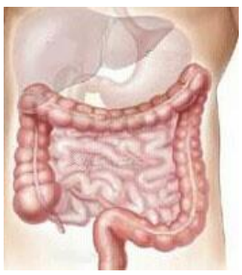
COLORECTAL CANCER RESEARCH UPDATES

Month Ending February 17, 2017



The following colorectal cancer research update extends from December 31, 2016 to February 17, 2017 inclusive and is intended for informational purposes only.

CONTENT

DRUGS / SYSTEMIC THERAPIES

1. Combination strategies for immunotherapy in GI cancers (Jan 12/17)

Current colorectal cancer (CRC) research in immunotherapy aims to create a more personalized, tailored approach to existing treatment regimens. While immunotherapy is not tumour-type specific, there are certain tumour types that are more responsive than others. Gastrointestinal (GI) cancers may be more difficult to treat with immunotherapy due to their low number of mutations and scarcity of infiltrating T cells (an important mediator cell of the immune system). Studies examining potential treatment combinations as a way to improve response to immunotherapy in GI cancers are hoping to provide the means to converting the less immune-responsive cancers into those that respond better to the treatment.

Combination with chemotherapy

To date, chemotherapy is the basis of treatment for most GI cancers. By itself it is known to have various immunogenic effects (i.e. stimulating the body's immune response). Chemotherapeutic agents such as anthracyclines and oxaliplatin initiate an immune response in the body by stimulating immunogenic cell death. Other drugs, such as gemcitabine, appear to positively regulate dendritic cells of the immune system, improving their ability to recognize foreign cells and respond accordingly. Care must be taken in the scheduling of chemotherapy and immunotherapy combinations, as supportive treatments given with chemotherapy may cause an unintended impact on the immune system.

Combination with radiotherapy

Recently, radiotherapy has presented itself to be a potential partner to immunotherapy by initiating an immune response in situ (at the tumour site) thereby taking advantage of the potentially numerous tumour-associated markers (antigens) there.

Combinations with agents targeting the tumour microenvironment

The tumour microenvironment consists of a vast array of immune cells, tumour vasculature (blood vessels that supply the tumour), lymphatics, as well as surrounding tissue cells including fat and muscle cells. For example, combining immunotherapy agents with anti-angiogenesis agents (agents which target the tumour vasculature) has demonstrated success in breast cancer mouse models in reprogramming an immunosuppressive tumour microenvironment to an immunosupportive environment.

Combinations with vaccines

Therapeutic vaccines work by priming the immune system against tumour cells by generating a tumour-specific immune response.

In conclusion, while GI cancers may be challenging to treat with immunotherapy, it may be possible to increase the ability of such cancers to respond to treatment with carefully designed combination therapies based on a solid understanding of the tumour environment and the immune system. Future studies aim to better assess response to treatment, minimize and treat autoimmune toxicities, and develop reliable biomarkers to be able to predict outcomes for such treatments.

http://gicasym.org/daily-news/combination-strategies-immunotherapy-gi-cancers

2. Study identifies potential biomarkers that predict for celecoxib CRC chemoprevention (Jan 22/17)

Celocoxib is a COX-2 selective non-steroidal anti-inflammatory drug (NSAID). The Adenoma Prevention With Celecoxib (APC) trial demonstrated that celocoxib reduced the incidence of post-polypectomy adenoma by 38% and advanced adenoma by 63% when used in patients with a high risk of developing colorectal adenomas. Due to the drug's small but significant increase in the risk of cardiovascular toxicity, no widespread adoption of the drug as a chemopreventive took place.

Recent research has re-examined the study to identify biological markers which could help predict response among patients. Prostaglandin E2 (PGE2) is an inflammatory mediator within the COX pathway that is implicated in carcinogenesis. COX-2 stimulates PGE2 expression, while 15-prostaglandin dehydrogenase (15-PGDH) degrades it, working with COX-2 to establish a PGE2 equilibrium. It was hypothesized that high COX-2 and 15-PDGH expression among individuals might be suggestive of the tumour-preventive efficacy of the selective COX-2 inhibitor celecoxib.

Both markers demonstrated predictive strength in celecoxib's chemopreventive effect – the 8% of individuals with high COX-2 expression demonstrated a 63% reduction in the risk of adenoma recurrence with celecoxib. The risk reduction with celecoxib was less strong among the 92% of individuals with low initial COX-2 expression. The absence of 15-PGDH at baseline (indicating higher PGE2 levels) predicted a reduced risk of adenoma recurrence with celecoxib, while no significant benefits of celecoxib were seen among individuals with 15-PGDH present at baseline. It was concluded that individuals with high PGE2 levels at baseline (high

COX-2 expression and/or absence of 15-PGDH) reached a 41% reduction in adenoma occurrence with celecoxib treatment. No benefit was observed among individuals with low PGE2 levels at baseline (low COX-2 expression and presence of 15-PGDH). Study results suggest that PGE2 is an important mediator in tumour formation in the colon for many individuals with adenoma.

http://gicasym.org/daily-news/study-identifies-potential-biomarkers-predict-celecoxib-crc-chemoprevention

3. Long-term use of low-dose aspirin helps prevent colorectal cancer, but also raises GI bleeding risk (Jan 23/17)

While long-term use of low-dose aspirin has demonstrated preventive effects in colorectal cancer (CRC), its adoption has remained controversial due to the increased risk of gastrointestinal bleeding. To date, few large-scale studies have compared risks and benefits of long-term aspirin use. A study conducted at the Chinese University of Hong Kong assessed the incidence and mortality of CRC and gastrointestinal bleeding among a population of 689,209 individuals. Aspirin users had been taking an average dose of 80mg for an average duration of 7.7 years. Among aspirin users, 2.8% were diagnosed with CRC and 1.02% died of the disease. 3.41% of non-users were diagnosed with cancer, and 1.65% died of the disease. Aspirin use demonstrated a significant reduction in CRC mortality, though 5.42% of users developed gastrointestinal bleeding and 0.41% died from it. In comparison, 3.14% of nonusers developed gastrointestinal bleeding and 0.35% died. Thus while long-term use of low-dose aspirin helps to prevent CRC, the associated gastrointestinal bleeding risk warrants further considerations of prophylactic use of aspirin to reduce the risks of this promising treatment.

Image courtesy of: http://restore.cityofhope.org/daily-aspirin-cancer-prevention

http://www.practiceupdate.com/news/14727/32/1?elsca1=emc_conf_ASCOGI2017Post1&elsca2=email&elsca3=practiceupdate_onc&elsca4=201711_ASCOGI2017Post1&elsca5=conference&rid=NTU2MjE4MDA1NzQS1&lid=10332481

4. Simultaneous EGFR and BRAF inhibition is proven effective in BRAF V600-mutated, metastatic colorectal cancer (Jan 19/17)

Results of the SWOG 1406 trial demonstrated that among patients with BRAF-mutant metastatic colorectal cancer (mCRC), the addition of the BRAF inhibitor vemurafenib to irinotecan and cetuximab increased progression-free survival (PFS) and disease control rate compared to treatment with irinotecan and cetuximab alone. BRAF mutations in metastatic colorectal cancer (mCRC) are associated with poor prognoses and 12-15 month median survival. To date, the use of BRAF inhibitors alone in the treatment of this subset of mCRC has not demonstrated clinical success. The addition of vemurafenib (a BRAF inhibitor) to a standard of care therapy of cetuximab (epidermal growth factor receptor (EGFR) inhibitor) and irinotecan demonstrated prolonged progression-free survival (PFS) and improved disease control rate in BRAF-mutated mCRC.

The SWOG 1406 study enrolled 106 patients with BRAF-mutated mCRC. Patients were randomly assigned to treatment with irinotecan and cetuximab with or without vemurafenib. When BRAF is inhibited by vemurafenib, a resulting upregulation of EGFR occurs; upregulation of EGFR is implicated in increased tumour activity. When given in combination with cetuximab EGFR inhibitor and irinotecan, greater antitumour activity was observed. A study examining the effects of the triple therapy on BRAF-mutant mCRC divided patients into two treatment arms: vemurafenib + cetuximab-irinotecan and cetuximab-irinotecan alone. It was found that PFS improved in the triple therapy arm with median PFS of 4.4 months vs 2.0 in the cetuximab-irinotecan group alone. The response rate was 16% vs. 4% and the disease control rate 67% vs. 22% for the vemurafenib and control arms, respectively. Adverse effects were significantly more common in the triple therapy group, including neutropenia (28% vs. 7%), anemia (13% vs. 0%) and nausea (15% vs. 0%). The research concludes that the effectiveness of the triple therapy is promising, though improvements to minimize adverse effects must be considered.

http://www.practiceupdate.com/news/14699/32/1?elsca1=emc_conf_ASCOGI2017Post1&elsca2=email&elsca3=practiceupdate_onc&elsca4=201711_ASCOGI2017Post1&elsca5=conference&rid=NTU2MjE4MDA1NzQS1&lid=10332481

5. Chemotherapy use and survival among young and middle-aged patients with colon cancer (Jan 25/17)

Treatment options for individuals with early-onset colon cancer are poorly defined, and effects of treatments on the patients' prognoses remain unclear. Young and middle-aged patients are 2 to 8 times more likely to receive postoperative systemic chemotherapy for colon cancer than older patients. Such additional use of postoperative systemic chemotherapy without matched survival improvement suggests that there may be overuse of chemotherapy among younger adults with colon cancer. A recent study aimed to investigate the effects of adjuvant chemotherapy plus surgery by age category (18-49, 50-64, and 65-75 years) and corresponding survival gains compared to individuals who only received surgery. The study included 3143 patients aged 18-75 years with confirmed primary colon cancer. The study found that while young and middle-aged patients between the age of 50 and 64 years were 2 to 8 times more likely to receive adjuvant chemotherapy, no significant differences were observed in survival among age groups. These findings suggest that there is a possible overuse of chemotherapy among young and middle-aged adults raising many quality of life concerns.

http://jamanetwork.com/journals/jamasurgery/article-abstract/2599142

SURGICAL THERAPIES

6. Young adult colorectal cancer clinic now available at Sunnybrook (Feb.1/17)

A recent study led by University of Toronto doctors has observed a rise in colorectal cancer rates in patients under the age of 50. The study mirrors findings from the U.S., Australia and Europe. The growing colorectal cancer rates in young people has come after decades of declining rates in people over 50, which have occurred most likely due to increased use of colorectal cancer screening (through population-based screening programs) which can identify and remove precancerous polyps.

Patients diagnosed under the age of 50 have a unique set of needs, challenges and worries. They are unlike those diagnosed over the age of 50. **Dr. Shady Ashamalla (colorectal cancer surgical oncologist),** and his team at the **Sunnybrook Health Sciences Centre** understand the needs of this patient population.

Dr. Ashamalla belongs to a multidisciplinary team of experts in the ***Young Adult Colorectal Cancer Clinic*** who will work with young colorectal cancer patients, regardless of disease stage, to create an individualized treatment plan to support each patient through their cancer journey. Their needs and concerns will be addressed as they relate to:

- Fertility concerns and issues
- Young children at home
- Dating/intimacy issues
- Challenges at work
- Concerns about hereditary cancer
- Relationships with family and friends
- Psychological stress due to any or all of the above

Patients will access a team of experts consisting of:

- Oncologists (medical, surgical, radiation)
- Social workers
- Psychologists
- Geneticists and a
- Nurse navigator

Should a patient wish to be referred to Sunnybrook, they may have their family doctor or their specialist **refer them to Sunnybrook via this e-referral form.** Once the referral is received, the **Young Adult Colorectal Cancer Clinic** will be notified if the patient is under the age of 50. An appointment will then be issued wherein the patient will meet with various members of the team to address their specific set of concerns. The Sunnybrook Team is dedicated to improving the quality of care for young adults afflicted with colorectal cancer.

http://sunnybrook.ca/content/?page=young-adult-colorectal-cancer-clinic

7. 2017 GI Cancers Symposium: Watch-and-wait approach for rectal cancer appears as an option for more patients (Jan 17/17)

Data from a recent study suggests that among some patients with rectal cancer, omitting surgery does not compromise disease outcomes. The survival rate among patients who received "watch-and-wait" care after primary cancer treatment was 91% - a number similar to survival rates among patients who undergo surgery. Given the fact that rectal surgery comes with the risk of numerous debilitating complications including colostomy and urinary and sexual problems, if surgery can be safely avoided, it is good news for many patients. Surgery, however, remains part of the standard of care for rectal cancer. In many countries, patients with stage II-IV rectal cancer receive chemotherapy and/or radiation prior to receiving surgery. Some researchers have suggested that some people with rectal cancer will undergo surgery post-chemoradiation therapy, even though it may not be necessary. Though the watch-and-wait surveillance may be effective for some patients with rectal cancer, it cannot be said as of yet whether this method should be integrated into standard of care. A study examined the effects of watch-and-wait among 802 patients who had no signs of recurrent rectal cancer following chemotherapy and radiation. After an average of 2.6 years, 25% of patients underwent surgery after a cancer recurrence was detected, and distant metastases occurred in 7% of patients. The 3-year survival rate was 91% among all patients, and 87% among those with local cancer recurrence. These data are similar to data from patients who undergo surgery. Despite the study's findings, in the end it is the patient's personal decision whether they will undergo surgery or not. Further data collection, including all available future and past data on watch-and-wait strategies in rectal cancer, is expected to occur in order to best inform international guidelines on treatment and monitoring of patients with rectal cancer.

http://www.ascopost.com/News/46284

8. Left- and right-sided CRC: what is the impact on clinical decisions? (Jan12/17)

Recent clinical data has demonstrated that left- and right-sided primary tumours have different prognoses in colorectal cancer (CRC). The right side of the colon contains the cecum, ascending colon, hepatic flexure, and transverse colon and is also referred to as the "midgut". The left side of the colon contains the splenic flexure, descending colon, sigmoid and rectum and is also referred to as the "hindgut". In general, patients with a primary tumour on the right side of the colon have a significantly shorter overall survival (OS) compared with patients with a primary tumour on the left side of the colon. While the efficacy of anti-epidermal growth factor receptor (anti-EGFR) antibodies in the treatment of right-sided tumours remains uncertain, various studies have clearly demonstrated the efficacy of first-line anti-EGFR antibodies in prolonging OS among patients with left-sided primary tumours.

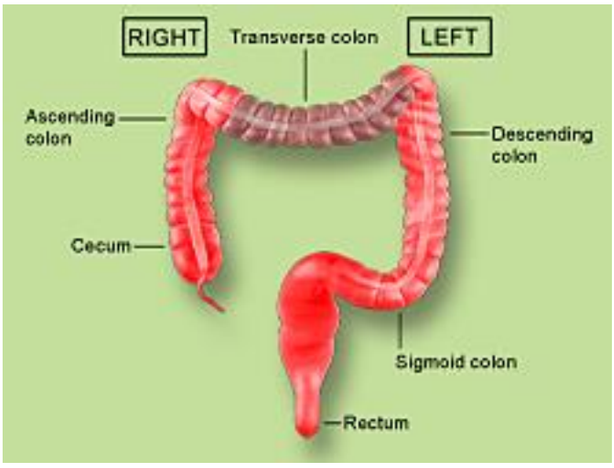


Image courtesy of: http://www.medscape.com/viewarticle/863537

Currently, there are four major CRC classification groups (Consensus Molecular Subtypes, CMS) based on genetic mutations and gene-expression data. For example, CMS1 contains high microsatellite instability (MSI), BRAF mutations and immune infiltration and activation. Despite such classification, about 13% of CRC cases remain unclassified because of the mixed makeup of tumours and the occurrence of rare forms of the disease. These unclassified CRC cases tend to be derived from stage II and III tumours, suggesting that CRC subgroup classifications may be very different among more advanced, metastatic forms of the disease. Similarly, such subclassifications have been unable to consistently define left- and right-sided tumours. This suggests a spectrum of change of tumour types from right- to left-sided tumours with different frequencies of molecular subtypes in different subsegments of the colon. With this knowledge, it is important for physicians not to exclude any biologic agent from use in a given treatment regimen solely based on the location of the primary tumour. Further research is necessary to create tests to determine the sensitivity of the tumour to each agent used in CRC treatment to better personalize the regimen. In addition, more extensive analysis of the primary tumour sample will enable better tailoring of the therapy to patients.

Colorectal cancer (CRC) is a highly heterogeneous disease that has proven difficult to classify. Recent efforts have focused in on the "sidedness" of the disease, demonstrating that the anatomic location of the

primary tumour within the colon is linked to varying outcomes of survival among patients with metastatic CRC. It has been observed that cancers which originate on the left of the colon (splenic flexure, descending colon, sigmoid colon and rectum) are linked to higher survival rates compared to cancers that originate on the right side (cecum, transverse and ascending colon).

The CALGB/SWOG 80405 trial demonstrated that left-sided tumours respond differently to biological therapies compared to right-sided tumours, suggesting molecular differences among the tumour types. Further studies on the molecular makeup of right- and left-sided tumours indicate that CRC contains a continuum of molecular alterations from the right to left side, rather than any clear-cut distinction between the sides.

Another study suggests that the sidedness of the tumour is also relevant among earlier stage CRC. Given that right-sided tumours often display worse outcomes compared with left-sided tumours, sidedness may be linked to recurrence risk and therefore suggest the need to strongly consider adjuvant therapies. Data from a small group of patients with stage III CRC revealed that recurrence rates were higher in right- versus left-sided tumours. Stage II or III tumours in the rectum had higher recurrence scores compared to stage II or III tumours in the left colon. Further studies are necessary to confirm the role of tumour location as a predictive indicator that warrants adjuvant chemotherapy.

http://gicasym.org/daily-news/left-and-right-sided-crc-what-impact-clinical-decisions

http://gicasym.org/daily-news/new-studies-offer-insight-implications-left-versus-right-sided-primary-tumor-location-crc

RADIATION THERAPY

9. MicroRNA regulation of radiation sensitivity in colorectal cancers (2017)

The current standard of care for patients with locally advanced colorectal cancer (CRC) is chemoradiation therapy (CRT) followed by surgery. While 10-25% of patients experience a complete response to CRT, patients with unresponsive cancer undergo extensive tumour excision that raises many quality of life issues. Thus, it may be observed that CRT is a predictor of overall survival of advanced CRC patients, emphasizing the importance of improving CRT response rates. Various factors governing the tumour microenvironment impact responses to CRT, such as specific tumour gene expression patterns. Existing evidence suggests that microRNAS (miRs) may play a key role in modifying tumour gene expression in response to radiation. Given that miR-processing machinery is often mutated in CRC, miRs have been implicated in the development of the disease. A recent study aimed to study miRs and understand whether differential expression of miRs regulates sensitivity of CRC to radiation, thereby making miR expression a potential biomarker to predict therapeutic response. Among rectal cancer patients who had either a partial response or no response to radiation therapy, RNA was isolated and examined. Seventeen miRs were identified that were differentially expressed in these patient subgroups. One in particular was found to inhibit cell proliferation and colony formation in the presence of radiation. These results suggest that miRs may modify cell survival pathways and therefore affect tumour sensitivity to radiation therapy.

http://meetinglibrary.asco.org/print/2545441

10. New Study Offered at the Odette Cancer Centre to Treat Recurrent Rectal Cancer (Feb.2/17)

Magnetic resonance--guided focused ultrasound (MRg--FU) is a non--invasive, outpatient modality being investigated for the thermal treatment of cancer. In MRg--FU, a specially designed transducer is used to focus a beam of low intensity ultrasound energy into a small volume at a specific target site in the body. MR is used to identify and delineate the tumour, focus the ultrasound beam on the target and provide real--time thermal mapping to ensure accurate heating of the designated target with minimal effect to the adjacent healthy tissue. The focused ultrasound beam produces therapeutic hyperthermia (40--42°C) in the target field causing protein denaturation and cell damage. Currently, there is no prospective clinical data reported on the use of MRg--FU in the setting of recurrent rectal cancer. Recurrent rectal cancer is a vexing clinical problem. Current retreatment protocols have limited efficacy. The addition of hyperthermia to radiation and chemotherapy may enhance the therapeutic response. With recent advances in technology, the investigators hypothesize that MRg--FU is technically feasible and can be safely used in combination with concurrent re--irradiation and chemotherapy for the treatment of recurrent rectal cancer without increased side--effects. The study is being offered at the Odette Cancer Centre. Here is the link to the study protocol:

https://clinicaltrials.gov/ct2/show/NCT02528175?term=magnetic+resonance+guided+focused+ultrasound&recr=Open&rank=1

SCREENING

11. Colonoscopy screening in older adults (Dec 25/16)

A recent study aimed to evaluate the effectiveness and safety of colonoscopy screening for the prevention of colorectal cancer (CRC) in older individuals aged 70-74 and 75-79 who are an often underrepresented group in study trials. Through an analysis of data from over one million Medicare beneficiaries aged 70-79 at average risk for CRC, it was found that colonoscopy screening only added a modest benefit in preventing CRC, an effect that was especially pronounced with older individuals. In the younger age group, colonoscopy reduced the 8-year risk for CRC from 2.6% to 2.2% and from 3.0% to 2.8% in the older group. It was observed that while the occurrence of adverse effects was low overall, it was greater among older individuals. Thus, while there is a modest benefit of colonoscopy screening in individuals aged 70-74, there is an even smaller benefit in older individuals. Findings from this study may help patients, doctors and policymakers make informed decisions about screening and prevention among this underrepresented population.

http://www.ascopost.com/issues/december-25-2016/colonoscopy-screening-in-older-adults/

12. New blood test for colorectal cancer recurrence: twice as sensitive as CEA test (Nov 10/16)

A blood test that detects circulating tumour DNA (ctDNA) for post-surgical surveillance of colorectal cancer (CRC) recurrence has been shown to detect twice the number of recurrence cases compared to carcinoembryonic antigen (CEA) testing. CEA testing is currently the standard-of-care for CRC recurrence monitoring in post-surgical patients. The ctDNA test screens for the presence of a modified form of two genes (BCAT1/IKZF1) which are associated with tumour growth and invasion. Recurrence rates among patients in remission from CRC is 30%, necessitating better methods for monitoring cancer recurrence if improved disease outcomes are to be reached. In a recent study, the sensitivity and specificity of the ctDNA test was compared to that of the CEA test among patients in remission undergoing surveillance. Out of the 122 participants evaluated, 28 had recurrence and 94 had no clinically detectable disease. Among the patients with recurrent disease, 67.9% tested positive in the ctDNA test while only 32.1% tested positive for CEA. Among the patients with no clinically detectable recurrence, no significant difference in the percentage that tested positive for ctDNA compared to CEA was identified. This test demonstrates promising results in detecting recurrence that CEA testing misses. Detecting early molecular changes that indicate underlying tumour growth may allow recurrent CRC to be detected in earlier stages of the disease when clinical intervention is more likely to be effective.

http://www.ascopost.com/issues/november-10-2016/new-blood-test-for-colorectal-cancer-recurrence-twice-as-sensitive-as-cea-test/

Young, GP, et al: A cross-sectional study comparing a blood test for methylated BCAT1 and IKZF1 tumour-derived DNA with CEA for detection of recurrent colorectal cancer. Cancer Med. October 11, 2016.

13. Molecular screening for Lynch Syndrome in young patients with colorectal adenomas (Feb 2/17)

MMR deficiency (dMMR) is one of the best understood forms of genetic instability in colorectal cancer (CRC), characterized by the loss of function of the mismatch repair pathway. Inability to repair errors in DNA replication allows mismatch mutations to occur across the genome, occurring especially in regions of repetitive DNA called microsatellites. This dysfunction leads to a phenomenon of microsatellite instability (MSI). High frequency MSI is the hallmark of the most common form of hereditary susceptibility to CRC, known as Lynch Syndrome, and is also observed in about 15-20% of sporadic colon cancers. Today, the frequency of dMMR in patients under 50 with adenomas without any known hereditary predisposition is unknown. The aim of a recent study was to define the frequency of dMMR in adenomas in patients under 50 years of age. For the study, patients with a personal history of CRC, polyposis syndrome, or inflammatory bowel disease prior to colonoscopy were excluded. Of the 208 patients, 266 polyps were identified via colonoscopy and 259 were stained using immunohistochemistry. Of all patients, only one patient (0.4%) was found to have dMMR on one polyp. The study concluded that routine screening of polyps in patients under 50 years old is not an effective means to identify Lynch Syndrome carriers. Further research must be conducted to identify the best methods for screening among this high-risk CRC group.

http://www.sciencedirect.com/science/article/pii/S1533002817300294

NUTRITION/ HEALTHY LIFESTYLE

14. Food and nutrition and colorectal cancer: patterns for prevention (Feb 1/17)

Countless studies over the years have highlighted the importance of diet in modifying the risk of colorectal cancer (CRC). The World Cancer Research Fund (WCRF)/American Institute for Cancer Research (AICR) Continuous Update Project Report systematically evaluates epidemiologic studies of diet and cancer risk to provide comprehensive evidence on the issue. The 2011 report revealed strong evidence to support that the consumption of foods containing dietary fibre is protective against CRC while the intake of red meat, processed meat and alcoholic beverages are causes of CRC. The report also demonstrated convincing evidence that physical activity protects against CRC while body fatness and particularly abdominal fatness contribute to the development of the disease. The report supported the consumption of garlic, milk and

calcium to be protective against the disease, whereas the evidence was more limited regarding the protective effects of non-starchy vegetables, fruits and foods containing vitamin D, or that foods containing iron, foods containing animal fats and sugary foods are causes of CRC. The interactions between diet and gut microbes are a growing topic in recent research, where diet is understood to have a strong influence on the amount and types of microbes present in the intestine. Gut microbial metabolism of foods produces compounds that may have positive or negative effects on CRC risk.

While growing emphasis is placed on identifying eating habits associated with lower cancer risk, it is important to recognize that while certain compounds found in everyday foods may have protective effects against the disease, they are not consumed in isolation. The role of diet in cancer prevention might be maximized when dietary patterns as a whole are considered, rather than any single-acting component. A variety of diet quality indices have been developed to help better understand the complexity of human diets and disease incidence, including the Healthy eating Index, the Alternative Healthy Eating Index, the Dietary Approaches to Stop Hypertension and indices based on the Mediterranean diet. In the future, experimental diets in animal studies that try to better capture the complexity of human diets may help to further characterize the effectiveness of certain diet patterns and their impact on CRC prevention.

http://cancerres.aacrjournals.org/content/77/3_Supplement/IA12

Johanna W. Lampe. Food and nutrition and colorectal cancer: Patterns for prevention. [abstract]. In: Proceedings of the AACR Special Conference on Colorectal Cancer: From Initiation to Outcomes; 2016 Sep 17-20; Tampa, FL. Philadelphia (PA): AACR; Cancer Res 2017;77(3 Suppl):Abstract nr IA12.

Image courtesy of: http://i.ndtvimg.com/i/2016-07/intestinal-gut-625_625x350_71468404450.jpg

OTHER

15. What role do bacteria have in the development of colon cancer? Jan 12/17)

The role of intestinal bacteria in the initiation and progression of colon cancer is a topic that has long been under study. Dr. Cynthia Sears of the Johns Hopkins University School of Medicine has been studying the role of microbes as contributors to the development of tumours in colon for over a decade, beginning her studies with a particular bacterium called enterotoxigenic *Bacteroides fragilis* ETBF). Her team was able to demonstrate that ETBF is, in fact, a carcinogen in mice. According to Dr. Sears, evidence demonstrates that 85-90% of colon cancer patients have ETBF present in their colon. The difficulty lies, however, in proving that ETBF is actually causing the cancer to develop. Especially in a disease like colon cancer that develops over 10 or more years, proving such causality remains a challenge as there are countless factors that may influence the rate at which colon cancer might arise. To gain such understanding, Dr. Sears and her team are studying hereditary colon cancer syndromes which have far more accelerated timelines of development. In this way, the researchers are able to study changes in the bacterial microbiota that may predispose a patient to the disease.

http://gicasym.org/daily-news/what-role-do-bacteria-have-development-colon-cancer