

A Study of Colorectal Cancer

Author: Michael Dooley

Major: Mechanical Engineering

Department of Microbiology and Molecular Genetics, Oklahoma State University, Stillwater, OK 74078, USA

Key Words:

Autophagy, Colorectal, Cancer

Colorectal cancer is a major cancer of the world, it accounts for nearly 10% of all cancers worldwide and affects predominantly the more highly developed western world. This cancer does not only have a high incidence rate but also has a high mortality rate. Risk factors vary by age, lifestyle, and family history. These risks can be mitigated by simple and effective lifestyle changes and screenings of high-risk populations, such as patients who have a family history of colorectal cancer. Early detection through preventive screening remains the best method to increase patient prognosis, with colonoscopy being the gold standard of detection methods. These screening methods have proven to be highly effective, but unfortunately have not made as meaningful changes in incidence rates or mortality rates. Many methods have been developed to treat colorectal cancer and more are being developed every year to fight this cancer. One new method is the use of the autophagy to help the auto immune system detect and kill cancer cells. Many problems exist in the fight of this cancer, those being the lack of awareness of the public, low screening rates, cost of care, and the cost of quality of life for the patient.

Introduction

Colorectal cancer is a major contributor to cancer in the world, it makes up for 10% of all new cancer diagnoses (1). Most cases of colorectal cancer are sporadic and have no family history of the disease. Patients with family history of colorectal cancer, in particular first-degree relatives have twice the incidence rate (2). Preventive screenings of colorectal cancer are possible and have lowered the mortality rate of colorectal cancer due to early detection. Risk factors such as age and lifestyle play a large part in the outcome of this cancer. Surgery in combination with chemotherapy and radiation therapy have been the primary treatments of this cancer and have better outcomes with earlier detection of this cancer. Though this disease is preventable and treatable, it remains one of the most widely spread cancers in the world. This paper will strive to address the risk factors, screening options, treatments, and the challenges of management/prevention of the disease.

Recent Progress

Colorectal cancer is a complex cancer with many underlying causes. In many cases colorectal cancer, the overexpression of epidermal growth factor (EGFR). EGFR makes up 80% of all cases of this cancer. Making the use of monoclonal antibodies to block this receptor and inhibits cell growth (1). This is one of many emerging immunotherapies that can help fight most colorectal cancers. Another method that is being developed is the use of autophagy to help the immune system better identify and fight cancer

cells growth. It does this by eliminating damaged organelles in cancer cells (3). Autophagy also shields the cells from inflammation preventing genome damage and transformation in a malignant cancer cell. Most progress in the treatment of colorectal cancer has been made in prevention of it. Another pathway that could be useful in fighting colorectal cancer would be the use of organellophagy. This method would selectively remove high energy mitochondria and thus degrade the cells energy until the cell stops cellular growth (3). The improvement of colonoscopies by use of high-resolution video chips. The current standard is a high-definition white light endoscopy (HWLE)(1). This coupled with the Third Eye Retro scope have made it possible to find lesions behind mucosal folds. The CT colonography uses a low-dose CT scanner to obtain images of the colon. CT colonography has also been shown to have a 96% success rate at detecting colorectal cancer (1). The improvement of colonoscopy is only one way that the screening methods have been improved, other methods such as the capsule endoscopy have opened the medical field to new ways to conduct routine screenings of the colon. These pill size cameras use wireless receivers to obtain images of the colon as it moves through the intestinal track. 2nd generation capsules have 88% success rate at finding adenomas (1). These methods become very important to have, because they help to reduce the overall price of having this disease, making it a cost saving exercise in many places. (1). Inflammation also has been shown to have a affect in the incidence rates of colorectal cancer. The observed decrease in the incidence rate of colorectal cancer may also be attributed to improvements in anti-inflammatory drugs. Treatment methods and preventative screenings have lowered the mortality rate of colorectal cancer, but it remains high at 40-50%

Discussion

These improvements in screening and treatments have reduced the mortality rate of colorectal cancer but these methods still have many problems. Screening is the best method to prevent colorectal cancer but without a population that is routinely screened and recorded, it will never become the cure for colorectal cancer. Many patients have no idea that they need to have screenings, and this is not just a lack of information from the medical industry, though that could also be improved, but patients have no idea about the medical history of their own families. These patients have no access to family medical records and thus live ignorant of if they may need a screening. It is estimated that 10% of the US population has a first-degree family member that has been diagnosed with colorectal cancer. This implication increases the risk factor of that family member twice (2). If the family member is a second-degree family member, then this risk factor is 75% higher than families that have no family history of colorectal cancer (2). These risks are even higher if that family member was under the age of 50 years, increasing the risk factor by 2 to 3 times (2). By finding ways to better report and inform families of their possible risk of colorectal cancer we can make large improvements in mortality rates for this disease. Preventive screenings are the best method to fight colorectal cancer but have their problems when it comes to how to best administer and keep information. Treatments have come a very long way to improving outcomes for many patients but still have their fair share of problems. Many of these treatments have major consequences for the quality of life for patients. Chemotherapies and radiotherapy can impair food consumption and physical activity (1). They also can cause other side effects such as anemia, abdominal pain, and weight loss. These side effects are what fuel the medical field to find better and more precise methods. This question of how-to better fight cancer is very complex because the situation for every cancer is practically unique and requires varying methods to treat it. The pathways and specific mutations require individualized treatments, but if we can better understand the pathways the cancer uses, we could use these pathways to find an Achilles heel as to say in fighting these cancers. This could also help to prevent patients from having as many severe side effects as possible and make better outcomes for long survival rates. This is why methods such as the use of autophagy, that drains the energy of fast-growing tumor cells, is a possible major advantage in the fight against colorectal cancer. It uses methods that already exist in the human

immune system to identify and hinder growth of malicious cells. The future of colorectal cancer treatment should be focused on minimizing the need for surgery. By doing this we can improve outcomes for patients and reduce surgical trauma (1). Improvements in our understanding of colorectal pathways will also help to better give us tools in the future to treat this disease. This is not to take away from the desperate need to increase and improve the field of medical screenings for at risk populations. Simply by taking the fight to colorectal cancer as soon as possible with early detection we can drastically decrease the mortality rate of patients and increase long term survival rates. Questions left unanswered are simply are we really experiencing a downward trend of colorectal cancer or perhaps are we having a false positive because of the improvement in anti-inflammatory medicine, which have shown to decrease the incidence rates of colorectal cancers. Also, with advances in medical technology we can finally overcome the stigma of the cost of cancer treatment so individuals can afford to have their medical screenings done in a timely and cost-effective manner. The cost of medical treatments prevents many patients from ever attempting to prevent their cancer through screenings and prevents them from seeking lifesaving procedures. These hurdles will continue to affect the mortality rate of patients of colorectal cancer.

References:

- 1.) Kuipers, Grady, W., Lieberman, D., Seufferlein, T., Sung, J. J., Boelens, P., de Velde, C., & Watanabe, T. (2015) Colorectal cancer. *Nature Reviews. Disease Primers*, 1(1), 15065–15065. <https://doi.org/10.1038/nrdp.2015.65>
- 2.) Lowery, Ahnen, D. J., Schroy, P. C., Hampel, H., Baxter, N., Boland, C. R., Burt, R. W., Butterly, L., Doerr, M., Doroshenk, M., Feero, W. G., Henrikson, N., Ladabaum, U., Lieberman, D., McFarland, E. G., Peterson, S. K., Raymond, M., Samadder, N. J., Syngal, S., ... Smith, R. (2016). Understanding the contribution of family history to colorectal cancer risk and its clinical implications: A state-of-the-science review. *Cancer*, 122(17), 2633–2645. <https://doi-org.argo.library.okstate.edu/10.1002/cncr.30080>
- 3.) Mokarram, Albokashy, M., Zarghooni, M., Moosavi, M. A., Sepehri, Z., Chen, Q. M., Hudecki, A., Sargazi, A., Alizadeh, J., Moghadam, A. R., Hashemi, M., Movassagh, H., Klonisch, T., Owji, A. A., Łos, M. J., & Ghavami, S. (2017). New frontiers in the treatment of colorectal cancer: Autophagy and the unfolded protein response as promising targets. *Autophagy*, 13(5), 781–819. <https://doi-org.argo.library.okstate.edu/10.1080/15548627.2017.1290751>