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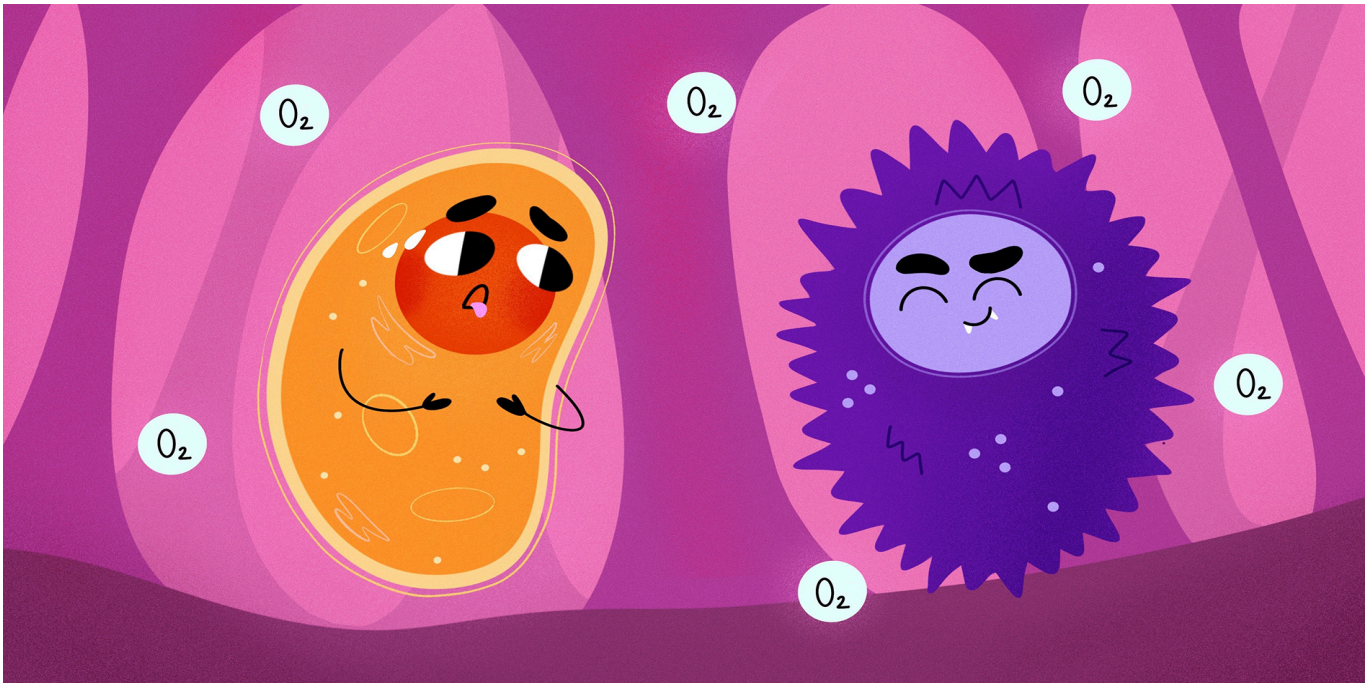


# WHY DO WE CARE HOW MUCH OXYGEN TUMORS HAVE?

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**AGES: 14–15**

**WILLIAM**

**AGE: 11**

The air we all breathe contains oxygen, which is essential for life. Each of the tiny cells that make up our bodies needs oxygen, although they need different amounts. Whenever a cell does not receive enough oxygen, it is said to be hypoxic, which means "low oxygen". Normally, if a cell is very hypoxic it stops working and eventually dies. As we age, things can go wrong in our bodies and tumors can develop. The cancer cells inside the tumor can experience hypoxia. Unlike normal cells, cancer cells can adapt to living in hypoxic conditions and survive instead of dying. Hypoxic cancer cells are very difficult to kill using the standard therapies given to cancer patients, so the degree of hypoxia is in a tumor can determine whether the cancer can be cured. We understand how hypoxia makes cancer worse, but we are still working on ways to get rid of hypoxic cancer cells.

## MISBEHAVING CELLS CAN LEAD TO CANCER

Our bodies are made up of tiny cells, all with jobs to do. For example, we have skin cells, bone cells, muscle cells, and many more. Usually,

when cells get old or broken, they stop doing their jobs and die. Occasionally, a cell misbehaves and instead of dying when it is damaged, it continues to grow and make more cells. People with **cancer** have lumps inside of them made up of these misbehaving cells, which are called **tumors**. In 2020, over 19 million people worldwide were told they had cancer and sadly about 10 million of them died from their disease. Most cancers happen in old people because it usually takes a long time for the cells to become out of control and form a tumor. Scientists spend a lot of time trying to work out why the cells that form tumors misbehave and do not die when they are supposed to.

**CANCER**

A group of diseases caused by the uncontrolled growth and spread of abnormal cells.

**TUMOR**

A mass or lump of abnormal cells.

## OXYGEN IS FUEL FOR CELLS

All our cells require fuel, in the form of oxygen and sugar, to produce the energy they need to function and grow. The oxygen comes from the air we breathe, while the rest of the fuel comes from the foods we eat. Oxygen travels through our lungs and into the blood. The heart then pumps the oxygen-loaded blood around the body to supply all the cells. Normal cells grow in a very organized way, next to blood vessels, so they get enough oxygen to survive. Cells growing out of control in a tumor grow in a very disorganized way, so sometimes they are too far away from the oxygen-delivering blood vessels (Figure 1). As a result, greedy cancer cells next to the blood vessels use up all the available oxygen, leaving very little or no oxygen for the cells further away. Whenever a cell does not have enough oxygen, we say it is experiencing **hypoxia** or that it is hypoxic [1]. You may have heard about climbers struggling with altitude sickness at the top of tall mountains. This happens because there is not enough oxygen high up in the atmosphere, so the climbers become hypoxic. So, why do we care if cancer cells get hypoxic? We want them to die, so surely when they struggle for oxygen it is a good thing, right? But remember, cancer cells are out of control—they do not play by the same rules that normal cells do. So instead of dying when they become hypoxic, cancer cells can adapt and get sneaky [2].

**HYPOXIA**

Condition that results when a part of the body does not get enough oxygen to function properly.

## CANCER CELLS ADAPT TO HYPOXIA

One of the things cancer cells can do if they find themselves short of oxygen is to make new blood vessels grow, to try to get more oxygen delivered. The process of growing new blood vessels is called **angiogenesis**. New blood vessels coming to the tumor help it grow, which is bad, but the vessels are not as good as normal ones, so they leak and cause more hypoxia. Imagine you are a tumor cell growing somewhere with very low oxygen. If you were a normal cell, you would have to put up with the situation until you died, but because you are a cancer cell, you do not have to follow the rules. Hypoxic cancer cells can move to look for another place in the body where there is

**ANGIOGENESIS**

The process by which new blood vessels are made.

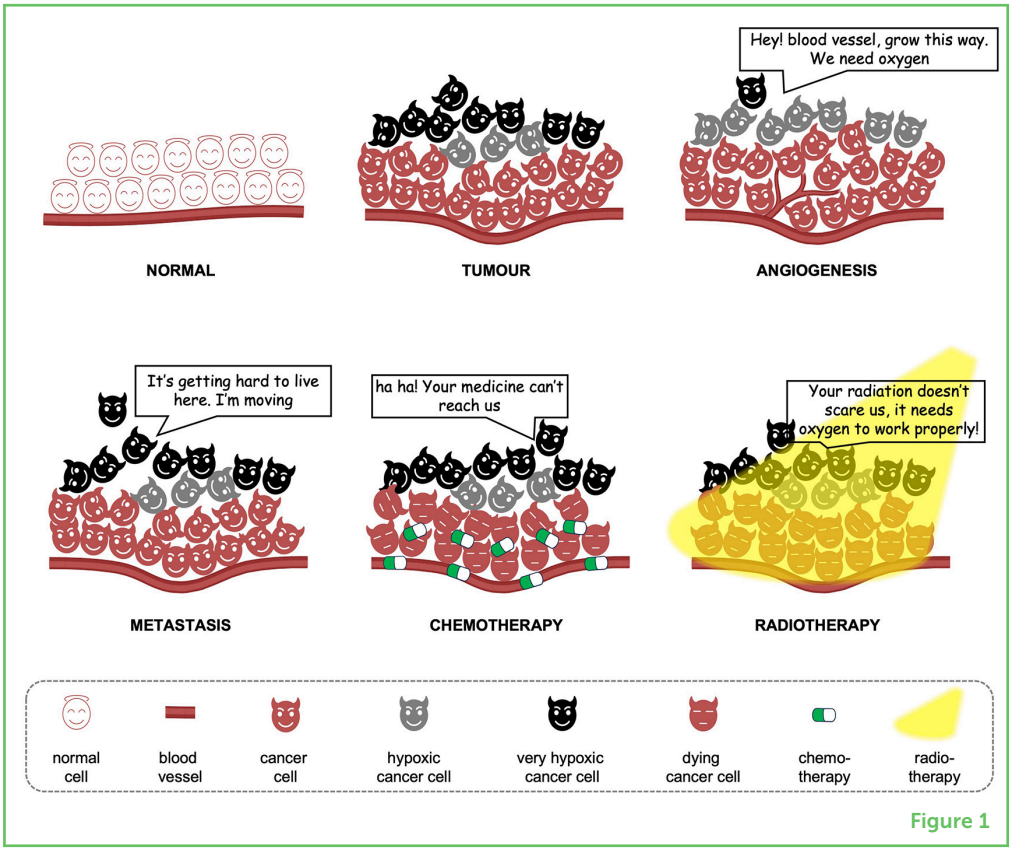


**Figure 1**

The normal cells are nicely arranged and organized, while the cancer cells in a tumor are disorganized and grow wherever they want to. As the cancer cells get further away from the oxygen-carrying blood vessel, they become hypoxic (gray) and eventually very hypoxic (black). The hypoxic cancer cells cause new blood vessels to grow (angiogenesis) and the cancer cells spread to other parts of the body (metastasis). The hypoxic cells are resistant to chemotherapy medicines delivered through the blood vessels, and to radiotherapy that is aimed at the main tumor.

**METASTASIS**

The movement of cancer cells around the body.

**ONCOLOGIST**

An oncologist is a type of doctor who treats people with cancer.

**CHEMOTHERAPY**

Medicines that are taken by cancer patients to help cure their cancer.

plenty of oxygen. The process by which cancer cells move around the body is called **metastasis** [3]. People with metastatic cancer have tumors in more than one place. Most of the people who die from cancer die because their cancer has metastasized. Tumors with lots of hypoxic cells are called aggressive cancers because of their ability to perform angiogenesis and to metastasize. However, being aggressive is not the only problem with hypoxic cancer cells. It is also harder for **oncologists** (cancer doctors) to kill these tumors. In fact, many studies have shown that the more hypoxic a tumor is when a patient starts their cancer treatment, the harder it is to cure the patient.

## HOW HYPOXIC CELLS SURVIVE CANCER TREATMENT

Many people with cancer are treated by a surgeon who finds the cancer and cuts it out of the body. The surgeon can only remove what they can see and find, though. So, if hypoxic cancer cells have already spread to other places in the body, they will be left behind and keep growing.

In addition to surgery, people with cancer receive medicines that are injected into their blood. This is called **chemotherapy**. Although there are many different types of chemotherapy, which the oncologist chooses based on the type of cancer being treated, they are mostly injected into the patient and carried around the body through blood

vessels. Now, remember some of the cancer cells are living so far from a functioning blood vessel that they do not receive enough oxygen, making them hypoxic. When there is cancer-killing medicine in the blood vessels, being far away is an advantage! The cells close to the vessel die, while those in the hypoxic zone survive.

**RADIOTHERAPY**

A cancer therapy in which radiation is aimed at the tumor to try to kill it.

Another very common way oncologists treat cancer is the use of radiation, called **radiotherapy**. There are lots of types of radiation, for example the sun's rays, the type that cooks our food in microwaves, and the X-rays doctors use to look at our bones. The radiation we use to kill cancer cells is full of very small particles, much smaller than a single cell. These particles have so much energy that, when they hit a cell, they cause so much damage that the cell usually dies. But again, there is a problem with the hypoxic cells. First of all, the oncologist aims the radiation beam at the tumor and blasts it, but this does not hit the hypoxic cells, which have metastasized to other places. Second, and more importantly, for the radiation to work well by causing lots of damage to cells, there needs to be plenty of oxygen around. So, the hypoxic cancer cells are more likely to survive radiotherapy [4].

## CAN WE GET RID OF HYPOXIC TUMOR CELLS?

So, what can we do about tumor hypoxia to help cancer patients? Scientists have been thinking about this problem for a long time and have not come up with an answer yet [5]. One of the problems is that, when a cancer patient is diagnosed, the oncologist cannot tell if the tumor is very hypoxic or not, so we need good tests for this. Some of the things that are being investigated are increasing the amount of oxygen in tumors, making medicines that work better when oxygen is low, and delivering radiation in such a way that it also kills the hypoxic cells.

Altogether, we know that cancer cells that get used to living in hypoxic conditions are more likely to perform angiogenesis to grow their own blood supply, as well as to metastasize to other parts of the body. Hypoxic cells are harder to treat by surgery, chemotherapy, and radiotherapy. Imagine that a tumor is made up of hundreds of cancer cells with oxygen (Storm Troopers) and one hypoxic cell (Darth Vader). We do not want Storm Troopers or Darth Vader in our bodies, but the Storm Troopers are a bit dumb, so we can easily kill them with a blast of radiation, for example. But, if we leave Darth Vader alive, even though there is only one of him, he will go on to raise another army and try to kill us in the future. This is why we care how much oxygen there is in tumors.

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## YOUNG REVIEWERS

**SCIENTIFIC HIGH SCHOOL GIUSEPPE MAZZINI, AGES: 14–15**

We are a group of 14 and 15 year old students. We like studying and playing sports. We love having fun together, doing projects or team work, where all of us try to do the best we can. Thanks to our different personalities and characteristics, each of us gives various ideas and the final result is truly unique and original. The review was

performed within the project "Project S.T.R.E.E.T.S.—Proposed activities ERN 2024 at Schools".

**WILLIAM, AGE: 11**

William is 11 years old and has an interest in cancer biology. His areas of interest include academics, specifically Math and Sciences, writing, sports, and also music. He is enrolled in the Johns Hopkins Center for Talented Youth program, a gifted educational program for school-age children. He is also the author of an educational children's book on colon cancer which is currently in press.

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