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47 Years of Research, Education, Advocacy, & Support
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Do You Have CF? A Colonoscopy Can Save Your Life

By Anna Payne

Last year, at the age of 34, I was living in a place of hope. I was thriving on Trikafta, working full time, serving as elected Supervisor for Middletown Township in Bucks County, Pennsylvania, and acting as Vice-Chair of the Pennsylvania Rare Disease Advisory Council. For the first time in a long time, I had hope for a future of a "healthy" life. I had big dreams and a lot of things I wanted to accomplish. But then I found a mass in my groin, and after a long, painful and circuitous diagnostic journey that included numerous invasive tests and long waits between them, I received the news no one wants to hear. "You have Stage 4 colon cancer."

Anna Payne

Known as the "silent cancer," colorectal cancer remains the third leading cause of cancer-related deaths in the U.S. among the general population. Those with cystic fibrosis have a significantly higher risk of colon cancer than the general population. For those with CF who have not had a transplant, their risk is five to ten times higher, while individuals with CF post-lung transplant have twenty times the risk as the general population.

What makes us especially vulnerable is that colon cancer symptoms can and often do mimic issues that we CF survivors experience daily. More research is needed to determine exactly why we're at such elevated risk for the disease, but it's believed to be linked to a mutation in the cystic fibrosis transmembrane conductance regulator (CFTR) gene.

The most effective tool for preventing this silent disease is a colonoscopy. Colon cancer always starts in the form of polyps, which, if found early, can be removed prior to becoming malignant. Colonoscopies are recommended for the general population at 45, yet despite our highly elevated risk, the current recommendation for a first screening colonoscopy for a person with CF is 40. That's too late and must change. Screenings can prevent about 60 percent of colorectal cancer deaths.

I was 34 years old when diagnosed; I had few symptoms and no known family history. Colon cancer grows slowly, and it's possible it's been in me for years. I initially sensed

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Identifying Biomaterials that Enable the Transplantation of Gene Corrected Airway Stem Cells to Treat Cystic Fibrosis

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Although many cystic fibrosis (CF) patients have benefitted from recently developed drugs (modulators), approximately 10% of patients still need a therapeutic option. The ideal therapy for CF is a gene therapy that corrects CF-causing mutations in their airway stem cells and generates a durable layer of corrected airway

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me to work remotely — as much as I'm able. My wonderful colleagues have carried the load in my absence. I miss them. I've even come to miss the 45-minute commute to my office with a stop to get a hot tea at Dunkin'.

Simple joys like eating — which most of us take for granted — are now a chore. I eat for calories, not pleasure. My diet changed drastically, and I no longer enjoy foods I'd grown up eating, such as macaroni and cheese and steak. If you looked in my cabinets now, you'd mainly find massive amounts of Fruit Loops and Apple Jacks.

I was shocked when my platinum blonde hair – with blue streaks – fell out in clumps. Losing hair is traumatic – it's about body image, one's sense of self, and feeling normal. Many have told me not to worry, that it will grow back, but I have no idea how long I will be on chemo, and whether that is true. While I have multiple wigs that allow me to feel like a different superstar each day, and a wide array of knitted hats, I often scrap these so I can emulate my idol, the Rock.

As a little girl, I spent a lot of time inpatient at St. Christopher's Hospital for Children in Philadelphia. Watching the Rock on the weekly Smackdown was a great escape. Amazingly, the Rock learned about my diagnosis and sent me a heartfelt video wishing me luck in my fight. It's been viewed millions of times on his Instagram page, and has allowed me to feel less isolated, with a virtual connection to countless people who channel their positivity toward me.

Prior to my diagnosis with colon cancer, I planned to travel across the globe. I wanted to hold a koala bear in Australia and visit Costa Rica. I planned to run for higher elected office. I had hopes and dreams that have been put on pause. I live in a world of uncertainty. Once again, I am learning to be comfortable living in the uncomfortable.

As science improves and evolves, so should our thinking. Cancer screenings must become a normal routine for cystic fibrosis adults, and the sooner the better. My hope is that the recommended age for a first colonoscopy will be lowered to 25 years for those with CF.

But you don't have to wait for that to happen. If you have symptoms, don't write them off as the usual CF GI issues. Go and get screened. You may end up saving your own life.

Symptoms of Colon Cancer Mimic CF-Related GI Issues

- A change in bowel habits (diarrhea, constipation) lasting for more than a few days;
- Cramping or abdominal (belly) pain;
- Bloating or full feeling;
- The feeling that you need to have a bowel movement that is not relieved by having one;
- Rectal bleeding with bright red blood;
- Blood in the stool;
- Weakness and fatigue

Identifying Biomaterials to Treat Cystic Fibrosis

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cells. Past gene therapy trials that attempted to deliver the CF gene into the lungs failed due to several technical challenges related to gene delivery. Hence, we are working to develop methods to correct airway stem cells outside the body followed by their transplantation into the sinuses and the bronchi of CF patients.

In working towards this aim, we first optimized gene editing using Cas9 to achieve 30-60% correction of the F508del in CF patient samples and restore 30-60% CFTR function. We have further improved on this system to insert the full coding sequence of CFTR in airway stem cells and restore CFTR function to levels seen in non-CF patients. Further clinical translation of this approach requires the transplantation of gene corrected airway stem cells. Cell transplantation into the lower airways has never been done in humans, and can be potentially life-threatening. Recognizing this, our aim is to first validate the use of this gene corrected airway stem cell therapy for treating CF sinus disease.

Transplantation of airway cells requires an injury to make space for the transplanted cells and a biomaterial to hold the cells in place after delivery into the sinus. In this project, we first screened several biomaterials for their ability to support the proliferation of airway basal stem cells. Among the materials tested, fibrinogen (a human protein involved in blood clot formation) best supported the growth of airway basal cells. Significantly, fibrinogen is already used in the clinic as a surgical glue, further facilitating clinical translation. Ongoing studies are testing the ability of fibrinogen scaffolds to facilitate airway basal stem cell transplantation into the sinuses.

Collaborative studies with Dr. Jayakar Nayak's lab helped us identify multiple injuries including clinically applicable mechanical injuries that facilitate the transplantation of airway basal stem cells into the sinuses of immunocompromised mouse models. Preliminary results indicate that both mouse and human basal stem cells can survive in the sinuses of mice for >4 months when transplanted using fibrinogen.

Ongoing studies are evaluating the ability of the transplanted cells to form a functional sinus epithelium. Upon the successful completion of these studies, we will approach the FDA to discuss our plans for the further clinical translation of this approach to treat CF sinus disease. The results from this clinical trial will inform future efforts to treat CF lung disease using gene corrected airway stem cells.

We are grateful to the Cystic Fibrosis Research Institute for its support of this research.