Cancer is a frightening disease. Creating evocative experiences and artwork around the science of cancer can be a challenge. How do you encourage people to engage with a disease that is so scary, a disease that has likely touched their lives and perhaps even stolen their loved ones? At Arizona State University, we have created a new and different kind of artwork/experience to communicate the science of cancer: a garden composed of plants both beautiful and monstrous, whose sculptural aesthetics derive from mutations during growth and development.

**Endless Forms Most Beautiful** illustrates two important aspects of the science of cancer: First, the ubiquity of cancer-like processes across all forms of life, and second, the promise of new therapies that aim for long-term control of cancer.

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**Endless Forms Most Beautiful** is a crested cactus garden that embodies both an aesthetic and a medically transformative approach to cancer. The cacti in this garden have mutations in their meristem cells causing uncontrolled growths—which are, by some definitions, cancer. The garden was installed near the new Biodesign Institute C building on the Arizona State University campus in Tempe. Crested cacti and other fasciated plants are examples of organisms that live with cancer but do not die from it. These plants help to widen the framework for thinking about what cancer is and how to live with it and, ultimately, inspired a new center, the Arizona Cancer Evolution (ACE) Center, which investigates cancer across forms of life.

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Athena Aktipis first encountered these striking plants (see Fig. 1) during a visit to Arizona almost 10 years ago. Their
elegance and grace despite their apparent deformity has a certain poetic beauty, and their ability to survive even with these cancer-like forms was inspiring. Aktipis's obsession with these plants began at that point, and it was partly her aesthetic interest in them that led her to broader questions: Are these mutated forms cancer? What does cancer look like across life, from coral to cacti?

Part of being a multicellular organism means having cells that divide and can mutate during a lifetime. The cacti in Endless Forms Most Beautiful have mutations in their meristem cells causing uncontrollable growths—which are, by some definitions, cancer. The mutations cause distinctive growths, sculptural in form, and these abnormal specimens are prized as beautiful and rare [1]. They are called crested or "fasciated" plants, fascination being the more general term for plants with mutations in their growth tips that cause these unusual forms.

After moving to Arizona, Aktipis and Carlo Maley worked with Caspian Robertson, director of the landscape design company Caspian Gardens, to create a series of drawings that would eventually end up as the final design for the garden.

Robertson had this to say about the experience:

I was delighted to have been asked to contribute to this fascinating project and have been amazed by the personal enthusiasm and care that those involved have given to it. The great thing about gardens as a medium is that they are ever adapting over time; just as the caricature of the project evolves, so too does the planting! This seems all the more poignant when designing on the theme of change being a natural and beautiful process, and it is my hope that this space will continue to transform and provoke thought for many years to come [2].

The questions about cancer across life, seeded partly by these crested cacti and their beauty, have grown into a large research program, which is now a significant part of the Arizona Cancer Evolution Center. The Arizona Cancer Evolution Center (ACE) is studying cancer across life in sponges, bats, whales, elephants and many other species.

The name of the garden, "Endless forms most beautiful," is based on the end of Darwin's first 1859 edition of On the Origin of Species, where he writes: "There is grandeur in this view of life . . . from so simple a beginning endless forms most beautiful and most wonderful have been, and are being, evolved" [3].

The idea for this garden was to represent two critical aspects of cancer:

1. Susceptibility to cancer is a fundamental part of all multicellular life, across the tree of life [4].
2. It is possible to live with cancer and cancer-like growths [5], as many of these cacti do.

Plants are radically different from animals and yet, as multicellular organisms, they too are susceptible to cancer-like phenomena. Plant tumors are characterized by both abnormal proliferation and large cell size, suggesting that not only are these cells dividing when they are not supposed to, they are also acquiring more resources than is their due. Some researchers have argued that plants are particularly resistant to cancer because their cells do not migrate through their bodies and are fixed in place with rigid cell walls, preventing cancerous cells from invading neighboring tissue and metastasizing to distant sites. In fact, plant tumors typically are not lethal. However, researchers have reported metastasis-like phenomena in plants, with tumor strands emanating from primary plant tumors [6]. Bacteria-free tumors have also been reported at secondary sites without the apparent presence of tumor strands [7]. So little is known about these phenomena and the genetic mutations that cause plant tumors that many exciting opportunities for discovery and await future researchers.

This garden is different from much of the art associated with cancer, which is usually created by patients and designed to have a therapeutic impact, because the aim is to create a work about the fascinating science of cancer. Artworks that explore the thinking behind the research are rare. Many previous artworks simply present the cells themselves as a beautiful and insidious visual narrative. However, the science of cancer is filled with fascinating concepts—like the way that cancer manifests across different forms of life—that few people have had the opportunity to consider. Engaging more deeply with the nature of cancer and its relationship to multicellular life may help cancer patients and their families see cancer differently and explore a different therapeutic approach that is aimed at cancer control rather than eradication [8].

As is true in most public artworks, there are multiple stakeholders. Because Robertson was not licensed in Arizona, we hired the MOORE/SWICK partnership, a local landscape architecture and planning firm that could assist him in adapting his design to Arizona conditions and design vernacular.

The process was paved with people who had their own relationship to cancer; Kevin Moore was no exception. He wore a machine, hanging from his shoulder, that was slowly leaching chemotherapy poisons into his veins during our planning meetings.

Ironically, I was going through my own cancer experience while working on this project. From the outset, I tried to maintain a positive outlook, refusing to think about my experience as a "battle" with the need to "beat" anything—an attitude I saw as too confrontational. I’ve preferred to understand my cancer for what it was, not a foreign enemy, but cells in my own body that have “gone rogue” and weren't caught by my immune system, that needed to be managed rather than beaten. I was encouraged to hear the scientists at the ASU Biodesign Institute talk about their current understanding and approach to cancer in the same terms [9].

Half of us will be diagnosed with cancer at some point in our lifetimes, and it is viewed as a devastating diagnosis [10]. However, there are many ways in which cancer can be transformative.

We found out that we needed to add yet another layer of
landscape architects, because we planned on installing the garden on the campus of Arizona State University. Lucky for us that layer was Byron Sampson, associate director and university landscape architect at ASU, who had yet another personal story to add to the mix.

Through the course of gaining additional insight [into the] meaning of the garden, I was able to discuss openly my own experiences and see them come to fruition in a beautiful garden. My father had passed away eleven years ago after a long “battle” with oral cancer, my mother is a breast cancer survivor and I am a brain cancer survivor, being diagnosed four years ago. In the ensuing conversations with Todd Briggs, the co-director of the Trueform Landscape Architecture Studio, his lead designer was adamant that she work on the project as she was a cancer survivor as well. This garden brought together many different people, all with similar stories and a unified understanding of the unique aspects of the meaning behind the garden [11].

The installation of the garden coincided with the start of clinical trials to test a strategy for living with, but not dying from, cancer called adaptive therapy [12]. Fittingly, the innovation behind these trials comes from agriculture and the strategies farmers have developed to manage pests. High-dose chemotherapy, like high doses of pesticides, kills most of the cells/pests but leaves behind mutants that are resistant (immune) to the drug. This is why, when a tumor recurs after therapy, it typically no longer responds to that therapy. However, that resistance usually comes at a cost. It either takes some energy to detoxify or expel the drug, or the variant that can avoid the drug is less well adapted to its environment than the sensitive cells/pests in the absence of drug. Farmers have learned that they can capitalize on the cost of resistance by not spraying a part of their fields, and thereby keep some sensitive pests around to out-compete the resistant pests. Typical high-dose chemotherapy kills all the chemo-sensitive cancer cells, leaving nothing to control the chemo-resistant cells. Bob Gatenby translated this insight to cancer therapy with a strategy called “adaptive therapy,” in which the dose of the chemotherapy is reduced or stopped if the tumor starts shrinking so as to preserve sensitive cells. If the tumor regrows, chemotherapy is started again, but now the tumor is mostly composed of sensitive cells, and so it continues to respond to the drug. In mouse experiments, Gatenby and colleagues were able to keep cancers under control indefinitely (with lower and lower doses of chemotherapy over time) [13]. The first pilot clinical trial tested adaptive therapy in castration-resistant metastatic prostate cancer and has been able to keep control of the cancer in 10 out of 11 men for over a median of 27 months, where, under standard therapy, they would have lost control of at least half of the men’s cancers within 16 months [14]. That trial is continuing and expanding. Meanwhile, we at the Arizona Cancer Evolution Center are about to open the first pilot trial of adaptive therapy in breast cancer at the Mayo Clinic Arizona, with Donald Northfelt and Karen Anderson. We see this garden in part as an embodiment of this new approach to cancer—to live with cancer as a normal part of life, pruning it back occasionally and managing it responsibly.

The garden is now installed and is still immature, filled with relatively new cacti; a triangular space (Color Plate B) that, given time, will grow into a fully realized landscape complete with a seating area. Additional cacti will be added as they are identified by the Tucson Cactus and Succulent Society Cactus Rescue Crew, which saves cacti and other native plants that would otherwise be destroyed during the development of Arizona real estate.

Pamela Winfrey, the scientific research curator for the project, developed an opportunity for people to write the names of people they know who have been impacted by cancer onto plant identification tags. These tags are then added to the garden. We are currently developing a sculpture that will house this ever-growing project. This adds to the feeling that this garden is for the community: a place that is theirs, a place of solace, sympathy and solidarity.

We envision the garden as a place where people can engage with the science of cancer while simultaneously having a peaceful and grounding aesthetic experience with the crested cacti and other plants in the garden. As one woman who contributed a tag said, “For me, this is a place of comfort.”

Many voices and collaborations have shaped this garden into an echo of Darwin’s thoughts when he wrote of the “grandeur in this view of life.” Our garden itself had “so simple a beginning” and from it “endless forms most beautiful and most wonderful have been, and are being, evolved” [15].

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References and Notes
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CASPIAN ROBERTSON is an award-winning landscape architect and the director of the garden design and construction company Caspian Gardens. His gardens have been installed in Saudi Arabia, the United States, the United Kingdom and Russia.

ATHENA AKTIPIS is a cooperation theorist, theoretical evolutionary biologist and cancer biologist. She is an assistant professor in the Department of Psychology at Arizona State University, codirector of the Human Generosity Project and co-founder and vice president of the International Society for Evolution, Ecology and Cancer. She is the author of The Cheating Cell: How Evolution Helps Us Understand and Treat Cancer, forthcoming from Princeton University Press.

CARLO MALEY is a cancer biologist, evolutionary biologist and computational biologist working at the intersection of those fields. His team applies evolutionary and ecological theory to problems in cancer. He is codirector of the newly formed Arizona Cancer Evolution Center (ACE) and cofounder and president of the International Society for Evolution, Ecology and Cancer.
COLOR PLATE B: **ENDLESS FORMS MOST BEAUTIFUL:**
A GARDEN SHOWS THAT CANCER IS A PART OF LIFE

Planting scheme by Caspian Robertson. An educational garden installation at Arizona State University, second iteration. (© Caspian Robertson) (See the article in this issue by Pamela Winfrey, Caspian Robertson, Carlo Maley and Athena Aktipis.)