

PEOPLE & IDEAS

Jerry Edward Chipuk: A powerhouse for mitochondrial biology

Marie Anne O'Donnell  and Nicole Inforinato

Chipuk studies the interaction between mitochondrial dynamics and cell death in cancer.

Upon graduating high school, Jerry Chipuk says, “I was unsure about college, but thought the arts would be in my future.” However, Chipuk took a tentative step toward the laboratory and an appreciation that “academic research is the art of science” by studying biology at Baldwin-Wallace College, Berea, OH. Although he enjoyed several summer research experiences and received the prize for “most promising biology student,” he was again uncertain what to do next. While deciding, he worked as a research assistant studying animal models of cystic fibrosis with the physician scientist Pamela B. Davis at Case Western Reserve University, Cleveland, OH. Chipuk describes Davis as “a powerhouse in both the laboratory and clinic, and I appreciated every moment of time in her department. I believe being in her laboratory solidified that research would be my next step.” Chipuk completed graduate courses in the department of pharmacology while working full-time, which further motivated him to apply to graduate school.

Chipuk became the first graduate student to join David Danielpour's laboratory, where he studied prostate cancer. As a new investigator, Danielpour could spend time providing Chipuk mentorship and support, and focusing his research efforts in the laboratory. Although being a new investigator's first graduate trainee can be risky, Chipuk describes his experience as very positive and he graduated quickly with three papers in the *Journal of Biological Chemistry* under his belt that explored signal transduction and apoptosis.

During his graduate research, Chipuk presented his first apoptosis-related poster at a Keystone Cell Death conference, organized by Douglas R. Green. Because Chipuk never wears his glasses, he had a front row seat near Green when he opened the conference with his usual enthusiasm and

charisma. Green's opening remarks were so captivating that Chipuk says, “It was love at first sight. I enjoyed everything about Doug: I already knew about his work, but I enjoyed witnessing his energy, wit, and positive nature. Without obtaining permission, I invited him to give the annual graduate student-hosted seminar. He accepted, and I asked him for a postdoctoral position while driving him to the Cleveland airport. I didn't waste any time. I joined his laboratory a few months later.”

In Green's laboratory, Chipuk investigated how tumor suppressor pathways, BCL-2 proteins, and mitochondrial biology affect cell death, producing nearly 20 papers. Chipuk describes this time as transformative in his development as a scientist and scholar, and it continues to inform how he runs his own research group today. Now at the Icahn School of Medicine at Mount Sinai, Chipuk recounts some of the key experiences that shaped his professional development and outlook on science and life.

Where did you grow up?

I grew up in Cleveland, OH, with immigrant parents and no siblings. Everyone that knows me understands why one child was enough—I'm a passionate, emotional, openly opinionated, and gregarious individual. No one in my family has a formal education, and my parents had no understanding of the educational system in the United States. That said, my family instilled a strong work ethic and persistence that enabled me to understand the need for dedication and focus, this originated in the garden and kitchen to produce outstanding meals.

When did your interest in science begin?

I cannot recall a specific moment that my interest in science started, but I was curious about the natural world and biology from an

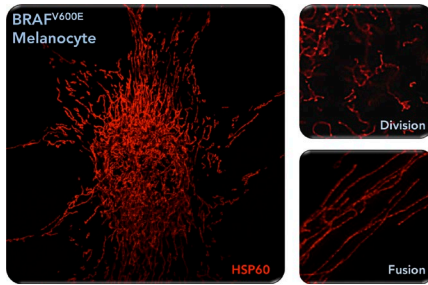


Jerry Edward Chipuk. PHOTO COURTESY OF CATHY CLARKE.

early age. I never had much interest in cartoons, television shows, toys, video games, etc. I was focused on the real components of the world. My first experiment was to determine how different surfaces affected the crystallization of salt solutions. I think I was around 10 years old and conducted the work in my grandmother's basement for a science fair.

What sustains your interest in mitochondria?

My laboratory has numerous research programs capturing the general cell biology principles behind human diseases including melanoma. I was initially intrigued by the mitochondrial biology literature because of its breadth and impact in disease. Mitochondrial biology includes proteins, lipids, membranes, DNA, dynamics, signaling, and metabolism. Despite being a mature field, the experimental results maintain impact and the applications to human disease are more relevant than ever. Finally, I've always been drawn to science because of the power of visual observation, and a lot of information can be gained by imaging the mitochondrial network—these organelles are beautiful!



Melanocytes harboring oncogenes can reside in the skin for decades before eventually escaping cellular senescence to promote melanoma. The Chipuk laboratory is interested in understanding how mitochondrial shape changes may contribute to the escape and transformation processes. Here, a human melanocyte induced to undergo senescence with BRAF^{V600E} was stained for HSP60 (red) to visualize mitochondria. IMAGES COURTESY OF JOSHUA KAMINETSKY, CHIPUK LABORATORY.

What are you currently working on and what do you envisage for the future?

My group focuses on the role of mitochondria in human health and disease. We study fundamental mechanisms related to mitochondrial biology, cellular homeostasis, apoptosis, cellular transformation, and cancer therapeutics (1–5). The laboratory is quite diverse in terms of expertise, as we use biochemistry, biophysics, cell biology, molecular biology, structural biology, and a considerable amount of imaging, metabolism, and assay development. For the upcoming years, we will likely stay on this path, as we have many projects moving forward in these fields.

In terms of professional development, I've recently been appointed an associate director of the Tisch Cancer Institute at the Icahn School of Medicine. It has been an interesting yet daunting experience, because I had little knowledge of how a National Cancer Institute-designated cancer center is organized or funded. The best aspect is working with senior investigators to learn the organization quickly; the worst part is the insecurity of knowing that I don't have all the experience related to the position. I just needed to quickly learn and do, and for the most part, it's been pretty successful.

What kind of approach do you bring to your work?

My approach is to complete goals one at a time, and not distract myself by worrying about the lists of items to complete. In my eyes, there really is no other way as stressing about what's not done doesn't make the work any easier or faster. I also work on my personal schedule, not everyone else's. That

way, I can enjoy my life while accomplishing my goals. For example, I can write anywhere in the world, I don't need to be in my office. Also, I never think about my successes or failures for an extended time; my favorite quote is from John Cage, "We need not destroy the past. It is already gone."

What did you learn during your training that prepared you for being a group leader?

I learned to not let others' successes and failures distract me from my goals and interests. There's plenty to obtain in the world, and sharing the rewards is the best approach to mutual happiness. However, I didn't realize that people in my laboratory would come to me for advice on topics unrelated to science. This isn't a negative, I just didn't recognize how leading a group of people involved so much nonscientific support.

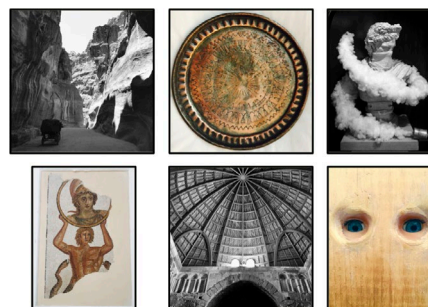
What has been the biggest challenge in your career so far?

Learning to accept that I cannot do everything that is asked, desired, or offered. At present, I am comfortable declining opportunities because I prefer to do a limited list of items with high quality, and not many things with poor quality or in a stressed manner. I've also learned to better value my time and input; it can take a while to convince yourself of your worth.

"Work on goals ahead of time and not at the deadline."

What is the best advice you have been given?

Work on goals (such as grants, papers, lectures, and presentations) ahead of time and not at the deadline. Do the least favorite things first and never waste time complaining because no one genuinely cares and everyone else is busy too.



A few examples of the art Chipuk has collected while traveling the globe. Photos courtesy of Jerry Chipuk.

What do you enjoy doing outside of the laboratory?

I have a broad spectrum of interests ranging from the arts to food, physical fitness, and travel. If I had to pick one that motivates me most, it would be travel. My favorite destinations are Israel, Iran, Palestine, Jordan, and Tunisia. I selected these countries because of the social, political, and cultural contrasts that define each experience. The architecture, food, music, arts, and people are beautiful and taught me a great deal about the differences and similarities between all cultures. Travel also provides the opportunity to think about science and my personal life in a different manner from being at home. I enjoy searching for the authentic around the world, and sharing it with others. Travel allows me to bring food and music from different cultures to my home but photography and collecting art from around the globe are my favorite pastimes. I am preparing a personal collection for when I am old and cannot physically explore the world. Political art seems to capture a higher interest for me, more than a simple beautiful piece.

Any tips for a successful research career?

I suggest finding something positive or enjoyable in everything that must be accomplished as an academic scientist. Accept how our products must be scrutinized and evaluated as the results will not always be positive. When grants don't get funded, think about being the reviewer; when papers don't go for review, think about the editor's position; when people in the laboratory do not meet expectations, remember when you may have not lived up to your best. Learn from every experience and, with an unbiased eye, evaluate your product in order to generate the best work. Also, mentor scientists within your own laboratory whom you enjoy seeing on a daily basis and are comfortable with representing your group. Finally, I think of academic science as a small business; I'm in charge of the product design, staffing, execution, production, advertising, and recruitment of capital for future products.

1. Chipuk, J.E., et al. 2012. *Cell*. 148:988–1000.
2. Serasinghe, M.N., et al. 2015. *Mol. Cell*. 57:521–536.
3. Renault, T.T., et al. 2015. *Mol. Cell*. 57:69–82.
4. Mendoza, A., et al. 2017. *Nature*. 546:158–161.
5. Serasinghe, M.N., et al. 2018. *Cell Death Dis*. 9:29.