ET IN ARCADIA EGO: ADDRESSING CANCER, DEATH AND IMMORTALITY USING SCIENCE

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Abstract

Charlotte Jarvis has collaborated with Hans Clevers to grow her own tumor. Here, the authors discuss the project's aims to examine mortality and create a dialogue with and about cancer.

Poussin's *Et in Arcadia Ego,* 1637–1638, hangs in the Louvre. The painting depicts four Classical shepherds discovering a stone monument within an idealized Tuscan landscape. The shepherds are reading the engraving *Et in Arcadia Ego* (*"Even in paradise I am here"*). The edifice is a tomb, and the first person "I" who speaks through the inscription is Death.

Unlike earlier paintings bearing the same inscription [1], Poussin omits any direct depiction, symbolic or otherwise, of Death itself. Death is unrendered yet terribly present. Furthermore, the beatific Classical figures within the paradisiacal setting remind us that Death exists even for perfect beings in a perfect world. It is not just with us, but *part* of us.

While we are built to live for about 80 years, our individual cells have much shorter lifespans. Stem cells allow us to outlive our constituent parts, replacing lost cells with fresh specimens. Of course, they also eventually wear out. The erosion of their DNA code causes their numbers to gradually dwindle. Yet, every once in a while, a specific mutation in their DNA doesn't make them weaker, but rather they start dividing more often, moving around and occupying nearby tissues; they have become cancer cells.

Our DNA code consists of 3 billion letters (a sequence of G, A, T and C). Stem cells require no more than four changes in this code to turn malignant [2]. Thus, the difference between cancer cells and normal stem cells is minute.

In 1971 then U.S. president Richard Nixon declared a "war on cancer" [3]. Four and a half decades later, the end of this war is not in sight. It has been exceedingly challenging to design drugs that will kill cancer cells, but leave other cells alone, because malignant tumours are built from our own cells. *Et in arcadia ego*, indeed.

Metaphors, Catharsis and Death (Charlotte)

In 2014, I (Charlotte) attended the funeral of a friend who died from kidney cancer at the age of 33. Before his death, I discussed the language of cancer at length with Martin, who, like other patients, was often described as *battling* or *fighting* cancer. These conflict metaphors (as opposed to journeys for example [4]) belie a desire to believe that if every patient fought hard enough, within him or herself, they would survive. This is clearly not the case. The image conjured of patients fighting cancer also, contradictorily, casts cancer as the external agent; something alien to be waged war against, so that dying of cancer becomes *both* the fault of the patient *and* the result of something "other" to their bodies.

I had previously made a number of biological artworks using cell cultures harvested from my own body, and I became interested in developing a piece of work that would interrogate these metaphors, challenge the idea of cancer as "other" to us and probe my relationship to mortality.

I wrote to Hans Clevers, from the Hubrecht Institute in Utrecht and asked if he would help me grow a tumour—something that would be biologically part of me, but grown outside of my body in a laboratory and ultimately exhibited, with me, in a gallery. The project would be called *Et in Arcadia Ego* and would aim to discuss cancer whilst realizing a confrontation between me and my own death, in homage to Poussin's painting.

The project would not attempt to represent the experience of cancer; to do so would be insulting to those with the real authority to speak. Rather, I hoped the project might contribute to finding new ways of visualizing and thinking about it. I hoped that the process of abstracting cancer through a scientific process—of literally removing it from the body and figuratively holding it at a distance—might help to see it more clearly. Additionally, I have always had a profound fear of death, which I felt more keenly after Martin died, and if I am honest I hoped that the project might be in some way cathartic—that it might make me less scared.

I hoped the piece would relate to three bodies of work—art involving growing and exhibiting cell cultures as pioneered by Oron Catts and Ionat Zurr, art that uses science and data to discuss cancer (*Blood and Bones* by Tom Corby and *La Cura* by Salvatore Iaconesi for example) and the long tradition of artists using their own bodies to make personal work with broader implications (Orlan, Stelarc, Kiera O'Reilly, etc.).

It was not without irony that I noted that the process of producing this work about mortality would necessitate making small parts of myself immortal [5]—a concept also explored by Marta De Menezes, who was working on *Immortality for Two* at around the same time. Perhaps this is another reason why cancer can feel like a perverse punch line—sometimes we die because parts of ourselves fail to.

How to Make Cancer (Hans)

One way researchers are attempting to solve the insidious enigma of how to treat cancer is to understand the process of mutation by which stem cells become cancer. When Charlotte wrote to me (Hans), my group was preparing a paper [6] that would further our understanding of this process by formally proving that it takes only four DNA mutations to convert a normal colon stem cell into a full-blown colon cancer cell.

In previous studies, we had developed technology to take a biopsy of colon tissue from a healthy mouse or human volunteer and culture this tissue in a petri dish for long periods. The ever-expanding structures created by the colon stem cells-in-a-dish are termed *organoids,* a.k.a. "mini-guts" [7].

To introduce defined mutations into the four best-known colon cancer genes (APC, P53, KRAS and SMAD4), we made use of groundbreaking technology developed by Jennifer Doudna and Emmanuelle Charpentier: CRISPR/CAS9 [8]. This technology allows us to introduce the four mutations in a stepwise fashion into the healthy colon stem cells.

To analyze the effects of the four mutations on the human colon stem cells, the mutant organoids were transplanted to mice. Only the organoids with all four mutations exhibited malignant behavior: they grew in an invasive fashion and metastasized to distant sites in the mouse body, eventually leading to its death [9]. In short, my group had successfully replicated the "natural" process by which healthy cells become cancer cells.

To a lab-based experimentalist, the cancer problem is just an intellectual challenge. So, when we turned normal cells into cancer cells, this carried no emotional charge. Charlotte's

question made us realize what actually had happened in our petri dishes. So I agreed to collaborate with her and replicate this process on an in vitro colony of her own cells. Whilst the mutations we would carry out would be common to all gut cancer, the cells themselves, having derived from Charlotte's body, would be distinct to her and as such potentially lethal to Charlotte, but harmless to anyone else.

Art and Ethics (Charlotte)

In order to initiate the project, we needed a sample of my (Charlotte's) colon tissue. This, however, proved harder than anticipated. Like all medical procedures, rectoscopy carries with it an (extremely small) associated risk, and for over a year I could not find a clinic willing to participate. This hesitance on the part of various medical institutions to carry out a low-risk procedure in the absence of medical *need* is understandable. However, the ethics become less straightforward when one considers that many of the same clinics *were* willing to carry out extensive cosmetic surgeries with considerably more associated risk and an equal absence of medical need.

Given the ease with which I could have booked any number of cosmetic procedures, it appeared that the objections I faced to the rectoscopy were less about the associated risk of me collecting and using my own cells and more about my reasons for wanting to do so, failing to conform to social norms regarding what I *should* want to do with parts of my own body. This part of the project was unexpected and can be viewed within the context of other pieces of art and writing that further explore medical ethics in relation to biological art [10].

Eventually, a sympathetic doctor was found through connections in Paris who agreed to do the procedure as a private consultation. The sample was taken and shipped to Utrecht, where Hans's lab initiated the seven-month process of mutating my healthy colon cells into cancer just in time for an exhibition at MU in Eindhoven.

Defeat, of a Sort (Charlotte)

The installation at MU, and later at Kapelica in Ljubljana, comprised two sets connected by a corridor. The first was a waiting room (see supplementary material), or more accurately, the *trope* of a waiting room. Screens showed abstract snippets of medical procedures, scientific experiments and disembodied parts of a waiting patient. Corkboards displayed documents including private emails, rectoscopy photos, lab imagery and sketchbook pages. During the exhibition, I (Charlotte) sat in this space, dressed in surgical gown, waiting.

Down a narrow corridor, the darker second space housed a spotlit mound of soil. Atop the earth sat a box—entirely mirrored, inside and out—creating an illusion of infinite space, within which my cancer sat housed in a petri dish.

This was not the cathartic object I had anticipated: The cells scare the living shit out of me (Fig. 1). I had thought that the scientific process would abstract cancer for me; that demystifying it would make it less frightening. It did not. The confrontation I have materialized is not one I have won. Although I recognize that this defeat at the hands of my own work is a meaningful, or at least compelling, outcome, I get no enjoyment from performing in the space. I hate being close to the cells. Although preserved in ethanol, as they are, the cells cannot harm me, and although I know them to be of my body, they still hold a kind of talismanic power for me. They may not be alien, but these parts of me remain incomprehensibly terrible.

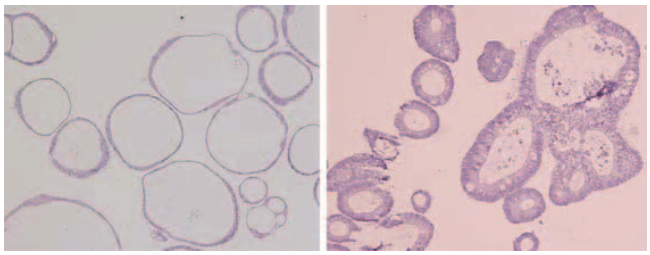

Fig. 1. Organoids, *Et in Arcadia Ego,* 2015. Healthy organoids, left, are structurally organized with single-layer epithelium. Cancerous organoids, right, are more solid and disorganized. (© Charlotte Jarvis. Photo Hans Clevers.)

Some time after the project was exhibited, Hans sent me an email. He said, "I tell the story of our project at scientific meetings and say that you exhibit yourself with your cancer cells. Colleagues walk up to me and say that examples like these are eye openers. We do study cancer as an abstraction, but your art project drives home that the real thing is never far away."

Poussin made an earlier, arguably less successful version of *Et in Arcadia Ego* in 1627. What Poussin decided to change in the later canvas, and what makes it more persuasive, is described by art historian Erwin Panofsky as "a contemplative absorption in the idea of mortality" [11]. The figures in the second painting are less dramatic: they are calm but resigned, sequentially describing the process of being confronted with mortality. One interprets the inscription; another appeals outwards bewildered and confused; the woman slouches, hand on hip in stunned contemplation; and the final figure gazes down, defeated.

References and Notes

1. For example Guercino's version painted between 1618 and 1622 featuring the typical *memento mori* skull.

2. J. Drost et al., "Sequential cancer mutations in cultured human intestinal stem cells," *Nature* **521** (2015) pp. 43–47.

3. R. Nixon (1971), <https://www.youtube.com/watch?v=E2dzEDnGqHY>, accessed 19 August 2016.

4. A number of articles and blogs have appeared recently that discuss cancer metaphors. See M. McCartney, "The Fight Is On: Military Metaphors for Cancer May Harm Patients," *BMJ* **349** (2014) g.5155; M. Gajewski, "May I take your metaphor?—how we talk about cancer" (2015) <http://scienceblog.cancerresearchuk.org/2015/09/28/may-i-take-your-metaphor-how-we-talk-about-cancer/>, accessed 20 November 2016; D. Hauser and R. Wassersug, "Do We Need to End the 'War' on Cancer?" (2015), <https://www.theguardian.com/commentisfree/2015/mar/22/saying-youre-fighting-a-war-on-cancer-could-make-you-lose-it>, accessed 20 November 2016.

5. Cancer cells are described as immortal because some (but not all) have no Hayflick Limit (the number of times a cell colony divides before division stops) due to the presence of an enzyme called *telomerase*, which maintains the end of the DNA strand after division.

6. Drost et al. [2] pp. 43–47.

7. A detailed protocol can be found in T. Sato et al., "Single lgr5 Gut Stem Cells Build Crypt-Villus Structures in vitro without a Stromal Niche," *Nature* **459** (2009) pp. 262–265.

8. J.A. Doudna and E. Charpentier, "Genome Editing. The New Frontier of Genome Engineering with CRISPR-Cas9," *Science* **346** (2014) p. 1258096 1–9.

9. Drost et al. [2] pp. 43–47.

10. For example, Gina Czarnecki's *Art and Ethics panel*, 2012 and Ionat Zurr and Oron Catts's paper "The Unnatural Relations between Artistic Research and Ethics Committees: An Artist's Perspective," published in *The Arts and Ethic, Library of Ethics and Applied Philosophy.*

11. E. Panofsky, "*Et in Arcadia Ego*: Poussin and the Elegiac Tradition" (1936), <https://lauradufresne.files.wordpress.com/2013/10/e-panofsky_et-in-arcadia-ego.pdf>, accessed 20 November 2016.