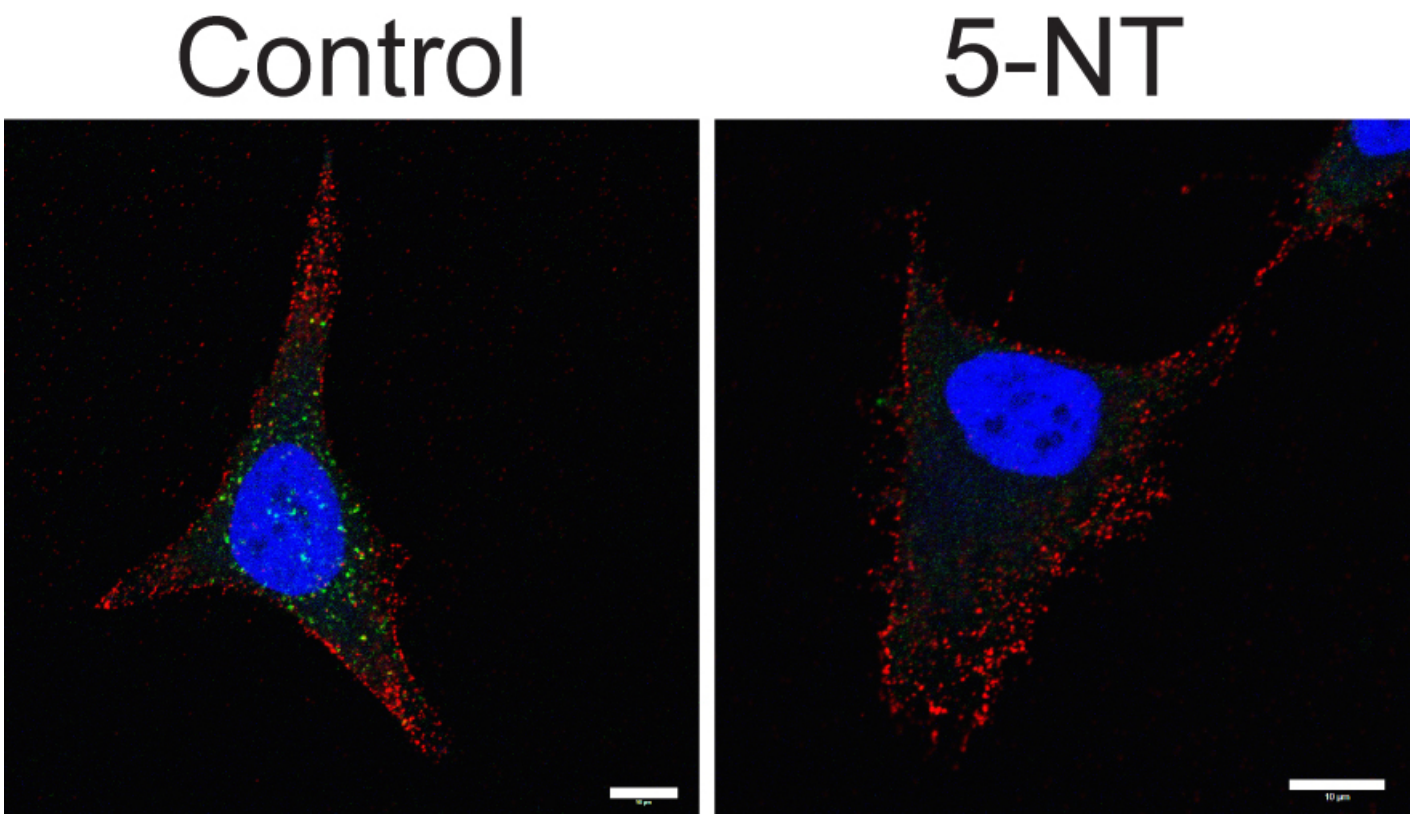
The drug that can inhibit infection by reovirus

Cellular diversity is, to some extent, determined by the molecules present within specific cells. For example, cells that make up the endothelium, the part of blood vessels that come in contact with blood, make specific proteins that are not made in other cells in the body. Viruses are obligate parasites as they need their host to replicate and spread. Viruses have evolved to infect specific cells that will allow them to create more copies of themselves. Some viruses like to infect cells in the brain, others infect cells that make up the immune system, while others infect cells that line the gastrointestinal tract. The goal of our study was to find chemicals or drugs that inhibit the ability of a virus, reovirus, to infect cells. By finding a drug that inhibits infection, in this case a drug that binds cell-surface proteins called serotonins, we can figure out which cellular molecules viruses use to replicate inside of cells, why viruses need these molecules, and perhaps use this drug to prevent disease caused by these viruses. This information also can help us determine why viruses infect some cells and not others, which can help us understand why viruses make us sick.



Control-treated cells on the left and 5-NT-treated cells on the right stained for Early Endosomal Antigen 1 (EEA1, green), a protein involved in the cellular transport network, and reovirus (red). Treatment with 5-NT causes EEA1 to disperse at early times of infection (compare green staining on Control cells to 5-NT-treated cells). Scale bars, 10 um.

In this study, we found that 5-nonyloxytryptamine (5-NT), a drug that binds serotonin receptors, can inhibit infection by reovirus. Serotonin receptors work by grabbing molecules found outside the cell, transmitting a signal to the inside of the cell, and causing the cell to respond to this signal by changing the production of cellular molecules, amongst other things. In the context of reovirus, it was not known why adding 5-NT to cells caused cells to be less susceptible to infection. We show that adding 5-NT to cells before the virus infects cells, but not after, blocks infection. This told us that 5-NT was affecting the ability of the virus to enter cells, but that once the virus had entered cells 5-NT could no longer block infection. Cells have a transport network that allows them to take molecules from one part of the cell to another, much like highways. Viruses have evolved to use one these transport networks to get inside the cell. We show that 5-NT blocks reovirus infection by causing a change in the cellular transport machinery (see the Figure), which affects how fast the virus can productively enter cells. We then show that 5-NT can impair infection by two other viruses, chikungunya virus and mouse hepatitis virus. Our study shows that 5-NT negatively affects the ability of three unrelated viruses to infect cells. At least in the context of reovirus, 5-NT blocks infection by affecting the cellular transport machinery the virus needs to get inside of cells. Our findings suggest that 5-NT could be used to block infection of viruses that infect cells that bare serotonin receptors on their surface.

Publication

Serotonin Receptor Agonist 5-Nonyloxytryptamine Alters the Kinetics of Reovirus Cell Entry.
Mainou BA, Ashbrook AW, Smith EC, Dorset DC, Denison MR, Dermody TS
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