

During the meeting of the LBMSDG on 29th September 2016, I presented how I had applied mass spectrometry (MS) in my doctoral research on small heat shock protein 27 (HSP27). This protein protects the cell under stress by interacting with partially folded protein substrates, and is implicated in a wide range of diseases from Parkinson's to cancer. It forms highly dynamic and heterogeneous complexes which can be interrogated within the gas phase. Here native MS was used as part of a multi-pronged approach including protein crystallography, ion-mobility MS, molecular dynamics simulations and solution-state NMR to probe the conformations of the HSP27 core domain and measure the effect of an unusual disulphide bond which is formed across the central interface. We found that this bond can act as a 'redox switch' and so modulate the dynamics and protective response of the protein. In my talk, I described how monomer exchange was monitored with MS and quantified the effect of the disulphide bond on the exchange kinetics. Native MS demonstrated the influence of disease-related mutations on the strength of this bond, and ion mobility MS was employed to look for conformational change on mutation following observations in the structural model from crystallography. Finally, native MS was used to follow binding competition between different parts of the protein to delineate the effect of modification on protein association. In summary, MS was a key player within a range of complementary structural biology techniques and provided essential insight on the regulation of an important stress-responsive protein.