Abstract (In English)

Mass spectrometry (MS) techniques are routinely used to probe the structure and dynamics of proteins and protein complexes. Although MS techniques lack the high resolution of data provided by X-ray crystallography, NMR, or cryo-EM, they excel in providing insights into analyte dynamics, structure, and interactions with other components, such as ligands.

This doctoral thesis presents a contribution to the field of structural biology employing and extending covalent labelling approaches, namely Fast Photochemical oxidation of Proteins (FPOP) and oxidation by singlet oxygen ($^1O_2$). These approaches were followed to study the structure, dynamics, and interaction of proteins, nucleic acids, and protein-DNA complexes in solution. Initially, FPOP was used to investigate the interaction interface of FOXO4 and DAF16-DNA response element and to show the possibilities of analyzing such a complex using both 'bottom-up' and 'top-down' approaches. Furthermore, an isotope depletion strategy combined with multiCASI-ECD proved effective in delivering structural information with the highest possible resolution for mapping protein-DNA interfaces. This research showcases how information derived from structural proteomic methods can guide the construction of *in-silico* models for protein-DNA complexes with dynamic structures or interactions, which remain unclear. Moreover, this thesis reports the first adoption of FPOP to induce hydroxyl radical-induced DNA damage coupled to high-resolution MS analysis. By studying damage to double-stranded IRE and FOXO4-IRE complex, we have elucidated the principles of DNA damage analysis by high-resolution LC-MS. By studying a ternary complex consisting of TEAD1-FOXO4-DNA, we have highlighted how FPOP can easily capture even minor conformational changes on DNA upon protein binding. And by MS structural analysis of the protein LOV2, we have further demonstrated that top-down technology is an effective tool for analyzing protein oxidative damage, as shown on a model protein covalently labelled by singlet oxygen ($^1O_2$).

Key words: Structural mass spectrometry, Fast photochemical oxidation of proteins (FPOP), protein-DNA complexes, FOXO4, TEAD1, DNA damage, photosensitizers, AsLOV2.