

NEW STRATEGIES FOR DRUG DISCOVERY – USE OF NON-COVALENT FOURIER TRANSFORM MASS SPECTROMETRY AS PART OF THE PROCESS

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Identifying the therapeutic properties of potential drug candidates remains a lottery process, with a mass-screening approach remaining the favoured method, after many years. Various proposals to intellectualise this approach have been put forward.

The recent increase in the amount of work on protein characterisation provides a useful starting point for this. Beginning with the large number of three dimensional structures in the protein data bank, and complimenting it with the SCOP classification of protein folding, proteins can now be classified into similar groups, defined by their three-dimensional structure.

It would follow that proteins of similar fold would also bind to similar ligands. Our aim is to test this theory using a variety of techniques – including non-covalent fourier transform mass spectrometry. Focusing on the zincin-like fold metalloproteases examples of natural products have been found from the literature that bind to proteins of these folds. Whether these proteins bind to thermolysin, has been tested by mass spectrometry. Results of these tested associations will be presented, along with an assessment of the mass spectrometry technique for this kind of work.