorectal cancer risk is unknown, but the digestion of processed meat may cause inflammation or immune system responses that might trigger tumor development, the researchers said. It's believed that genetics, lifestyle and environment contribute to colorectal cancer risk. "It is conceivable that selected individuals at higher risk of colorectal cancer based on genomic profiling could be targeted for screening, diet modification and other prevention strategies," study coauthor Jane Figueiredo maintains.

http://www.cleveland.com/healthfit/index.ssf/2013/10/could_eating_red_meat_increase.html

12. Sedentary Behavior Linked to Precancerous Colorectal Tumours' Recurrence (Oct.30/13)

Men who spend the most time engaged in sedentary behaviors are at greatest risk for recurrence of colorectal adenomas, benign tumors that are known precursors of colorectal cancers. The majority of

colorectal cancers arise from precursors called colorectal adenomatous polyps, or colorectal adenomas, which can be removed during a colonoscopy. Although there is extensive evidence supporting an association between higher overall levels of physical activity and reduced risk of colorectal cancer, few studies have focused on the impact of sedentary behavior on colorectal cancer risk. Sedentary behavior is emerging as a risk factor for poor health. Even among those who fulfill daily recommendations for physical activity, lengthy periods of sedentary behavior have been associated with early morbidity and mortality, leading to the 'active couch potato' paradigm. This study is the first to specifically investigate the association between sedentary behavior and recurrence of colorectal adenomas. Given the substantial increase in risk of colorectal adenoma recurrence (45%) researchers observed for men with the highest sedentary time, they believe it would be beneficial to see 'reduce prolonged sitting time' added to the list of public health recommendations currently in place for health promotion and disease prevention. Researchers performed a pooled analysis of participants of two randomized, double-blind, placebo-controlled phase III clinical trials conducted at the University of Arizona Cancer Center in Tucson and the Mel and Enid Zuckerman College of Public Health: The Wheat Bran Fiber Study and the Ursodeoxycholic Acid Trial. All participants in the trials had one or more colorectal adenomas removed during a colonoscopy conducted in the six months prior to their trial enrollment. Among the participants were 1,730 who had completed a self-administered questionnaire that included questions about leisure, recreational, household, and other categories of activity at enrollment, and had undergone a follow-up colonoscopy. When the researchers analyzed all the data together, they found no association between activity type and colorectal adenoma recurrence. However, when they examined the data for men and women separately, they found that men who reported spending more than 11.38 hours a day engaged in sedentary behaviors, such as writing, typing or working on a computer, and reading, were 45% more likely to experience colorectal adenoma recurrence compared with men who spent fewer than 6.90 sedentary hours a day. No association between sedentary time and colorectal adenoma recurrence was observed for women. Further analysis showed that men who reported high levels of sedentary behaviors and low levels of participation in recreational activities such as walking, jogging, and playing golf, were 41% more likely to experience colorectal adenoma recurrence compared with men who reported low levels of both sedentary behaviors and recreational activity. According to the study authors, this confirms that sedentary behavior appears to independently contribute to increased cancer risk beyond the accompanying reduction in physical activity. The researchers plan to conduct further studies to determine more clearly the role of sedentary behavior in cancer risk.

Columbia University's Mailman School of Public Health (2013, October 29). Sedentary behavior linked to recurrence of precancerous colorectal tumors

http://www.sciencedaily.com/releases/2013/10/131029143002.htm

13. Calcium Carbonate, Vitamin E Prevent Cured Meat-Induced Colorectal Cancer (Nov.10/13)

Processed meat intake has been associated with increased colorectal cancer risk. The results of this study have shown that cured meat promotes carcinogen-induced precancerous lesions and increases specific biomarkers in the colon of rats. Researchers investigated whether cured meat modulates biomarkers of cancer risk in human volunteers and whether specific agents can suppress cured meat–induced precancerous lesions in rats and associated biomarkers in rats and humans. Six additives (calcium carbonate, inulin, rutin, carnosol, α-tocopherol, and trisodium pyrophosphate) were added to cured meat given to groups of rats for 14 d, and fecal biomarkers were measured. On the basis of these results, calcium and tocopherol were kept for the following additional experiments: cured meat, with or without calcium or tocopherol, was given to dimethylhydrazine-initiated rats (47% meat diet for 100 d) and to human volunteers in a crossover study (180 g/d for 4 d). Cured meat increased nitroso compounds and lipoperoxidation in human stools. Calcium normalized both biomarkers in rats and human feces, whereas tocopherol only decreased nitro compounds in rats and lipoperoxidation in feces of volunteers. Last, calcium and tocopherol reduced the number of mucin-depleted foci per colon in rats compared with nonsupplemented cured meat. Data suggest that the addition of calcium carbonate to the diet or α-tocopherol to cured meat may reduce colorectal cancer risk associated with cured-meat intake

Fabrice, Pierre, et al., Calcium and alpha tocopherol suppress cured-meat promotion of chemically induced colon carcinogenesis in rats and reduce associated biomarkers in human volunteers. The Amer J of Clin Nutrition. First published September 11, 2013.