Abstract: Radical SAM enzymes (1) use a [4Fe-4S] cluster to cleave S-adenosylmethionine to generate the 5’-deoxyadenosyl radical, which abstracts an H-atom from a given rSAM enzyme’s substrate to initiate catalysis. In the maturation of the [Fe-Fe] hydrogenase H-cluster, the radical SAM enzyme HydG lyses tyrosine to generate the CO and CN ligands of the H-cluster of [FeFe] hydrogenase, ultimately building an organometallic Fe(CO)₂CN(cysteine) moiety that incorporates an iron atom derived from a unique 5-Fe Fe-S cluster (see figure) (2-7). How these “synthons” are pairwise introduced into the formation of the H-cluster, along with the molecular and enzymatic origin of the azadithiolate bridge component of this catalytic cluster, are a current experimental focus of the laboratory. We are also revisiting details of the initial radical SAM tyrosine radical reactions (2) and trying to understand the yet unknown details of CN and CO formation and binding to the “dangler Fe” of the 5-Fe cluster with a combination of experiments and computational chemistry.