

I am writing to apply for the Career Scientist Award. I thank the RNA Society for starting this award, because staff scientists contribute a lot to the health, safety, productivity, and creativity of research groups, and it's good to recognize these contributions.

I started as a research technician in Tom Cech's lab at CU Boulder in 1978. We were in an old teaching lab in the Chemistry Building, with soapstone lab bench tops. Tom was teaching a lot, so I was responsible for organizing the lab, ordering supplies, and doing many of the experiments. In the first decade my work was funded by NIH grants, but then in 1988 Tom became an HHMI investigator and I became an HHMI Senior Associate and later a Senior Scientist.

Initially, we were studying transcription of the ribosomal RNA genes in isolated nuclei of Tetrahymena. The nuclei synthesized pre-rRNA, which ran as a heterogeneous smear on gels, but there was also a very sharp band at around 400 nt. I had to learn Southern hybridization to map its position on the gene, and it turned out to be the excised intron. Because RNA splicing was happening in vitro, we switched our attention from transcription to splicing. Of course, we didn't expect that the RNA would be self-splicing. This started a very exciting period in the lab, when I had to learn RNA technology including fingerprinting to chase down the mechanism of splicing. We published the self-splicing paper in Cell in 1982, and then in 1989 Tom got the phone call from the Nobel Committee. He invited me and my family to join him in Stockholm for the very memorable celebration.

All the time we were studying RNA splicing, others in the lab (starting with Dan Gottschling) were working on telomere end-binding proteins in ciliates. Around 1996, Tom asked me to switch to research on telomeres and telomerase, which led me into the world of yeast molecular biology. I worked on a lot of team projects during this period, and I enjoyed working with Joachim Lingner, Christine Chapon, Anita Seto, April Livengood, Elaine Podell and others. The lab began working more and more on human telomerase, and in 2005 I made the switch, learning to work with human tissue culture cells. I have used mutagenesis, biochemistry and cellular assays to help understand how human telomerase is regulated by telomere-binding proteins and how it is recruited to telomeres. This is still my research area today, with emphasis on the CST telomere-binding protein. For example, I performed all the cellular assays for our recent Science paper describing the cryo-EM structure of human CST.

I really enjoy planning and carrying out experiments in the lab, and at the same time I enjoy working with young people and helping them become independent scientists. I've worked with many German students from CU's Regensburg exchange program, as well as undergraduates from the Meyerhoff Scholars Program and HHMI's EXROP program.

I realize that many excellent research scientists will apply for the Career Scientist award, and I am happy to have my application considered along with theirs.