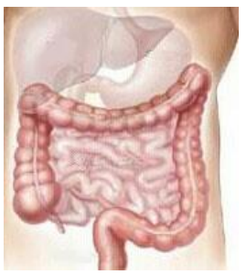
COLORECTAL CANCER RESEARCH UPDATES

Month Ending October 14, 2016



The following colorectal cancer research update extends from August 19th, 2016 – October 14th, 2016 inclusive and is intended for informational purposes only.

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DRUGS / SYSTEMIC THERAPIES

1. High surgical conversion rate in advanced colorectal cancer (Aug 25/16)

Results from a phase II trial suggest that a 4-month regimen of FOLFOXIRI (folinic acid, 5-fluorouracil, oxaliplatin and irinotecan) plus cetuximab (an epidermal growth factor receptor (EGFR)) followed by maintenance with cetuximab has significant activity in the treatment of colorectal cancer (CRC). A high surgical conversion rate was also reported, which researchers say may have a positive impact on overall survival rates. Participants of the study were patients with inoperable colorectal cancer with RAS/BRAF wildtype metastatic disease. Patients were treated with FOLFOXIRI plus cetuximab followed by either cetuximab or bevacizumab (a vascular endothelial growth factor inhibitor) maintenance. While overall response rates among the two treatment arms were similar, achieving 92% for the cetuximab arm and 89% for the bevacizumab arm, the curative surgical rate observed among the cetuximab arm was significantly higher: 45.8% compared to 29.8% for the bevacizumab arm. Safety concerns for the combination of FOLFOXIRI with an anti-EGFR agent such as cetuximab included grade 3/4 diarrhea in 25-94% of patients.

http://journals.lww.com/oncologytimes/Fulltext/2016/08250/High_Surgical_Conversion_Rate_in_Advanced.13.aspx

2. Alternative metrics (measures) of response correlate with O.S. in FIRE-3 trial (Aug 29/16)

Findings from the FIRE-3 study indicate that alternative measures of response to treatment, including early tumour shrinkage and depth of response, were linked to the overall survival benefit associated with FOLFIRI (5-fluorouracil, leucovorin, irinotecan) plus cetuximab as well as FOLFIRI plus bevacizumab treatment among patients with RAS wildtype metastatic colorectal cancer (mCRC). Among the RAS wildtype patient group, the FOLFIRI plus cetuximab group achieved a median overall survival of 33.1 months compared to 25 months for the FOLFIRI plus bevacizumab group. The investigator-assessed objective response (the proportion of patients with tumour size reduction of a predefined amount and for a minimum time period) and progression-free survival (the length of time during and after treatment that a patient lives with the disease but it does not get worse) was similar among the two treatment regimens. Patients with RAS wildtype mCRC who received FOLFIRI plus cetuximab achieved better objective response, frequency of early tumour shrinkage and median depth of response compared to those receiving FOLFIRI plus bevacizumab. This study provides a novel framework that connects alternative measures of response to overall survival.

http://www.cancertherapyadvisor.com/gastrointestinal-cancers/colorectal-cancer-mcrc-alternative-metrics-survival-folfirox/article/518947/

Stintzing S, Modest DP, Rossius L, et al. FOLFIRI plus cetuximab versus FOLFIRI plus bevacizumab for metastatic colorectal cancer (FIRE-3): a post-hoc analysis of tumour dynamics in the final RAS wild-type subgroup of this randomized double-blind phase 3 trial. Lancet Oncol. 2016 Aug 26. doi: 10.1016/S1470-2045(16)30269-8

3. Fingerprints disappear during capecitabine (xeloda) therapy (Aug 29/16)

Capecitabine (*Xeloda*), a widely used chemotherapy agent in the treatment of colorectal and breast cancer, can result in the temporary loss of fingerprints among patients. Researchers indicate that fingerprints return within 2 to 4 weeks after the end of treatment. Given the increasing importance of fingerprints in a person's ability to participate in public life, from applying to passports, logging into electronic devices, to entering certain countries including the United States, physicians should be aware of the possible loss of fingerprints during capecitabine treatment and patients should be well informed of this potential consequence of treatment. Hand-foot syndrome is one of the side effects of the drug, which results in redness and blistering of the palms occurring in about 60% of patients. This side effect is believed to be linked to the loss of fingerprints. A study conducted in partnership with the police force in the Netherlands aimed to examine this correlation between hand-foot syndrome and loss of fingerprints. The study revealed that patients can develop hand-foot syndrome without losing fingerprints, and vice versa. It is suggested that patients undergoing treatment with capecitabine should carry a doctor's note stating that they are undergoing treatment and that their fingerprints could be affected if they are planning to travel abroad.

http://www.medscape.com/viewarticle/868086

4. CRC biomarkers exert growing influence on prognosis and treatment (Sept 02/16)

Molecular testing for colorectal cancer has the potential to better personalize treatments based on the patient's particular biomarker (a measurable substance in an organism whose presence is indicative of disease, infection or environmental exposure) profile and tumour markers. Based on the current research, panellists at the 2016 American Society of Clinical Oncology (ASCO) Annual Meeting agreed that patients with recently diagnosed metastatic colorectal cancer (mCRC) should receive KRAS, RAS and BRAF testing and be assessed for microsatellite instability (MSI). With KRAS and RAS testing, it has been observed that an additional 13-16% of extended RAS mutations can be identified which could impact treatment. While BRAF testing will not direct therapy, it should be analyzed because it is an indicator of poor prognosis – a patient with a BRAF mutation has a probable survival of about 1 year. MSI testing examines tumours for mutations in DNA mismatch repair genes which cause errors in the repair of repetitive sequences and thus, the MSI of tumours. MSI testing, however, proves challenging in that it presents results that are difficult to interpret, many of which do not have practical value (i.e. there are mutations for which no drug is available).

While blood-based colorectal cancer testing has the potential to detect a wider variety of genetic mutations at a given time, the major challenge remains finding mutations for which a practical response, i.e. drug therapy, is possible. The general consensus among panellists was that finding the best treatment for actionable mutations will remain a process of trial and error. Molecular profiling trials, however, are making new treatments available for patients who have already undergone standard options or cannot afford to pay for new medications. In one molecular profiling trial, MATCH, molecularly targeted cancer drugs are provided to patients in exchange for reporting whether the drugs worked.

Increasing evidence on the impact of tumour location on patient prognosis suggests it may have important treatment implications. ASCO panellists examined data from a retrospective analysis of a federally funded phase III trial CALGB/SWOG 80405 which compared bevacizumab and cetuximab in combination with chemotherapy as initial therapy for mCRC. The analysis demonstrated that patients with tumours originating on the left side of the colon (descending colon, sigmoid colon and rectum) had significantly longer median overall survival (OS) compared to patients with right-sided tumours (cecum and ascending colon). The trend held true whether the patients received cetuximab or bevacizumab. While the difference in OS between right and left-sided tumours is not fully understood, it is important to note that the right colon is formed from the midgut tissue during embryonic development and the left colon originates from the hindgut, resulting in a dramatic difference in the types of detectable tumour markers. Furthermore, it has been observed that a higher incidence of BRAF mutations occurs in right-sided tumours, resulting in poorer prognoses in such cancers. Panelists agreed that further studies are required to more thoroughly understand the biologic profile of left versus right-sided tumours.

http://www.onclive.com/publications/oncology-live/2016/vol-17-no-17/crc-biomarkers-exert-growing-influence-on-prognosis-and-treatment

Venook AP, Niedzwiecki D, Innocenti F, et al. Impact of primary (1º) tumor location on overall survival (OS) and progression-free survival (PFS) in patients (pts) with metastatic colorectal cancer (mCRC): analysis of CALGB/SWOG 80405 (Alliance). J Clin Oncol. 2016;34(suppl; abstr 3504)

5. Tumour microenvironment acts as a mechanism of resistance to chemotherapy (Sept 06/16)

Researchers from the Bellvitge Biomedical Research Institute have published a new study which emphasizes the importance of the tumour environment in resisting treatment in colorectal cancer. Certain molecules (i.e. cytokines and chemokines) secreted by carcinoma associated fibroblasts (CAFs), a type of normal cell that is closely associated with primary tumour cells, induce processes that slow down the cell cycle thereby affecting how quickly tumour cells proliferate. These factors stabilize and activate particular proteins that minimize the effectiveness of conventional chemotherapy. Researchers are hoping to attain a better understanding of how the tumour microenvironment contributes to cancer progression and the development of resistance to therapies given that most tumours are treated with conventional cytotoxic (toxic to living cells) therapies thereby placing drug resistance as the main obstacle to their effectiveness.

https://www.sciencedaily.com/releases/2016/09/160906084839.htm

Samuel Gonçalves-Ribeiro, Natalia Guillen Díaz-Maroto, Mireia Berdiel-Acer, Antonio Soriano, Jordi Guardiola, Mercedes Martínez-Villacampa, Ramon Salazar, Gabriel Capellà, Alberto Villanueva, Eva Martínez-Balibrea, David G. Molleví. Carcinoma-associated fibroblasts affect sensitivity to oxaliplatin and 5FU in colorectal cancer cells. Oncotarget, 2014

6. Controlled studies needed to clarify aspirin's role in cancer prevention (Sept 10/16)

While regular aspirin use as a cancer preventive among the general population is not recommended by health care professionals, guidelines now indicate its use among patients with active cardiovascular disease or those at high risk for cardiovascular disease as it conveys a protective benefit with a reduction in the risk for colorectal cancer. A 30-year follow-up on two large population-based prospective patient studies including more than 88,000 women and 47,000 men assessed long-term aspirin use, including metrics such as quantification of dose and duration of usage. Aspirin use resulted in a mere 3% reduction in the risk for overall cancers, fuelled mainly by a 15% lower risk for gastrointestinal cancer and a 19% reduced risk for colorectal cancer in particular. Researchers estimated that more than 29,000 cases of gastrointestinal cancers could be prevented per year by regular aspirin therapy use. Such benefits were both time and dose

dependant, with aspirin usage required for at least 6 years or longer and a minimum use of at least one half to 1.5 standard aspirin tablets per week.

The COX-2 pathway is implicated in pre-cancerous conditions of colorectal and gastroesophageal cancers including polyps and chronic gastritis; aspirin's role as a COX-2 inhibitor explains its effectiveness in minimizing risk for such cancers. Countless studies, however, have suggested the variable effectiveness of aspirin in reducing incidence of colorectal cancer based on the presence of certain mutations (e.g. PIK3CA kinase mutations) or the expression of certain cellular biomarkers (e.g. human leukocyte antigen class I). Ongoing research is necessary in order to clarify potential biomarkers to identify which patients are mostly likely to benefit from aspirin therapy.

Currently, oncologists routinely recommend aspirin use among patients who have undergone curative treatment of colorectal cancer. It is also suggested that patients with the Lynch syndrome (an inherited disorder that increases the risk of many types of cancer, particularly colorectal cancer) gene take aspirin as part of their cancer-preventive therapy. The US Preventive Services Task Force indicates that regular low-dose aspirin use should be a consideration for prevention of cardiovascular disease and colorectal cancer in patients between the ages of 40 and 70 who are not at risk for stroke or gastrointestinal bleeding. As with any therapy, the advantages must be weighed against the disadvantages – regular use may increase risk for gastrointestinal bleeding and hemorrhagic stroke. Further studies are necessary to evaluate the potential risks and benefits of aspirin as a preventive therapy.

http://www.healio.com/hematology-oncology/gastrointestinal-cancer/news/print/hemonc-today/%7B42ff8114-0446-4b9e-8349-ff3eb24b7fa6%7D/controlled-studies-needed-to-clarify-aspirins-role-in-cancer-prevention

7. New retrospective analyses confirm Vectibix (Panitumumab) treatment provided survival benefit over chemotherapy with or without bevacizumab (avastin) in metastatic colorectal cancer patients with tumours of left-sided origin (Oct 10/16)

Amgen has announced results from retrospective analyses of studies with Vectibix (panitumumab) in metastatic colorectal cancer (mCRC) patients. The retrospective analysis of the PEAK study in mCRC patients with RAS wildtype primary tumours originating in the **left-sided colon** demonstrates that patients who received Vectibix plus FOLFOX 6 achieved 43.4 months median overall survival (OS), a 11.4 month increase when compared to FOLFOX6 plus bevacizumab. Furthermore, for the same patient population, the retrospective analysis of the PRIME study demonstrated that Vectibix plus FOLFOX4 increased OS by 6.7 months compared to FOLFOX4 alone. Progression-free survival which is the length of time during and after treatment that a patient lives with the disease but it does not get worse (PFS) among such patients in the PEAK and PRIME retrospective analyses was also greater in the Vectibix plus FOLFOX chemotherapy arms compared to FOLFOX chemotherapy alone. These analyses revealed that about 80% of tumours originate in the left side of the colon. Right-sided colon tumours are associated with a poorer prognosis compared to left-sided colon tumours. The subgroup of patients with RAS wildtype mCRC with right-sided tumours achieved greater response rates to **Vectibix and chemotherapy** compared to chemotherapy with or without bevacizumab. Further research is necessary, however, in order to make better conclusions regarding the response to treatment for patients with right-sided tumours. Whether a tumour originates in the left or right colon is becoming more important as predictor for differences in tumour biology and mutation load, providing physicians with another metric to help inform treatment decisions for mCRC patients.

http://www.prnewswire.com/news-releases/new-retrospective-analyses-confirm-vectibix-panitumumab-treatment-provided-survival-benefit-over-chemotherapy-with-or-without-bevacizumab-in-metastatic-colorectal-cancer-patients-with-tumors-of-left-sided-origin-300341514.html

SURGICAL THERAPIES

8. Young adult colorectal cancer clinic now available at Sunnybrook (Oct 11/16)

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

SCREENING

9. Blood test for colorectal cancer: the last resort? (Aug 31/16)

A new blood-based screening test may help increase the numbers of Americans in the target age group getting screened for colorectal cancer. The Epi proColon blood-based colorectal screening test gained approval from the US Food and Drug Administration (FDA) in April of 2016. The test screens the blood for the presence of methylated Septin 9 DNA, a biomarker (a measurable substance that indicates the presence of a disease, infection or environmental exposure) that is found in increased quantities in colorectal cancer. While the Epi proColon's advantages include its rapidity of testing, how easy it is to complete, and its non-invasiveness, the molecular test is less sensitive and less accurate than a routine colonoscopy in detecting the presence of cancer. To date, this new test has not been shown to reduce mortality from colon cancer. Many researchers believe, however, that any screening is better than no screening at all. According to the National Health Interview Survey data, overall annual screening use in the US is well below the target numbers with no improvements in screening rates from 2010 to 2013 for colorectal cancer. Emphasis must be placed on proper follow-up and discussion of the test results in order to determine the screening effectiveness of the test, not merely focusing on the fact that it is easy to employ. Researchers stress that this new blood test is not meant to replace any of the better tests that are currently available, and is recommended primarily for individuals that have declined other types of screening. Currently, colonoscopy has proven to be the best test to prevent cancer since it detects the presence of polyps – for every 1% increase in polyp detection, there is a 3% reduction in the incidence of colon cancer and 4% reduction in death. The new Epi proColon test merely detects the presence of cancer but will not detect precancerous polyps, highlighting its inferiority in cancer prevention compared to colonoscopy.

The Epi proColon currently has limited evidence that evaluates its use. The updated 2016 guidelines on cancer screening by the US Preventive Services Task Force (USPSTF) currently recommends seven different screening strategies (colonoscopy, fecal immunochemical testing (FIT) for occult blood, guaiac-based fecal occult blood testing, sigmoidoscopy alone, sigmoidoscopy plus FIT, the FIT-DNA test, and computed tomographic colonography). The Epi proColon blood test was not included in their

recommendations given the USPSTF's requirement for sensitivity levels about 90% or higher (the new test demonstrated a sensitivity to detect colorectal cancer under 50%). It is emphasized that the test is indicated for people at average risk for colorectal cancer, are 50 years or older and have been offered and have a history of not undergoing screening by the tests recommended by the USPSTF guidelines.

http://www.medscape.com/viewarticle/868226

10. Virtual colonoscopy gets top marks as cancer screening exam (Aug 30/16)

CT colonography, or "virtual colonoscopy" is a less invasive screening method than the conventional colonoscopy and can detect polyps as well as cancer and other diseases. Currently in the US, the federal government is obligating all private insurance companies to cover such virtual colonoscopies, while Medicare is yet to extend their coverage to the new screening method. According to Colon Cancer Alliance, a third of individuals who should be getting screened for colorectal cancer do not get a colonoscopy.

Image: http://www.fairview.org/healthlibrary/Article/40536

CT colonography could increase screening rates among such individuals and minimize cancer incidence. Given that colorectal cancer is almost always treatable when found early by screening, the cost involved in screening and prevention of the disease is exponentially less than to treat cancer found at more advanced stages. A recent study demonstrated that screening Medicare patients with CT colonography would cost 29% less than with traditional colonoscopy and save up to $1.7 billion per screening cycle. Virtual colonoscopy as a option for individuals covered under Medicare may be a choice that more individuals are more likely to choose, in particular, the elderly.

http://www.hendersondailynews.com/online_features/community_cares/virtual-colonoscopy-gets-top-marks-as-cancer-screening-exam/article_026719ff-c5e2-54bf-9f10-8bfae8c77108.html

11. Benefits of colon cancer screening decrease after age 75 (Sept 28/16)

For patients aged 70-74, screening for colorectal cancer with colonoscopy remains modestly effective at preventing the disease. Above this age group, however, the benefits appear to diminish as the risk of adverse events from the procedure increase. A prospective observational study followed over 1 million Medicare recipients between the ages of 70 and 79 with average colorectal cancer risk. Among individuals between the ages of 70-74, the 8-year risk of a colorectal cancer diagnosis was 2.19% among those who were screened with a colonoscopy compared to 2.62% among those who were not screened. Among individuals aged 75-79, the 8-year risk of a colorectal cancer diagnosis was 2.84% in those who were screened with a colonoscopy and 2.97% in those who were not screened. The 30-day risk for any adverse event (e.g. gastrointestinal bleeding, perforations and cardiovascular events) requiring hospitalization or an emergency room visit in the colonoscopy group was 5.6/1000 individuals aged 70-74, and doubled to 10.3/1000 individuals aged 75-79. Current screening guidelines from the US Preventive Services Task Force recommend routine screening for men and women between the ages of 50-75 using any method, including colonoscopy. Findings from the observational study confirm such guidelines, with individualized decisions for screening above the age of 75.

http://www.cancernetwork.com/screening/benefits-colon-cancer-screening-decrease-after-age-75

12. What does a positive Cologuard test mean? (Oct 03/16)

Cologuard is a commercially-available screening test for colorectal cancer that is convenient, non-invasive and easy for patients to access and complete at home. Unlike colonoscopy, there is no pre-procedure bowel preparation necessary and no special diet must be followed. The Cologuard test examines stools for certain DNA mutations and other abnormalities to determine if the test results are positive or negative. A study following 10,000 patients at average-risk of colon cancer had patients use the Cologuard test followed by colonoscopy as the gold-standard colorectal cancer screening test. Results form the study demonstrated that the Cologuard test had high sensitivity (92%) in detecting the presence of colorectal cancer, though was significantly less sensitive at detecting advanced adenomatous (pre-cancerous) polyps (42%). When an individual receives a positive result from their Cologuard test, they must then be screened with a

colonoscopy to examine the colon in more detail. A negative Cologuard test means than there is a less than 1% chance of having cancer found on colonoscopy. About 34% of individuals with negative test results will have precancerous polyps found via colonoscopy, while 66% of individuals with a negative result will also have a negative colonoscopy. Thus while Cologuard rarely will miss the presence of cancer, it is not ideal for detecting polyps and results in false positive results 45% of the time and false negatives 34% of the time. Healthcare professionals emphasize that while the test is indeed a good screening test, it is not a replacement for colonoscopy which remains the gold-standard for colorectal cancer screening. For individuals who decline screening via colonoscopy, Cologuard is a good test that may help improve population-based screening rates.

http://www.gastroendonews.com/Retroflexions/Article/09-16/What-does-a-positive-Cologuard-test-mean-/38052

OTHER

13. Not all tumour cells are equal (Aug 18/16)

Tumour heterogeneity refers to the diverse nature of human tumour cells in their ability to grow at an exponential rate in the patient, their ability to survive in diverse environments and adapt to changes including the administration of chemotherapy and radiotherapy. Such heterogeneity is believed to be the consequence of the existence of many different types of cancer cells contained within a single tumour. Furthermore, the epigenetic changes (changes in the activity of genes which control tumour activity) could also be heterogeneous. Within a single tumour, there are different regions which are each under distinct epigenetic control. Researchers have identified that the most epigenetically diverse region of the tumour is the invasive front, which is the part of the tumour that directly interacts with neighbouring normal tissues. Furthermore, it has been observed that the part of the tumour that is most reminiscent of metastatic cancer stages is in fact the oldest region of the tumour, indicating that the tumour's tendency to spread is a characteristic that may appear even in early stages of cancer development. Data has demonstrated that the more similar the regions of the tumour, the more aggressive the tumour is, suggesting that the cell population with the greatest proliferative capacity may have already been selected. Thus, measurements of the level of heterogeneity of tumours may be used as a predictor for the tumour's prognosis and the possibility to develop resistance to therapies.

https://www.sciencedaily.com/releases/2016/08/160818093317.htm

Anna Martínez-Cardús, Sebastian Moran, Eva Musulen, Cátia Moutinho, Jose L. Manzano, Eva Martinez-Balibrea, Montserrat Tierno, Elena Élez, Stefania Landolfi, Patricia Lorden, Carles Arribas, Fabian Müller, Christoph Bock, Josep Tabernero, Manel Esteller. Epigenetic Homogeneity Within Colorectal Tumors Predicts Shorter Relapse-free and Overall Survival Times for Patients With Loco-regional Cancer. Gastroenterology, 2016.

14. Tumour location relevant in metastatic colorectal cancer treatment (Sept 10/16)

Evidence from numerous clinical trials indicates that colorectal cancer originating in the right side of the colon manifests as a different disease than colorectal cancer that originates in the left side of the colon. This indicates that a different approach to treatment is necessary depending on the sidedness of the tumours. It is known that the right-sided colon originates from the mid gut and the left-sided colon originates from the hind gut, two distinct tissues in embryonic development. These distinct tissues result in different tumours with different behaviours and cellular make-up. Researchers have suggested that the sidedness of tumours may be a good predictor for targeted agents and possibly for chemotherapy. Right-sided tumours tend to have DNA mutations such as BRAF, PIK3CA kinase and KRAS mutations, as well as greater microsatellite instability (MSI), all of which lead to a poorer prognosis. Left-sided tumours tend to have more chromosomal mutations as well as increased expression of the HER pathway, resulting in amplification of EGFR receptor, HER1 and HER2 proteins. A retrospective analysis of the SWOG 80405 trial confirmed that left-sided and right-sided tumours had different responses to the same drugs. Survival outcomes in patients with KRAS wildtype metastatic colorectal cancer were significantly longer among those with left-sided tumours compared to right-sided tumours. Median overall survival by targeted therapy with cetuximab resulting in a 19.3-month difference between patients with left-sided tumours versus right sided tumours, with left-sidedness resulting in a significantly better prognosis.

Researchers also point to gender to explain differences at the molecular level among colorectal cancer cases. The difference in males between the right and left colon is 148 genes, while for women the difference is 2,371 genes. Researchers note that while the absolute number of genes is not what matters the most, it is the differential pathways that are activated via these genes that is implicated in colorectal cancer incidence.

Researchers emphasize the importance of considering sidedness of colorectal tumours alongside the typical markers such as age, stage and the typical markers RAS, BRAF and microsatellite instability (MSI). Further research is much needed to find better treatments for right-sided colorectal cancer given the poor results of any targeted therapy currently available.

http://journals.lww.com/oncologytimes/Fulltext/2016/09100/Tumor_Location_Relevant_in_Metastatic_Colorectal.14.aspx

15. Gene mutations that lead to more aggressive colorectal cancer in African American patients discovered (Sept 02/16)

Researchers have identified new gene mutations that are only found in colorectal cancers among African Americans. Such gene mutations are associated with tumours that are highly aggressive and more likely to recur and metastasize. The study is important given that colorectal cancers tend to be more aggressive in African Americans compared to Caucasians and other groups. Colorectal cancer rates have decreased by about 30% among Caucasian men while rates have increased by 28% among African American men since 1960. The study highlights the importance of genetic analysis as a tool in cancer prevention and treatment – colon cancer in African Americans is a distinct disease to be treated differently from colon cancer that occurs among Caucasians or other groups.

https://www.sciencedaily.com/releases/2016/09/160902161812.htm

NUTRITION/HEALTHY LIFESTYLE

16. Colon polyp risk reduced 33% by legumes (beans) and 40% by brown rice in the diet: Study (Aug 17/16)

A study found that eating legumes at least three times a week and brown rice at least once a week was linked to a reduction in colon polyps and risk for colorectal cancer. The study also found that eating cooked vegetables at least once a day reduced the risk of colon polyps by 2.4%, while consuming dried fruit three times a week reduced the risk of developing colon polyps by 26%. The fibre content of beans, brown rice and dried fruit is known to protect against potential carcinogens. The detoxifying compounds found in cruciferous vegetables such as broccoli and cabbage are known to be protective against colorectal cancer. Other dietary suggestions to prevent colon polyps include:

Eating foods that contain curcumin and quercetin: curcumin, a compound found in turmeric, as well as quercetin, a compound found in onions, are both shown to reduce polyp size.

Reducing fat intake, particularly from animal sources: studies have shown that diets high in animal fats increase the risk of intestinal polyps and colon cancer. A diet high in healthy fats from plant oils, nuts and fatty fish have been shown to prevent polyps and decrease the risk of colon cancer.

Getting enough vitamin D: adequate vitamin D intake has been shown to prevent polyps from developing. Sources of vitamin D include exposure to sunlight, eggs and fortified cereals and milk.

Maintain a healthy calcium-magnesium ratio: the pairing of calcium and magnesium has been shown to have a protective effect against polyps. Maintaining these minerals in a proportion of 2:1 calcium to magnesium is recommended for this protective effect.

Eating foods that contain sulphoraphane: sulphoraphane is a compound found in broccoli and other vegetables in the cruciferous family (i.e. cabbage, bok choy, brussel sprouts).

http://www.belmarrahealth.com/colon-polyp-risk-reduced-33-percent-legumes-beans-40-percent-brown-rice-diet-study/

17. Obesity more prevalent in cancer survivors (Aug 23/16)

Findings from a recent study reveal that obesity was more prevalent among individuals who had a history of cancer, specifically colorectal and breast cancers, compared to individuals with no history of cancer. Of the 32,447 cancer survivors followed in the study, breast, prostate and colorectal cancers were the most common. Results from the study analysis demonstrated the prevalence of obesity increased in cancer survivors from 22% to 32% from 1997 to 2014. The rate of obesity also increased among adults with a history of cancer from 21% to 29%. Study data found that the rates of obesity increased more rapidly among female cancer survivors versus male cancer survivors and women with no history of cancer. African Americans in general tended to be the most affected survivors of cancer. For female colorectal cancer survivors, the study found that young, non-Hispanic blacks within 2 to 9 years from initial diagnosis had the highest increasing rates of obesity. For male colorectal cancer survivors, the study revealed that the highest increase in obesity was among older, non-Hispanic blacks who were 10 or more years from initial diagnosis. Study results demonstrate that obesity is becoming an increasingly important public health burden among cancer survivors, and specific weight management interventions aimed to help cancer survivors are becoming increasingly necessary.

http://www.specialtypharmacytimes.com/news/obesity-more-prevalent-in-cancer-survivors

18. Antioxidant compounds, curcumin and silymarin, promising for colon cancer treatment: study (Aug 30/16)

Curcumin is a plant compound found in turmeric and is well known for its anti-inflammatory properties. Silymarin is a compound found in milk thistle and has been used to treat liver disease. Studies have shown

that the two compounds when used simultaneously produce an anti-cancer effect in colon cancer cells, promoting cell death and halting cell proliferation and metastasis. Curcumin's anti-cancer effects have been previously noted in breast cancer and prostate cancer research. Silymarin has been approved by the European Commission and the World Health Organization for use in a standardized concentration of 70-80% to treat toxic liver damage and as a complementary treatment in chronic inflammatory liver disease and hepatic cirrhosis. The anti-cancer effects of curcumin and silymarin provides a promising alternative approach to standard cancer treatment, which runs high risks of toxicity and adverse effects. Further research is needed to determine effective dosage and formulations of the compounds.

http://www.ctvnews.ca/health/antioxidant-compounds-curcumin-and-silymarin-promising-for-colon- cancer-treatment-study-1.3050006

19. Can Vitamin A fight colon cancer? Retinoic acid "dramatically reduces" tumour growth (Aug 31/16)

Vitamin A is an essential vitamin in promoting good eyesight and proper functioning of the immune system. A new study from the Stanford University School of Medicine demonstrates a connection between retinoic acid, a compound formed in the body from vitamin A, and the suppression of colorectal cancer incidence in mice and humans. Since the intestine is a major site of absorption of nutrients and molecules that we ingest through our food, it is constantly exposed to foreign organisms. The resulting immune functioning of the intestine is highly complex. Today, a clear link has been established between inflammatory bowel disease, ulcerative colitis, and the predisposition to developing colorectal cancer. Retinoic acid has a complex relationship with immune-related inflammation and gut microorganisms. It is difficult to study, however, due to is rapid degradation when exposed to light. This study demonstrated a role for retinoic acid deficiency in colorectal cancer, and researchers hope to expand this understanding by determining the specific microorganisms that may be responsible for such changes.

http://www.medicaldaily.com/can-vitamin-fight-colon-cancer-retinoic-acid-dramatically-reduces-tumor-growth-396687

Engleman E, Prestwood T, DeMaio M, Reticker-Flynn N, Kenkel J, Carmi Y, et al. Retinoic acid suppresses colorectal cancer development, Stanford study finds. Immunity. 2016.

20. "Healthy" sweeteners, protein-powerhouse quinoa and other nutrition myths, debunked (Sept 14/16)

Nutrition information and advice is constantly changing and it is often difficult to know what to believe. Five common nutrition myths are clarified below according to the cited article:

Processed meat causes cancer

The World Health Organization's report indicates that eating 50g of processed meat every day, or the equivalent of about one hot dog, increased the relative risk of colorectal cancer by 18%. While the average person has a 5% risk of developing the cancer, this risk increases to 6% if a person's diet is rich in processed meats. Indeed, processed meats should not be eaten in excess and red meat consumption should be limited to no more than 18 oz. per week.

Natural sweeteners are better than regular sugar

When it comes to sugar consumption, the quantity consumed overall is more important than the kind of sweetener consumed. While some sugars are indeed less refined and do not cause the same insulin spike as refined white sugar, the total amount of sugar consumed is still more important. Guidelines suggest no more than 6 teaspoons of added sugar for women and 9 teaspoons for men per day.

Sea salt is healthier than table salt

While sea salt does contain more trace minerals than regular table salt, these minerals are found in such small quantities that they have little impact on the body. The important fact is that sea salt contains the same amount of sodium as table salt, and it is precisely the amount of sodium that we consume that is important to monitor: excess of salt (more than 2,300 mg/day) can increase your risk of stroke, kidney disease and high blood pressure.

Quinoa is super-high in protein

While quinoa is one of the few plant-based foods to contain all nine essential amino acids (a "complete" protein), it is not a high protein food. While meat or poultry contains about 25g of protein per 3 oz. serving, quinoa contains 3g per 3 oz. serving. Quinoa contains 40g of carbohydrates per cup, thus it serves better as a grain than a protein.

Cleansing helps remove toxins from the body

Cleansing includes using juices, herbs and laxatives to help the body remove toxins, boost energy and stimulate weight loss. The skin, intestines, liver and kidneys, however, naturally detox the body through the

production of sweat, urine and feces. To facilitate the natural detox of the body, a diet high in fiber, lots of pure water and exercise, as well as eliminating cigarettes, alcohol and processed foods can do the trick.

http://www.theoaklandpress.com/health/20160914/healthy-sweeteners-protein-powerhouse-quinoa-and-other-nutrition-myths-debunked