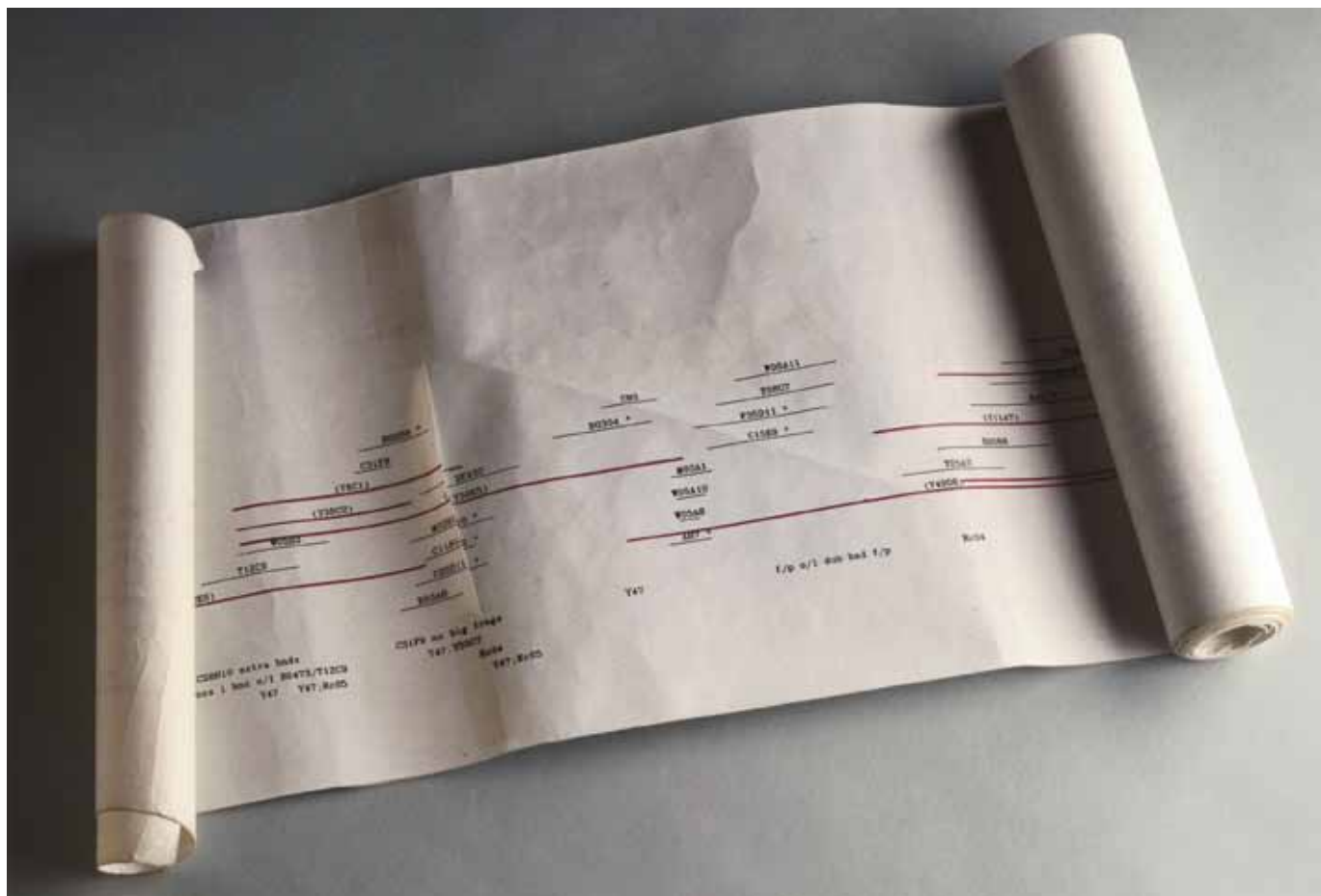


C. elegans Physical Map, circa 1989



By the 1980s, Sydney Brenner’s “worm project” was in full swing. Brenner and his crack team of researchers at the Laboratory of Molecular Biology (LMB) in Cambridge, UK, had already constructed a detailed genetic map of the nematode *Caenorhabditis elegans* and described the worm’s embryonic and nervous system development in exquisite four-dimensional detail. What was missing, however, was an efficient way to isolate the genes for molecular analysis.

To address this problem, Alan Coulson and John Sulston developed a high-resolution “fingerprinting” technique to line up DNA fragments cloned using hybrid plasmid vectors called cosmids; by 1984 they had successfully assembled a physical map that spanned about 60% of the worm genome. Bob Waterston of Washington University in St. Louis, who spent a sabbatical at the LMB in 1985, then devised a different approach to complete the map. Together with Coulson and Sulston, he created yeast artificial chromosome (YAC) clones for the worm DNA that linked together all the pieces of the cosmid-based map to achieve near-complete coverage of the genome.

In 1989, the researchers brought their draft of the physical map to the *C. elegans* meeting in Cold Spring Harbor, NY. Coulson printed the map onto hundreds of letter-sized pieces of paper and taped them together to make long scrolls of the worm’s six chromosomes, each around 5.5 to 7.5 meters in length. (Chromosome II is shown here.) “I stuck these, one above another, to the wall right across the back of the Bush lecture theater where poster sessions were held,” he says. Throughout the meeting, researchers came up to the banners to study the short black lines (the cosmids) and the longer red lines (the YACs).

James Watson, then head of the Human Genome Project, was keen to try sequencing model organisms before launching into the human sequence. He saw the map and remarked, “You can’t see it without wanting to sequence it, can you?” Sulston wrote in his book, *The Common Thread*. A meeting was hastily arranged in Watson’s Cold Spring Harbor office, and the rest is history—less than a decade later, the worm became the first multicellular organism with a completely sequenced genome. ■