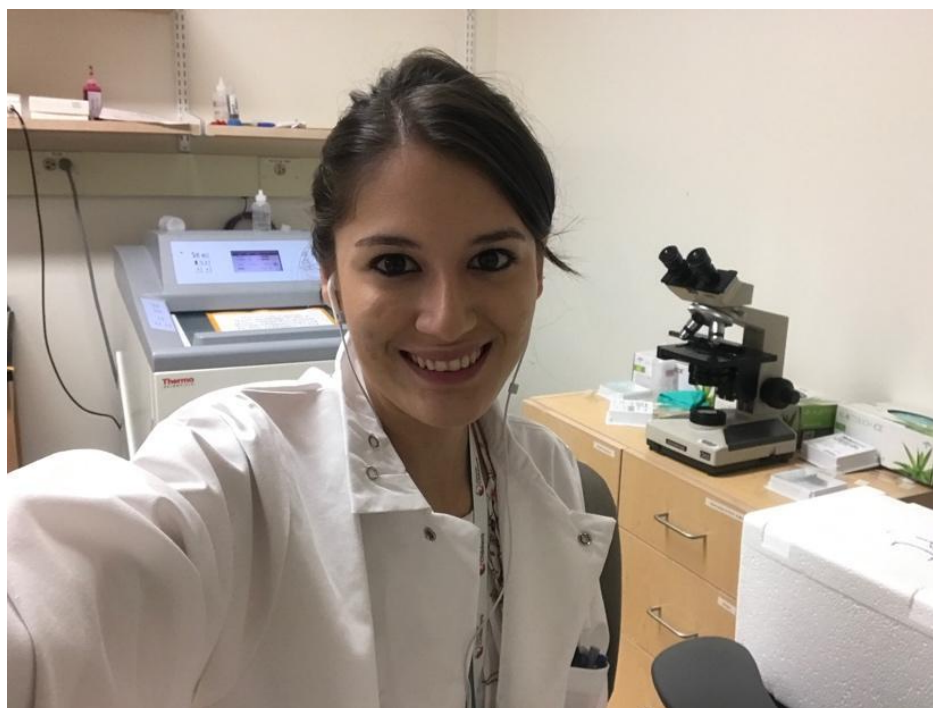


How do molecules outside the cell affect the nervous system?

Featured Scientist: Jennifer Patritti-Cram (she/hers), PhD candidate (Anticipated: Summer2021), University of Cincinnati & Cincinnati Children's Hospital



Jennifer in the laboratory preparing to cut tissue sections of mouse spinal cords and tumors.

Birthplace: Valencia, Venezuela

My Research: I'm interested in understanding how a type of tumor called **neurofibromas** form in the nervous system. We use mice to study the **neurofibroma** disease and see how these tumors form. Our goal is to identify genes important to the formation of **neurofibromas**. We want to provide therapies to patients that suffer from a specific version of this disease: **neurofibromatosis type 1**.

Research Goals: After obtaining my doctoral degree, I will pursue a career in Intellectual Property Law and Policy. This means I will not be doing research. Instead, I will use my scientific knowledge to advise scientists on how to protect their scientific inventions.

Career Goals: I plan to use my knowledge in neuroscience and cancer biology to help scientists protect their inventions. I am also interested in science policy. I plan to use my training to advocate for policies that increase funds for important research and help to increase Latino representation in science fields.

Hobbies: I like to take hikes with my dogs and watch Netflix.

Favorite Thing About Science: My favorite thing about science is how we are creating new knowledge through research. My most fulfilling time as a scientist is when I discover something new that only I know. Then, as part of my job as a scientist, I get to share that knowledge with other scientists and people around the world.

My Team: My lab is very cooperative. We all help each other with experimental design and with performing experiments. We also have several collaborations with other labs in the United States.

Organism of Study: The house mouse (*Mus musculus*)



Photo by George Shuklin from [Wikimedia Commons](#)

Field of Study: Neurobiology & Cancer Biology.

What is Neurobiology & Cancer Biology? Neurobiology is a type of biology that focuses on the nervous system. Cancer biology focuses on the mechanisms that regulate the spread of cancer. This can include the study of cell growth, the transformation of normal cells into cancer cells, and the spread, or **metastasis**, of cancer cells.

Check Out My Original [Paper](#): “Purinergic Signaling in Peripheral Nervous System Glial Cells”



QR code that links to the original publication

Citation: Patritti-Cram J, Coover RA, Jankowski MP, Ratner N. Purinergic signaling in peripheral nervous system glial cells. *Glia*. 2021 Aug;69(8):1837-1851. (PMCID: PMC8192487).

Research At A Glance: This article is a review, it summarizes our knowledge of a particular topic. In this review, we address specific ways that cells communicate with each other and how that can control cell function. We focus on a type of molecule called **purines**, which are located outside of the cell. When **purines** bind to the cell, they can cause changes in how the cell functions and how it communicates with other cells. To make this change happen, the **purine** must bind to a specific type of chemical structure called a **receptor**, which is located on the outside surface of a cell. When the **purine** binds to a **receptor**, it can trigger a change in how that cell communicates with other cells. When this happens, it is called **purinergic signaling**. Our review focuses on **purinergic signaling** and how it affects a specific cell type in the body called **glial cells**. **Glial cells** surround our nerve cells to provide the support and protection that they need to work properly. Our nerve cells transmit information across the body. They help us to interpret tactile information, like touching a door knob, help us to control muscle contractions, and play a role in how we experience pain. In our review, we focus on a particular type of **glial cell** called **Schwann cells**.

In this review, we provide a summary of all the known **receptors** that **purines** can bind to. We refer to these receptors as **purinergic receptors**. We also provide a summary of the molecules that turn on to block those **receptors**, a summary of all the **receptors** that **purines** can bind to in mouse **Schwann cells**, and explain how they work. The nervous system is made up of two parts, the **central nervous system (CNS)**, which includes the brain and the spinal cord, and the **peripheral nervous system (PNS)**, which connects the rest of the body to the **CNS**. In our review, we discuss which **purines** might be found in the **PNS**. We review the role of **purinergic signaling** in several diseases and how it may impact how we experience pain. We conclude the review by arguing that scientists should focus on **purinergic receptors** when we develop drugs to treat diseases that impact the **PNS**.

Highlights: In this article, we provided a summary about how **purinergic signaling** happens in normal nerve cells (Figure 1), how **purine molecules** can impact tumors (Figure 2), and how **purinergic receptors** can regulate pain (Figure 3). Each figure below gives a summary of the main points made in our article. Figure 1 shows what happens in a normal nerve cell. When nerve cells receive an electrical signal, the **axon** of the nerve cell will receive and send the signal to other nerve cells, muscles, and glands. The electrical signal triggers the release of different types of **purine** molecules. These **purines** bind to **purinergic receptors** on the surface of **Schwann cells** to trigger cell responses. **Schwann cells** will perform different functions based on which type of **purinergic receptor** becomes bound by the **purine** molecule.

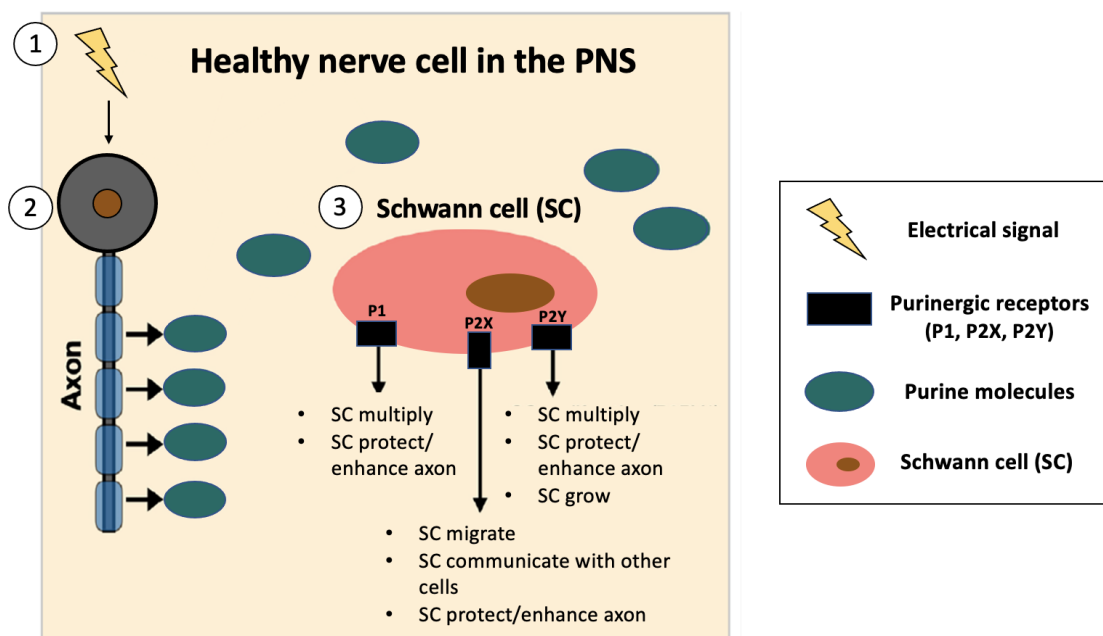


Figure 1. Purinergic signaling in a normal nerve cell in the **peripheral nervous system (PNS)** in three steps: 1) the nerve cell is stimulated by an electrical signal, 2) **purine molecules** are released, and 3) **purine molecules** bind to **purinergic receptors** to control how **Schwann cells** function, grow, and multiply. *Figure adapted from Patrilli-Cram et al. 2021.*

Figure 2 shows the roles of **purine molecules** in tumor cells when they are located in the **PNS**. Tumors have many **purine molecules**. These **purine molecules** activate **purinergic receptors** in the immune cells inside the tumor. The immune cells will then respond and contribute to fight tumor growth.

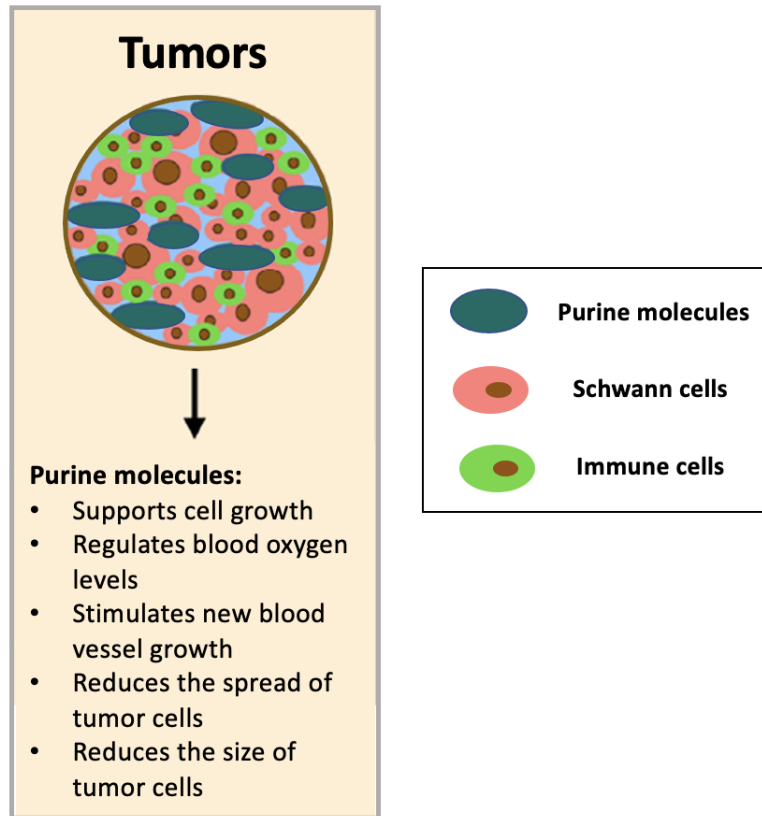


Figure 2. The role of **purine molecules** in peripheral nerve tumors. *Figure adapted from Patritti-Cram et al. 2021.*

Figure 3 shows the roles of **purine molecules** in regulating our pain response. **Purinergic receptors** have different roles in pain. Some help alleviate pain and inflammation, while others produce the pain sensation itself. We still need more research to clarify the role of **purinergic receptors** in pain.

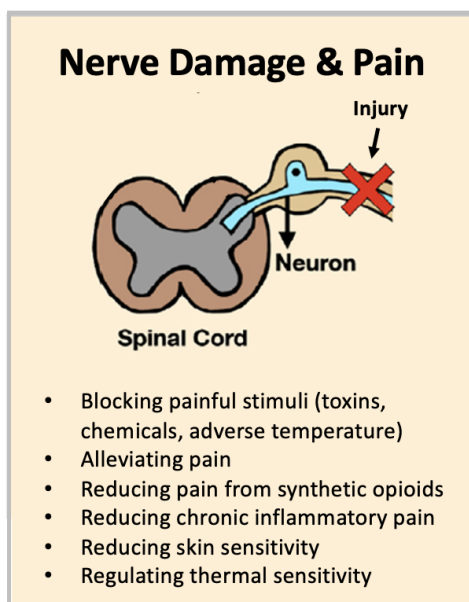


Figure 3. The role of **purinergic receptors** in the regulation of pain. *Figure adapted from Patritti-Cram et al. 2021.*

What My Science Looks Like: As part of this paper, we did an experiment to identify the **purinergic receptors** found in mouse **Schwann cells**. We isolated the **Schwann cells** from mice and performed a laboratory technique called **reverse transcription polymerase chain reaction (RT-PCR)**. RT-PCR allows us to count how much DNA is in a sample. In this case, we wanted to know which **purinergic receptors** were in mouse **Schwann cells** and how abundant they were.

Figure 4 shows the results of this test when we were looking for one type of **purinergic receptor**, **P2X**. Recall that **P2X** receptors help **Schwann cells** to communicate with other cells, migrate, and protect the **axon** of the nerve cell (Figure 1). The x-axis in Figure 4 shows each **P2X** receptor we found and the y-axis shows the **cycle threshold (CT)** value. The **CT** is the number of cycles required for the DNA to be detected in our sample. If a **CT** value is low, this means that there was more DNA in our sample because it took fewer cycles to be detected. So, in this case, a low **CT** means that the **purinergic receptor** was more abundant in our sample. As you can see, the **P2X** receptor “P2RX4” was the most abundant in mouse **Schwann cells**, while “P2RX1” was the least abundant. Our results are interesting because we can now give scientists a specific list of **purinergic receptors** that are present in mouse **Schwann cells**. This list can provide scientists with insight on how these receptors might impact how **Schwann cells** function in diseases that affect the **peripheral nervous system**.

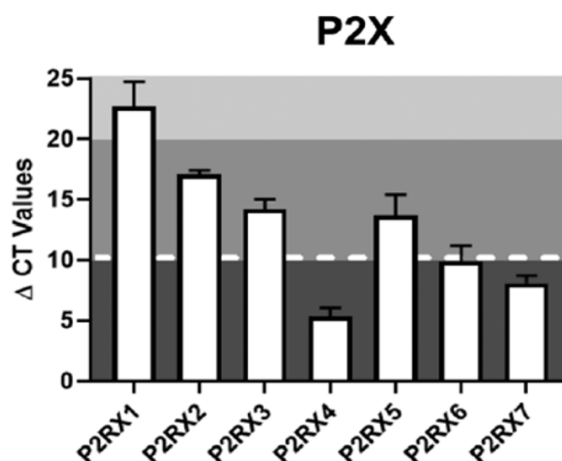


Figure 4. P2X purinergic receptors in mouse **Schwann cells**. We found that the following **P2X** receptors are expressed in mouse **Schwann cells**: P2RX2, P2RX3, P2RX4, P2RX5, P2RX6, P2RX7. Any receptor below the white dotted line was considered to be of high abundance in our sample. *Figure adapted from Patriitti-Cram et al. 2021.*

The Big Picture: My research is important because it can help scientists develop therapies for patients that suffer from diseases that impact the nervous system. Currently, over 100,000 Americans suffer from **neurofibromatosis type 1 (NF1)**. Patients with **NF1** have an increased risk of developing tumors (**neurofibromas**) in the **peripheral nervous system**. **Neurofibromas** can cause nerve damage and can compress vital organs. They are tumors composed of many types of cells that are not working properly. One type of the cell that plays a very important role in **neurofibroma** development are **Schwann cells**. **Schwann cells** are specialized cells that surround all the nerves in our body. In healthy humans, **Schwann cells** help to support nerve function. In **neurofibroma** patients, **Schwann cells** do not function properly and will multiply uncontrollably. This leads to the development of **neurofibroma** tumors. To date, there is no cure for this disease. Therefore, the main goal of my research is to understand how these **neurofibroma** tumors form and develop therapies for patients that suffer from this disease.

In our lab, we use mice to study **NF1**. We use mice because the genetics of mice closely resemble that of humans. Mice develop **neurofibroma** tumors in similar places in the body and at a similar rate. In both humans and mice, **Schwann cells** are at the center of **neurofibroma** formation. They express many different **purinergic receptors** and it's important for scientists to understand the role of these receptors so that we can learn about how **Schwann cells** function in the body. In our review, we clarify and organize the body of research on this topic. Our research can help scientists understand how **purines** impact diseases of the nervous system.

Decoding the Language:

Central nervous system (CNS): The CNS consists of two parts, the brain and the spinal cord.

Cycle threshold (CT): The CT is a way to express the abundance of DNA in a sample during an RT-PCR reaction. Each time the DNA is amplified, this can be considered one cycle. If many cycles are required to detect the DNA, then there is a small amount of DNA in the sample. If

very few cycles are required to detect the DNA, then there is a large amount of DNA in the sample.

Glial cells: Glial cells are cells in the nervous system that do not produce electrical impulses. They make a fatty substance called the myelin sheath, which wraps around nerve fibers to insulate them and increase the speed at which electrical impulses are conducted. They also provide support and protection for neurons.

Metastasis: Metastasis is the spread of cancer cells from the place where they first formed to another part of the body.

Neurofibroma: A neurofibroma is a type of nerve tumor that forms soft bumps on or under the skin.

Neurofibromatosis type 1 (NF1): Neurofibromatosis type 1 is a genetic disorder that causes tumors, called neurofibromas, to grow in peripheral nerves.

P2X: P2X is a type of purinergic receptor located at the cell membrane that gets activated when a molecule called adenosine 5'-triphosphate (ATP) binds to the receptor. When ATP binds to P2X receptors, molecules that were outside the cell can then move inside the cell. These molecules are sodium, potassium, and calcium and are essential for any cell to function properly.

Peripheral nervous system: The peripheral nervous system is the nerves outside of the brain and the spinal cord.

Purine molecules: Purine molecules are made up of carbon and nitrogen atoms. When the human body produces them, they are called endogenous purines.

Purinergic receptors: Purinergic receptors are a family of molecules or receptors that are found in the cellular membranes of almost all mammalian tissues.

Purinergic signaling: Purinergic signaling is a type of cell signaling that takes place when a purine molecule binds to a receptor embedded in the membrane of a cell. The bound receptor allows other molecules like sodium, potassium, and calcium to enter the cell, triggering a response that allows the cell to communicate with other cells.

Reverse transcription polymerase chain reaction (RT-PCR): RT-PCR is a laboratory technique used to amplify specific DNA targets. To do so, researchers will add a fluorescent tag to DNA and amplify the DNA in a machine. Each time the DNA is amplified, the fluorescent tag glows and the machine records how often the DNA fluoresces. This technique allows scientists to determine how much DNA is in a sample.

Schwann cell: A Schwann cell is a type of glial cell in the peripheral nervous system that helps to form the myelin sheath around nerve fibers.

Learn More:

Children's Tumor Foundation article about [Neurofibromatosis type 1](#)

New Medical LifeSciences article about [Schwann cells](#)

Other research papers from the scientific literature:

Abbracchio, Maria P., et al. "Purinergic signalling in the nervous system: an overview." *Trends in neurosciences* 32.1 ([2009](#)): 19-29.

Burnstock, Geoffrey. "Purinergic signalling and disorders of the central nervous system." *Nature reviews Drug discovery* 7.7 ([2008](#)): 575-590.

Burnstock, Geoffrey. "Purinergic signalling: therapeutic developments." *Frontiers in pharmacology* 8 ([2017](#)): 661.

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