Who or what inspired you to become a scientist?
During my fifth semester as a student in Ecuador, I engaged in extensive volunteer work, where I encountered a rare type of cancer in dogs known as transmissible venereal tumor. The unusual nature and transmissibility of this cancer sparked my curiosity. My interest in this field was further fueled when Dr. Elizabeth Murchison from the Transmissible Cancer Group at the University of Cambridge recognized my potential and invited me to Cambridge and the Wellcome Trust Sanger Institute. Witnessing Dr. Murchison, a remarkable female scientist, in action and observing her incredible achievements inspired me profoundly. She became a significant role model and motivated me to pursue a career in science.

What is the main question or challenge in disease biology you are addressing in this paper? How did you go about investigating your question or challenge?
The Bacillus Calmette–Guérin (BCG) vaccine is the longest-used cancer immunotherapeutic agent. Despite its success in maintaining a high 5-year recurrence-free survival rate (~74%) in bladder cancer, the initial mechanisms of its action remain largely unknown. Consequently, there is a lack of diagnostic tools to identify patients who will not respond to treatment or who will develop resistance. To address this gap, we aimed to uncover the earliest cellular mechanisms involved in BCG-induced tumor clearance. We developed a 4-day assay using the bladder cancer zebrafish xenograft model. In this model, we injected the BCG vaccine intratumorally twice: first at 1 day post injection (dpi) and again with a booster injection at 3 dpi, simulating the induction treatment given to patients. Xenografts were then analyzed using single-cell high-resolution microscopy.

How would you explain the main findings of your paper to non-scientific family and friends?
Cancer treatment often involves harsh drugs that kill tumors but also damage healthy tissues, causing severe side effects. To address this, a new approach called immunotherapy boosts the body’s defenses, the immune system, to fight cancer. One successful example is the use of the BCG vaccine, initially developed for tuberculosis, to treat non-muscle invasive bladder cancer. However, not all patients respond to this treatment, and it remains unclear who will benefit beforehand. To investigate, we developed an assay using zebrafish, which are small and transparent, allowing real-time observation with microscopy. We injected human bladder cancer cells into zebrafish, treated them with BCG, and analyzed the results. We discovered that BCG attracts immune cells called macrophages to the tumor, where they actively kill and remove cancer cells, rather than just signaling to other immune cells as previously believed. Comparing the traditional BCG vaccine with a new version, VPM1002, we found that VPM1002 induced a stronger immune response and was more effective at killing cancer cells. Thus, our results showed the importance of macrophages in the response to BCG immunotherapy and that our zebrafish model can also help us differentiate among different vaccines and their effect in killing cancer.

This study challenges the notion that an adaptive response is needed for an initial effective BCG-induced tumor clearance.
Advantages that align perfectly with our research goals and choosing DMM to publish our paper offers several key benefits. Why did you choose DMM for your paper?

Choosing DMM to publish our paper offers several key advantages that align perfectly with our research goals and findings. DMM is renowned for its focus on the use of model organisms to understand human disease mechanisms, which is central to our study utilizing the zebrafish xenograft model. The journal’s audience, comprising researchers interested in disease mechanisms and model development, ensures that our innovative use of zebrafish for real-time single-cell-resolution microscopy and immune response analysis will reach a highly relevant and engaged audience. Additionally, DMM’s emphasis on translational research highlights the practical implications of our work in developing more effective immunotherapies and personalized medicine approaches. Publishing in DMM will not only validate our methodological advancements, but also enhance the visibility and impact of our findings within the scientific community, fostering further research and collaboration in the field of cancer immunotherapy.

What are the potential implications of these results for disease biology and the possible impact on patients?

This study challenges the notion that an adaptive response is needed for an initial effective BCG-induced tumor clearance. It also demonstrates that macrophages do not just act as non-specific phagocytes nor professional antigen-presenting cells, but that they are able to target and kill cancer cells through the release of cytokines. This highlights the importance of evaluating the inflammatory potential of macrophage infiltrates within the tumor microenvironment, in particular related to TNF expression. This suggests that patients with low inflammatory profiles in their tumors could benefit from prior treatment with immunomodulators or could be offered alternative options without undergoing BCG treatment and developing severe side effects. It also presents the kinetics of macrophages as potential targets for the co-stimulation of immunotherapy. By immunomodulating the innate immune compartment, cancer clearance can be potentially boosted and treatment outcomes could be improved. Additionally, we present the zebrafish xenograft model as a promising in vivo preclinical model that has the resolution to test different immunomodulatory treatments aimed at the innate immune system.

Given your current role, what challenges do you face and what changes could improve the professional lives of other scientists in this role?

Science in Ecuador is still a developing field, facing significant challenges due to inadequate public policies and limited funding, especially for young women. Conducting scientific research is expensive, and importing equipment and reagents often leads to delays. Despite these obstacles, the scientific community in Ecuador is growing, with researchers collaborating on cooperative projects. We have adapted many scientific approaches and methodologies to fit the country’s unique circumstances, enabling us to perform high-quality research with limited resources. Additionally, women in science are gaining more recognition and, by highlighting our struggles, we are actively advocating for policymakers to create a more supportive environment for scientific advancement in Ecuador.

What’s next for you?

I hope to continue my work in Ecuador, advancing science in ways that are beneficial and relevant to our national reality. I remain dedicated to teaching and showcasing the diversity of female scientists to my students. My aspiration is to become a role model for them, inspiring and motivating them to pursue careers in science, much like Dr. Elizabeth Murchison did for me.

Tell us something interesting about yourself that wouldn’t be on your CV

I am a tattoo collector who loves having different artists’ work showcased on my skin, transforming myself into a living canvas. I live with my adopted dog and cat from Portugal, both of whom have European passports and Ecuadorian national IDs, which I find adorable and love to share with others. I’m a food enthusiast, always on the lookout for diverse restaurants and cuisines. I enjoy bringing my friends with me on these adventures, they always compliment my good taste.

Reference