

One on One with... Jean Rivier



Rivier's "worry woods" are one of his solutions for alleviating the stress of everyday life.

ON THE DESK IN JEAN RIVIER'S STUDY AT THE SALK INSTITUTE lies a palm-sized piece of ironwood—a talisman that speaks to both his extracurricular and professional passions. The espresso-colored chunk of wood has served, like a worry stone, as an outlet for anxious energy, evidenced by a thumb-wide groove worn into one side from years of rubbing.

Most surfaces in his office are covered with similar wooden objects, such as small figurines—dolphins, owls and other animals—carved by indigenous peoples in Mexico and collected during his visits to the country. Inspired by these works, he started making sculptures himself from scraps of hardwoods found during his hikes in the mountains east of San Diego. That Rivier designed a piece of wood as a stress reliever suggests his hobby aligns with his scientific research, which has focused largely on understanding how stress manifests itself in the body at a molecular level and on searching for a drug to neutralize the effects of pathogens, both physical and emotional.

Rivier has spent his career as a Salk professor studying a class of stress hormones called corticotropin-releasing factors (CRFs). He showed that CRFs are responsible for many of the body's reactions to stress, including disabling the immune system in irritable bowel syndrome (IBS). In an attempt to develop treatments for these conditions, he designed peptide molecules that block CRF receptors. In the process of studying these CRF-blocking molecules, Rivier discovered that they also restore hair growth and even prevent hair loss in mice that normally go bald quite early in life due to overproduction of CRF. He recently founded a company called Sentia Medical Sciences Inc. and obtained exclusive rights to CRF-targeted molecules from the Salk Institute. Aside from his contributions to understanding stress, his work has resulted in eight drugs used to diagnose and treat neuroendocrine tumors, prostate cancer, hypogonadism, pituitary dwarfism and intractable pain.



Rivier acquired a piece of this felled dead cedar tree from Cuyamaca Rancho State Park. He put together a scaffolding to offload the enormous piece of wood, which he carved into a chair and two boards (so far).





*Use nature for inspiration
Use experimentation for creation
Use perseverance for accomplishments
Find pleasure in leisure*

–Jean Rivier

How did you start collecting wooden figurines?

It was during a Christmas trip to Bahia Kino with my family. I saw these striking ironwood figures carved by the Seri Indians, who have been confined for more than a century in two reservations along the western coast of the Sea of Cortez. Inspired by their commercial success, more than 200 Mexican artists started to mass produce such carvings that they sold to tourists—including me, until they ran out of wood 10 years ago.

You carve wood yourself. What's the appeal?

Wood is malleable, but when you shape it, you need to work with the grain. It reminds you that you are part of nature. There is a connection between emotion and touch. There is something atavistic in working with wood. You return to a simpler rung on the evolutionary ladder. We take for granted the beauty of nature, and working with wood brings you back to that. Spiders make beautiful webs and birds make these amazing nests. Modern humans live in highly artificial surroundings, and sometimes we need to return to a simpler time, to get away from the chronic stress of the modern world.

Are we more stressed than we used to be?

I think so. Not necessarily in terms of intensity but definitely in terms of duration, unpredictability and inescapability. Our ancestors had a lot to

worry about, but much of their stress was acute—it came and it went.

On the whole, we now deal with chronic stress that we aren't adapted for. Job pressures, long commutes, economic slumps, mobile phones beeping at us 24 hours a day, you name it, it's nonstop.

When you are stressed, your body copes through the fight-or-flight response, which alters and compromises your metabolism and your immune, reproductive and cardiovascular systems, among other things. When stress is chronic, it puts you at risk for severe anxiety disorders. Our hypothesis is that neutralizing the effects of stress will restore the systems' homeostasis and health.

Why has it been so difficult to develop drugs that effectively target chronic stress?

There are several reasons, in part, because the pharmaceutical industry has focused on the symptoms of stress-related diseases and not the underlying causes. People had high blood pressure, so industry developed beta-blockers. People had acid reflux, so industry developed pH buffers. Also, the pharmaceutical industry stubbornly believed that drugs must be orally active, which excluded the vastly untapped potential of peptides that are commonly destroyed in the stomach.



From left: Joachim Spiess, Catherine Rivier, Jean Rivier and Wylie Vale at the Salk Institute in 1980 after isolating CRF.

It's only in the very recent past that some companies have realized the power of a healthy immune system to beat cancer as an alternative to chemotherapy and radiation. Whereas they came up with “omic” (expensive) solutions, they still ignore the use of CRF peptide antagonists shown to be effective in inducing homeostasis. Despite decades of research, stress has not been conquered. By contributing to the design of potent CRF receptor-selective antagonists that were shown to beat IBS symptoms in early weaned piglets, and preliminarily in humans, I'm confident that sometime in the future, we will have such a drug for treatment in humans.

You started your own company to develop CRF-targeted drugs, right?

That's right. Salk is “Where cures begin” but you have to take the next step. I founded Sentia to take the CRF antagonists we developed to the clinical trial stage. We worked with Salk's Office of Technology Development on filing patents and obtaining licensing. The next step is finding investors and testing the drugs in clinical trials.

In the meantime, how do we cope with our “age of anxiety” in today's world?

In my view, eating right, exercising, practicing yoga, meditating, being hypnotized and having many friends are examples of ways to cope. Psychotherapy may be helpful. I will keep up woodworking. I like to say that ‘worry wood whittles stress away.’ 🪵



Bottles of different forms of atresin, a class of CRF-antagonist drug candidates that Rivier developed to target the body's stress system.