HEALING ARTS

A Lesson in Participatory Research for a Rare Mutation of Cystic Fibrosis

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When I handed in my final biology exam in ninth grade, I thought I was leaving my biology education behind me—forever. In fact, I did, for 17 years—through the rest of high school, then college and graduate school.

My college and graduate education focused on communication theories of information dissemination and philosophical frameworks for moral behavior. Words were my currency. As far as I was concerned, cells lived in Excel documents, protein in my food.

While I may have banished biology from my thoughts, I could not escape its effects on my body. Indeed, my preferences for communication and philosophy could not protect me from my insidious biological flaws; over these same years, cystic fibrosis was ravaging my body with its relentless progression.

On January 31, 2012, biology came crashing back into my life. It was the day the FDA approved the breakthrough drug Ivacaftor, at once giving rise to unprecedented hope for the cystic fibrosis (CF) community and also, ironically, shattering our solidarity. The first-ever drug to treat the root cause of CF and not just the symptoms, ivacaftor was approved only for a small subset of CF patients with a particular genetic mutation. The rest of us were left in the shadows.

This was my introduction to personalized medicine, my re-introduction to ninth grade biology, and brought the blunt realization that the power to change my genetic destiny just might lie in my own two hands. It was terrifying on the one hand, wholly empowering on the other.

I dove back into biology, quickly learning that with over 1,900 mutations and countless numbers of heterozygotes, we were less a uniform population and more like a kingdom of cystic fibrosis trans-membrane conductance regulator (CFTR) mutants unified under the CF umbrella, each with our own variation of this crazy, complex disease.

Still, nearly 90 % shared at least one copy—and 50 %, two copies—of the most common CF mutation, Delta F508. This common thread made Delta F508 the logical next focus on the quest to extend the proof of concept established by ivacaftor to everyone with CF.

It turns out that even within the CFTR mutant kingdom, I am a rare breed. With two copies of a relatively rare w1282× mutation, the so-called "Ashkenazi Jewish mutation," my genetic composition places me in territory so uncharted, at least in the US, that there are no published statistics to indicate the size of my micro-community. I am a rarity among the rare, an orphan of an orphan disease.

At times, it can feel a bit lonely and bleak in this corner of the kingdom. But rather than become demoralized, I decided to take action.

The FDA approval of Ivacaftor came at a fortuitous time. A month earlier, my family, friends, and I had launched "Emily's Entourage," a nonprofit organization that raises funds and awareness to help find a cure for CF. Our motivation stemmed from the realization that I was teetering on the verge of end-stage CF, where the only option is lung transplant, and even that brings a whole new set of complications and short survival rates. My situation was dire.

The approval of Ivacaftor infused our efforts with a new degree of intensity and laser-like focus on our mission: to accelerate research and bring attention to those who would not benefit from the promising research in the pipeline—the forgotten CF orphans.

Just like that, Emily's Entourage assumed a brand-new role in the clinical research ecosystem. No longer willing to merely raise funds and spread awareness as foundations had long done, we were demanding our place at the research agenda-setting table.

Unbeknownst to us, we were ushering in a new model for conducting clinical research: participatory research, in which patients and foundations become active drivers of the research agenda, fostering a collaborative approach to clinical research and emerging as citizen and foundation scientists.

Initially reluctant to enter the business of vetting and driving research, we soon realized that the research agenda often gets set by factors like funding availability and scientific serendipity, whereby inklings of interest set researchers on sometimes wandering paths of scientific inquiry that lead to further interest, study, and then eventually expertise in a particular subject matter.

If we wanted more research on my rare mutation and other CF orphan mutations, it was up to us to get it. After

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all, nobody had a bigger vested interest in advancing this line of research than we did, and the reality was—and remains—that I did not have time to wait for research to unfold on the normal time line. The onus was on us to accelerate research and to act fast.

Armed with this sense of urgency and obligation, we set off. Our goals were threefold: to raise as much money as possible; to engage leading researchers with demonstrated interest, expertise, and capability in this area; and to funnel Emily's Entourage funds towards rapidly advancing research on the CF orphan mutations.

In just two and a half years, we have come a long way. We are fast approaching the million-dollar mark in dollars raised and have assembled a committed scientific advisory board of highly respected researchers, clinicians, and health industry leaders.

Perhaps the best evidence of our success thus far is that we just selected our first Emily's Entourage grant recipient, a leading researcher at a top-notch academic institution. The research project involves testing thousands of small-molecule compounds on a wild-type cell line genetically modified to express my CF mutation. To think that sentence came from my own biology-ungifted mind is, well, just mind-boggling. It's been a steep learning curve, to say the least.

We have learned that research funding is not the only barrier between CF orphans and their respective breakthroughs. That's why Emily's Entourage is also assembling the first-of-its-kind conference focused on w1282×, with the potential to generalize to other nonsense mutations. In fact, we believe that bringing together the best and brightest in this area to facilitate brainstorming, dialogue, and collaboration may indeed be our most important role.

This is participatory research at its finest. Participatory research is an extension of participatory medicine, a well-established healthcare model that encourages active involvement and partnership amongst all stakeholders, including patients and clinicians, in every aspect of health management. The model effectively empowers patients to expand their advocacy and participation to the research arena as well, which has the specific potential to transform the study of rare diseases.

In fact, this may be the perfect time for this new model of participatory research to thrive. With healthcare's shift towards consumerism and the growing focus on patient engagement encouraged by the Affordable Care Act, the national appetite for patient empowerment and activation is stronger than ever. As medicine becomes increasingly personalized, tailored to individual genomic and molecular characteristics, groups of people with diseases previously united under umbrella terms like cystic fibrosis will continue to undergo the same fragmentation that the CF community has at the therapeutic level. Rareness may become the rule, not the exception.

In this new world of personalized medicine, individuals with rare diseases can play influential roles as citizen and foundation scientists and research drivers. Emily's Entourage has gotten a head start.

On a personal level, I feel grateful to be surrounded by such a fearless, pioneering group of supporters and believers. For the first time in my life, hope feels tangible. There are no words to describe how motivating or empowering that is for me.

At the same time, I am keenly aware that not everyone has the opportunity to actively participate in this new research paradigm. It is critical to acknowledge that with participatory research's promise comes risk, particularly around widening already-rampant disparities in healthcare and research. We realize that we cannot resolve what is at its core a fundamental flaw of our country's health system, but Emily's Entourage has pledged not to rest until everyone with CF gets his or her lifesaver.

So while biology was not my subject of choice in ninth grade, it has become my subject of necessity. In fact, the ability of the human mind, body, and spirit to adapt and shift gears when faced with adversity has become a hallmark of my disease experience. Indeed, if there is one thing I have learned on this journey, it is that bemoaning the things you cannot control is a waste of time and energy. You get a lot farther and feel a lot better when you focus your energy on things you can change.

Emily's Entourage has allowed me to place my rare mutation on the research radar. It has given me a voice and a way to channel negative emotions into a productive outlet, to transform what could be crippling fear, sadness, and distress about the future into something infinitely bigger and more powerful—hope.

Hope for more tools to fight this disease, for fewer hospital stays and more healthy days, for a deep breath, for a future for the whole CFTR mutant kingdom.

Disclaimer: *Ms. Kramer-Golinkoff is co-founder of Emily's Entourage, a 501(c)(3) nonprofit organization funded through private donations; she is also related to a member of the JGIM editorial team. That individual played no part in the evaluation of this manuscript. The opinions and conclusions of this article do not represent the views of AHRQ and no statement in this report should be construed as an official position or endorsement by AHRQ or of the U.S. Department of Health and Human Services.*

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