Transfer RNA (tRNA) must interact with a staggering variety of proteins and other RNAs to effect translation of the genetic code into proteins with high fidelity. To fine tune this task, the structures of many nucleosides in tRNA are found to be enzymatically modified in all organisms. Nearly all of the reactions are carried out post-transcriptionally, meaning the modification enzymes have to recognize a specific base in the highly structured tRNA molecule. Many of the reactions are biochemically unprecedented and many of the modifications are linked to human disease states. Our goal is to identify the enzymes and the genes coding for them as well as the chemical mechanism of the enzymatic reaction. Thus, we combine a variety of techniques that range from organic chemistry to biochemistry and bacterial genetics.

Many of the modified bases we study contain sulfur. We recently discovered that the cysteine desulfurase IscS is required for the biosynthesis of all sulfur containing tRNA bases and many enzyme cofactors in E. coli. The mechanism for sulfur transfer involves protein bound persulfides (RSSH) which are rare and unstable.

We have been able to follow the flow of sulfur from IscS to tRNA binding proteins to the tRNA. Current work is directed toward discovering how many protein substrates exist for this novel type of sulfur transfer.

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**Drug Action**


5. R. Kambampati and C. T. Lauhon "Evidence for the transfer of sulfane sulfur from IscS to thii during the in vitro biosynthesis of 4-Thiouridine in Escherichia coli tRNA" J. Biol. Chem. 275, 10727-10730 (2000).
