

# Tetrodotoxin and Homer Simpson

by Frank Deis

In the second season of The Simpsons ('90-'91) the episode "One Fish, Two Fish, Blowfish, Blue Fish" (#7F11) features a trip to a sushi restaurant. Lisa complains that the family has fallen into a rut (Meatloaf Night, Pork Chop Night) so they go out to eat at "The Happy Sumo." The restaurant has a karaoke bar, where "Richie Sakai, an anesthesiologist" sings "Gypsies, Tramps and Thieves." Rich Sakai is actually the producer of this episode. Bart and Lisa perform the theme from the movie "Shaft."

Meanwhile Homer is trying everything on the menu. The problem arises that he orders Fugu, the blowfish, during an interlude where the master sushi chef is visiting with Mrs. Krabapple in the parking lot. The lowly assistant sushi chef attempts to dissect out the toxic parts (liver, other viscera, and skin) but has had no experience. When the master comes back, he is horrified and explains to Homer that he may have just eaten "poison." "No need to panic – there's a map to the hospital on the back of the menu!"

The scene with Dr. Hibbert is amusing, but the prognosis (no pain for 24 hours, then "your heart will explode") is unrealistic. Tetrodotoxin blocks neurotransmission by stopping up the Voltage Gated Sodium Channel, to which it binds with "great avidity." The  $K_i$  (dissociation constant) is about 0.001 mM which is to say 1 nM (page 358, Berg/Stryer V). As pointed out in class, the positively charged guanidinium moiety enters the channel, but then of course the rest of the molecule can't fit through the hole, so it acts like a cork in a bottle. Numbness, paralysis, convulsions and death occur within 4 to 6 hours.

The puffer fish (*Fugu rubripes*) is important in Molecular Biology research. Dr. Sydney Brenner selected it as an important species to sequence because it has one of the smallest genomes of any vertebrate. It is essentially "all genes" compared to the human genome which is cluttered with "junk" and repeating DNA between the genes. Comparing our genome to the *Fugu* genome makes it much easier to find the functional human genes.

Tetrodotoxin also figures in the film, "The Serpent and the Rainbow" (1988) about zombies in Haiti. The plot comes from a book written by botanist Dr. Wade Davis suggesting that the half-dead state can be brought on with the help of that poison. This idea is controversial.

It is difficult to find sushi restaurants in New Jersey which serve Fugu. I found it on a menu in Somerville. The menu listing said "Danger!" and the waitress wished me "good luck!" when she served it. When cooked it tastes very much like chicken breast. I used to catch blowfish in the Chesapeake Bay, and we would take them home and cook them with no thought of the potential toxicity. There have been no cases of confirmed poisoning from the Atlantic pufferfish (*Spheroides maculatus*) but there are reports that extracts of that species were highly toxic in mice.