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'Zovaldi' For Zika? Hepatitis C Technology to the Rescue

By Josh Bloom — March 8, 2016

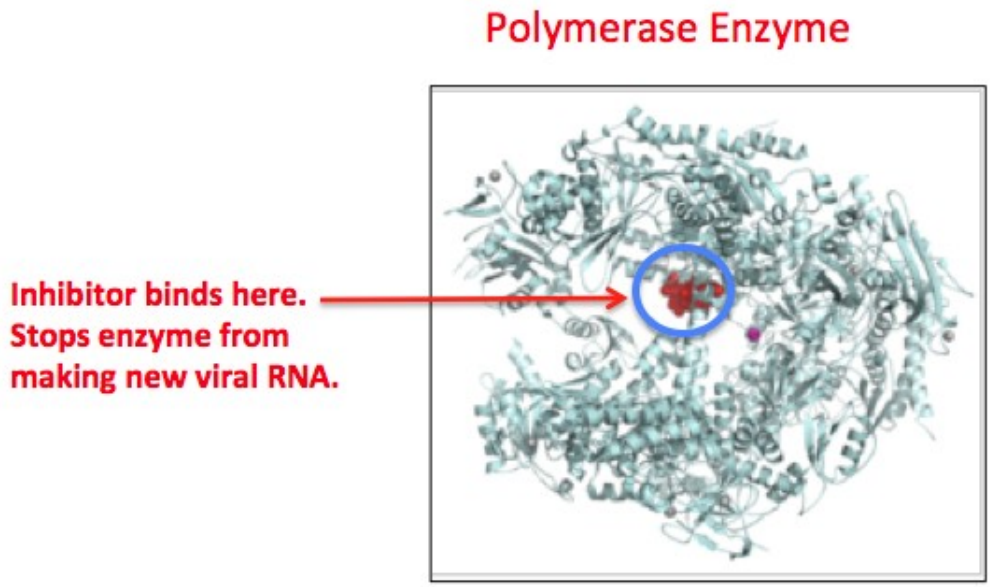
The headlines didn't exactly jump off the page: "BioCryst's Zika drug shows promise in mice." Big deal. All kinds of companies and research labs are feverishly looking at ways to treat or prevent Zika, should it become endemic to large parts of the United States this summer.

But this one stuck out as especially interesting. Why? Because there are two striking similarities in how the company's pre-clinical drug candidate BCX443 works in mice, and how Gilead's Sovaldi — the "$1,000-per-day pill" that finally cured hepatitis C — work.

First, Zika and hepatitis C are both in the flaviviridae family of viruses, which also includes yellow fever, Dengue and West Nile. Second, both drugs work in the same way: by preventing the virus from synthesizing new RNA, thus stopping its replication. This is pretty cool.

A number of RNA viruses carry an enzyme called RNA-dependent RNA polymerase (RdRp), which is mercifully just called polymerase. The enzyme has only one function: to take RNA fragments, which are called base pairs, and make a string of about 600 of them hooked together. This "string" then becomes the genetic material of a newly-formed virus, which will then repeat the process.

This is one of roughly a dozen steps that is required for the virus to replicate itself, and is the same step that Sovaldi uses to bring hepatitis C replication to a screeching halt. The following picture is the structure of hepatitis C polymerase bound to an inhibitor. The method used to solve these structures is called x-ray crystallography (the "Cryst" part of the company's name).



HCV polymerase bound to an inhibitor. Source: Protein Data Bank.

The really important question is: Will this drug work against Zika? Only a fool would predict the chances of success of a drug that hasn't even been tested in a single human, but this one has more going for it than most. Here's why:

1. The same concept worked spectacularly for Sovaldi
2. Zika and HCV are in the same family
3. Unlike other diseases, mouse models of infection are usually pretty good at predicting success in people

Perhaps just as important, I recently consulted [1] vaccine and infectious disease expert, Dr. Paul Offit of the Children's Hospital of Philadelphia (also a former trustee here at The Council). He said that it would take years to develop a vaccine for Zika.

If there is a piece of wood nearby, perhaps you should knock it — and then wish BioCryst the best of luck.

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