Internal proton transfer between an enzyme and substrate is a common feature of many enzyme mechanisms. Likewise, internal proton transfer between the chromophore of green fluorescent protein (GFP) and amino acids on the inside of the beta barrel are important both in the ground and excited state. I will discuss an interesting connection between the proton transfer dynamics in GFP and those in an enzyme, ketosteroid isomerase (KSI), bound to substrate analogs. In both cases there is a tug of war between the protein and bound substrate analog or chromophore that depends on their affinities for a proton and which can be tuned either by changing the substrate/chromophore or the protein. This can be observed in the ground state by optical methods (absorption and IR) as well as by nmr, or in the excited state by time-resolved fluorescence or visible pump-IR probe measurements. In both cases the proton dynamics have important functional consequences.