

The kingdoms of Carl Woese

Larry Gold^{a,b,1}

^aSomaLogic, Boulder, CO 80301; and ^bMolecular, Cellular, and Developmental Biology, University of Colorado Boulder, Boulder, CO 80309

Carl Woese is dead. He was diagnosed with pancreatic cancer in late June, learned that it was inoperable, lived for several months in Urbana, IL, and died at home in December. He was 84. We will miss him for a long time.

I met Carl in the summer of 1961. He was working at General Electric in Schenectady and had just arrived from Yale, having been hired as a biophysicist. He had purchased all of the stuff of a biophysicist: spectrophotometers, a Model E centrifuge, and more. All of those things were in their original cardboard boxes, never to be unpacked (had it been up to Carl, they would still be in their boxes). I was 19, he was 32, and the mentoring began.

From the first moment one felt Carl's quiet, his strength, his determination to solve something that mattered; he had no interest whatsoever in the next (obvious) experiment. At that time, Carl was thinking about coding and wondering if the universal genetic code was a frozen accident or a chemical inevitability. His work led from coding, through the ribosome (including his wonderful ratchet mechanism, a published model for how to get from RNA alone to a prim-

itive translational apparatus, a model that used three nucleotides per amino acid and had wobble built in), and in an astonishingly creative burst, to the notion that ribosomal RNA contained the crucial lineage information for all of biology.

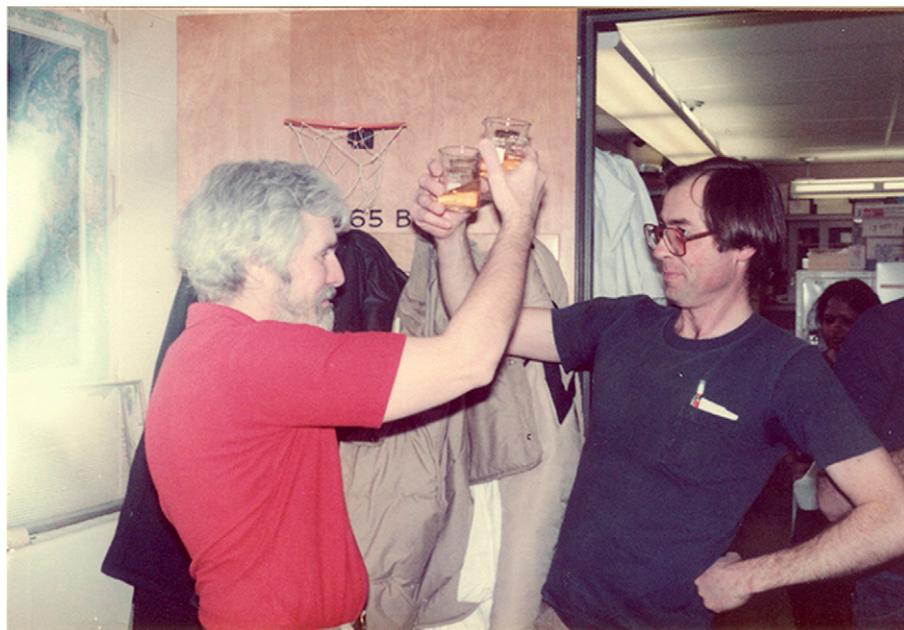
Carl had integrated his fundamental understandings that life had to have evolved through the translational apparatus, that the ribosome was thus ancient, and that the sequences of ribosomal RNA were going to be the right metric to use to follow evolution. Carl used the primacy of translation as the breakout event for life to identify the most likely candidate for a descent marker, and then had the further sense to focus on ribosomal RNA rather than ribosomal proteins. He pursued his idea productively for roughly 50 years. (Absent Carl's work, the avalanche of sequences we now collect would have been difficult to organize into something coherent; today we have no difficulties with sequence organization.)

Entire genomes are not really descent markers, and certainly neither is biochemistry. The replication and transcription ap-

paratuses throughout the three kingdoms are far more varied than the translational machinery, which is immensely conserved. Carl knew that RNA and DNA polymerases and all their associated factors were not ancient and he would never have focused on those wonderful machines; Carl sought the most ancient nucleic acid he could identify, an RNA that was part of the key breakout event for life. I am sure that Carl felt that the later choice of DNA was a consequence of the earlier evolution of RNA into the translation apparatus.

Carl contemplated deeply the pre-Darwinian/prespeciation threshold and also the later moment during which speciated creatures inhabited one of his three kingdoms to survive for the long haul. He was a huge proponent of lateral gene transfer in that pre-Darwinian moment. I always thought that Carl's interest in biology was aimed primarily at the time before and during the breakout of the three kingdoms. Yet Carl would not wonder out loud why there were three kingdoms: why not two or four, or even one? I would ask Carl and he would dismiss the question. I still wonder about the answer, but I guess we will have to sort that out without his help. Ribosomal RNA became *the* descent marker, and Carl's genius was not dependent on the number of kingdoms.

What Carl accomplished in his life was extraordinary. The arguments about his contributions took the form of asking if he was as important as or more important than Watson and Crick, or Darwin (or Wallace, as Carl would have interjected). Many people felt strongly that Carl ought to have won a Nobel Prize. I once wrote about Tom Cech and his Nobel Prize (which he richly deserved), and I concluded that there are so many great contributors and so few prizes that the task of the Nobel Committee is hopeless. Although Carl wanted—as do many others—to have been a recipient, it was not to be. Carl felt somehow that anointment by the Nobel Committee would mean that the heavyweights admired his work, something he craved. Even though he noticed what people thought about his work (which always surprised his friends), he was driven by the work and not the reward. Carl also enormously enjoyed just talking with young



Friendship in the Kingdom: Carl Woese and Norm Pace in 1981.

¹E-mail: lgold@somallogic.com.

scientists. He loved their open minds and their freedom from conventional thinking. He collected students around him his entire life; I was lucky to have been one. Carl was a mentor until the end (Fig. 1).

Carl carried an impish sense of humor, with a warm laugh that would light up a room. He didn't tell jokes (although in the early moments at General Electric he did recite bawdy limericks), he let his Jewish molecular biology friends tell jokes for him, which we did as an obligation. Carl played small jokes on people, with an acute sense of pleasing the people he loved (many people were picked up at the Urbana airport by a big white limo): there was always a feeling that he was honoring his friends. On one of my trips to Urbana a group met me at the gate (ah, the old days, *at the gate*. . .) with a gift: a black T-shirt that simply said *Ficananda*. Carl was, I think (and only for a while), *Evolveananda*, a lover of evolution. I never knew how Carl knew that I love fresh figs.

Sometime around 1988 I tried to hire Carl at the University of Colorado in Boulder. I was a departmental Chair and, like all

Chairs, I wanted to improve our department. In my mind Carl was the answer to that quest, and I invited him to visit and to give a seminar. He came, and during his talk he pointed to an "oligo spot" on a slide and said something like "this spot, the sequence AUUCCUCCUUAUACAAUAA-UUCCUAACUCUUAAG (I just made that sequence up as poetic license), is found in all small ribosomal subunit RNAs," at which point the audience tittered because he rattled off the exact sequence from memory. Carl heard the tittering and sternly admonished the audience to "not laugh at ribosomal RNA sequences because they are sacred." Carl felt called to his work. Even two decades ago the notion of a "calling" was out of the ordinary. Today that notion is further away, and that is part of what Carl taught us and part of why we are diminished by his death. Carl was the perfect anticareerist. We all ought to mentor away from careerism, as Carl did.

In his last weeks Carl talked about his fear of death and his inability to decide if he believed in some kind of spirit or energy;

maybe Carl did move to Boulder without telling us. He understood the existential predicament but he died without resolution, as far as we know, as do most people.

How can Carl remain a mentor for us? He might have said to follow your passions, study what you must, surround yourself with good people who like to giggle and work hard, respect the history of science and thought, read all of the time (but ignore the most recent trends), pay attention for a lifetime to your calling, and be respectful of the lineages that got us here. For the Institute for Genomic Biology he left in Urbana, and for the hopes of medicine and biology as a value for society, it would also be wise to remember that Carl liked technology. After all, he did do Sanger RNA sequencing when most of us were afraid the tanks would explode! Carl hated technology that had no deeper purpose than showing off—he hated show-offs—and he loved the sacred. Carl was dedicated—always—to important questions and, like the physicist that he was, he had no difficulties keeping those thoughts in the very front of his brain.