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Highlight

I love you Toxoplasma gondii☆

Q1 Q3

In December 1996, con artist and prison escape specialist Steven Jay Russell decided that he had seen enough of the inside of the Maximum Security Estelle Unit in Huntsville (Texas). Therefore he got his hands on a spare prisoner's uniform as well as a handful of Magic Marker pens, dyed the uniform the same shade of green as the prison doctors' scrubs and simply walked out the front gate in order to reunite with the man he loved.[1]

Escape stories have great storytelling potential. The true ones, like the one of Vincenzo Curcio, an associate of the Sicilian mafia, who broke out of jail by sawing through the bars of his cell using dental floss.[2] The fictional ones, like Alexandre Dumas' literature classic *The Count of Monte Cristo* or the eternal number one of the international movie database (IMDb) *The Shawshank Redemption.* And the real ones turned into Hollywood material, such as the life of Steven Jay Russell, which became *I Love you Philip Morris* in 2009.

Unlike human prisoners, it is rather the entry of intracellular pathogens into the host cells than their exit that has attracted a great deal of attention.

All animosities aside, the panoply of ingenious access strategies crafted over time by the arms race of co-evolution between man and microbe deserves true respect [1]. They mainly rely on an extensive ability to hijack all kinds of host cellular features – co-receptors, the endocytosis machinery and surprisingly, the cell–cell adhesion complex, technically meant to form impenetrable barriers and not entry portals [2,3]. The hijacking continues at full capacity of course inside the host cell, a rather comfortable lifestyle supplying essential nutrients, protection from the immune system and in the case of viruses, the entire genetic expression apparatus. However, what happens once the business inside the host cell is done is equally fascinating [4,5], and beautifully shown in a "live version" by Lúcio Caldas and colleagues through super resolution and electron microscopy [6]. Just like human prisoners, pathogens don't lack imagination when it comes to make a run for it.

Most pathogens master the manipulation of the host cell choice between life and death. During the replicative or latent phase of infection, intracellular pathogens usually repress programmed cell death signals [7]. When the time for dissemination is ripe however, they can spark off these signals to break free. Depending on the cell type and the presence of TNFα, *Mycobateria* for instance can trigger necroptosis, a very lytic and proinflammatory version of suicide, resulting in the rupture of the host cell's membrane and spilling out of its contents, including the bacteria [8]. *Shigella*, *Salmonella* and some fungal pathogens in turn provoke pyroptosis, another lytic host cell death with similar consequences [7].

Brute force is of course always an option. The fungal pathogen *Aspergillus* for example produces germ tubes and hyphae that can puncture the host cell membrane while inducing apoptosis *via* gliotoxin [9,10]. Although it looks equally violent, the ability of *Shigella* and *Listeria* to get themselves catapulted around inside the cell and into its neighbors by taking over the control of actin polymerization actually leaves the host intact because it relies on a combination of protrusion formation by one and gobbling up by another cell [11]. Some vacuolar pathogens, such as *Chlamydia* and *Cryptococcus*, have perfected the use of these compartments as packaging to be spit out back into freedom by macrophages under the charming name of "vomocytosis" [12], while *Legionella* exits its primary amoeba host through classical exocytosis and *Brucella* might hitchhike in autophagosomes [5].

Herpesviruses, on the other hand, seem to have it way harder. An exception even among viruses, they have to bud twice – first into the inner nuclear membrane, then into a cytoplasmic (Golgi or endosomes) membrane [13].

Speaking of viruses – Steven Jay Russel's last escape consisted in pretending that he was dying of AIDS after having ingested large amounts of laxatives in order to loose much weight and falsified his medical record. Thought to be on his last legs, he was sent to a hospice, which he left easily, then mailed his own death certificate to the Texas court.

1. Biosketch of Dr. Lúcio Ayres Caldas

Dr. Lúcio Ayres Caldes graduated on biology with a master's degree in the area of molecular virology and a doctoral degree in biology of protozoans at the Institute of Biophysics Carlos Chagas Filho (Federal University of Rio de Janeiro,

☆ Article highlight based on "A structural analysis of the natural egress of *Toxoplasma gondii*" by Lúcio Ayres Caldas et al. [6].

[1] http://nowiknow.com/the-man-who-walked-out-of-prison-a-few-times/.

[2] http://www.abc.net.au/science/articles/2001/04/04/271768.htm.

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Brazil). Nowadays he is a postdoctoral fellow in the group of Professor Wanderley de Souza at the same institute. He is working on the interactions of *Toxoplasma gondii* with the host cell as well as Flavivirus morphogenesis by using laser and electron microscopy. Besides he is a member of an inter-institutional research group on epistemology (http://www.epistemologia.ufrj.br/) and has been publishing papers on epistemological obstacles on the fields of physics and biology.

2. Interview

1. What was your motivation to investigate closely the natural egress of T. gondii ?

This stage of *T. gondii* cellular cycle is still poorly understood. Moreover, the knowledge of the interactions that take place in this step, in a structural level, can contribute to decipher new roles for known molecules, and analogue mechanisms of other pathogens interactions with the host cell.

2. What was your first reaction when you faced the results? Did you expect them?

Considering that the host cell is not a placid place, and the variety of signalling pathways that may converge to the parasite exit, we expected unreported kinds of interactions. After all, we should not search for the lost keys under the light pole just because there is light there. On the other hand, since calcium mobilization was shown to be upstream from many other players of *T. gondii* egress triggering, it is conceivable that no great differences show up when comparing "natural" egress with calcium ionophore induced egress.

3. How will the project go on?

This study opened several fronts. We noticed that some molecules are intriguing players, and we wish to use them as a tool to further exploit the *T. gondii*/host cell interactions.

4. What is the take-home message of the article?

In a structural level, *T. gondii* non-induced egress was shown to be very similar to calcium ionophore induced egress. Furthermore, several signals, yet not well perceived, may contribute to the exit, suggesting that there are a lot of doors for *T. gondii* egress but the protozoan is never able to choose. Neither is the cell.

5. Do you have a personal motto, quote or leading sentence?

I think the quotes we have on mind change according to the conjuncture. Nowadays, in Brazil, the scarce economic resources directed to the sciences field, within a profound economical (and political) crisis (which are immanent to our system), raises the quote of serious and catastrophic situations. This quote, which sarcastically fits to the way this crisis has been treated in my country, was recently remembered by the Slovenian psychoanalyst Slavoj Zizek as follows:

There is an (apocryphal, for sure) anecdote about the exchange of telegrams between German and Austrian army headquarters in the middle of the First World War: the Germans sent the message "Here, on our part of the front, the situation is serious, but not catastrophic," to which the Austrians replied "Here, the situation is catastrophic, but not serious."

6. What advice would you give to the young next-generation scientists?

Rigorous sciences require us to be materialist to the bone. This materialist conception of the world and history (in opposition to the idealistic, naïve ones) allows us to realize that reality is more creative than the stories we frequently create about it. I think we should always try to avoid the common sense and those epistemological obstacles described by Gaston Bachelard in his studies. Besides that, just as Alan Chalmers used to say about the route we go through sciences: "We start off confused and end up confused on a higher level."

7. What is your favourite hang-out method after a tough day at the lab?

Judo. I practice it since I was a child.

8. In your opinion, what are the three most important (scientific) discoveries of the last decade?

The CRISPR system is (still), which was shown to be very promising, as well as the development of the synthetic bacteria (see Hutchison, C.A. et al. Science 351, 1414 (2016)), and, evidently the Higgs Boson (together with the recent observation of gravitational waves, once predicted by Einstein's theory of relativity).

9. If you could travel back in time – what historical personality would you like to meet and what scientific discovery to assist to?

As a biologist, I don't think would be simplistic to claim that Darwin's evolution theory was one of the 3 most important

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