ASET Colloquium

Structure, Function and Architecture of the FdsABG Formate Dehydrogenase from Cupriavidus nectar

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We have examined the rapid reaction kinetics and spectroscopic properties of the molybdenum-containing, NAD+-dependent FdsABG formate dehydrogenase from Cupriavidus necator and characterized the electron paramagnetic resonance signal of the molybdenum center in its Mo(V) state, demonstrating the direct transfer of the substrate Ca hydrogen to the molybdenum center in the course of the reaction. We propose a reaction mechanism involving direct hydride transfer from formate to a molybdenum-sulfur group of the molybdenum center. We have also examined the ability of the enzyme to catalyze the reverse of the physiological reaction, the reduction of CO2 to formate. Despite reports to the contrary, we find the enzyme kinetically competent to catalyze the reverse reaction. CO2-saturated buffers are found to be superior to bicarbonate in supporting catalysis in the reverse direction, indicating that the substrate in the reverse direction is CO2. Accumulation of formate in the reverse reaction is quantified and found to stoichiometrically account for consumption of NADH. It appears likely that all molybdenum- and tungsten-containing enzymes acting on formate or CO2 operate via the same hydride transfer mechanism and are effective in catalyzing the reversible interconversion of CO2 and formate. Those enzymes such as the C. necator FdsABG formate dehydrogenase that possess cysteine rather than selenocysteine coordinated to the active site metal, are air-stable and have great potential for industrial applications.