

WEAK AFFINITY CHROMATOGRAPHY (WAC) AS A NEW APPROACH FOR FRAGMENT –BASED DRUG DISCOVERY

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Abstract: Weak Affinity Chromatography (WAC), in combination with mass spectroscopy (MS), is an HPLC method that measures the interactions of analytes to targets such as protein that is immobilized on a high-performance supporting matrix. Based on the retention times of the analytes, affinities can easily be measured of their interactions to target.

Recently, the technology has been introduced and optimized for fragment screening in drug discovery,¹ where affinities in the range from high mM to low μ M can be determined by analysis in one step with a single concentration of sample. WAC-MS is characterized by its cost-efficiency, robustness and ease to use, high throughput and low consumption of target and sample. The WAC-technology can be performed on a standard LC/MS platform and it allows analysis of fragments in complex mixtures.²

WAC-MS has already been applied to a variety of protein targets including proteases, kinases and chaperones as well as challenging ones such as transmembrane proteins. Frequently, hits picked out by WAC correlated well with hits from other screening methods such as SPR,³ NMR, TSA or ITC.⁴ The number of applications is growing both from our and external labs and we are sure that WAC-MS will be an important and complementary tool for fragment-based drug discovery especially when different screening techniques are considered.

References

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