WuXi AppTec

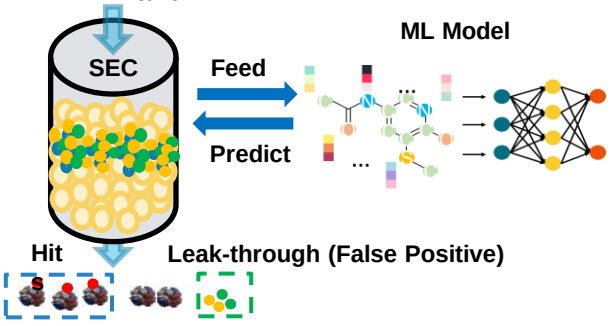
WuXi Biology

Affinity Selection Mass Spectrometry (ASMS)

Abstract: GLUT1 serves as the conduit for transporting glucose from the extracellular milieu into the cell, thereby fueling cellular physiological activities via glucose metabolism. Its overexpression has been documented in various tumor cells, establishing GLUT1 as a promising therapeutic target. During an ASMS screening of GLUT1, a counter screening had been introduced to effectively mitigate false positives arising from surfactants in the protein buffer, and ASMS integrates ML modeling, resulting in a 5.8-fold enhancement in screening efficiency which shorten the process of the screening scope while concurrently reducing costs. Through this strategy, GLUT1 binder had been identified with a Kd of 35.7 μM while inhibits cellular glucose transport activity with an IC50 of 2.3 μM.

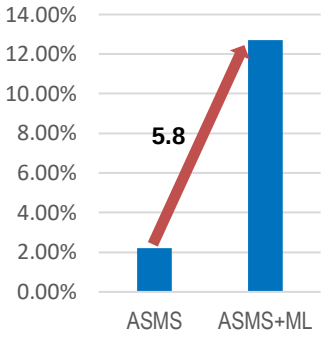
Application of ML-enriched ASMS for Hit Discovery Targeting the Membrane Protein GLUT1

1 **Target - Compounds Mixture**



◆ Schematic representation of ML-enriched ASMS

2 **Primary Hit Rate**



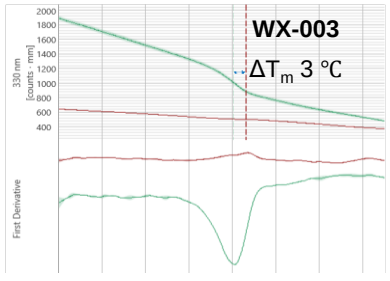
◆ Primary hit rates observed in ASMS and ML-enriched ASMS for GLUT1

3

Method	Hit Confirmation Rate (%)
ASMS	48%
ASMS+ML	49%

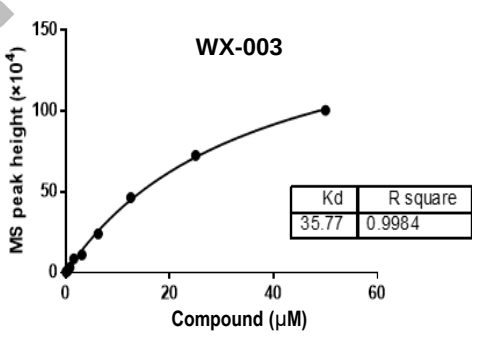
◆ Hit confirmation rates assessed by nanoDSF

4



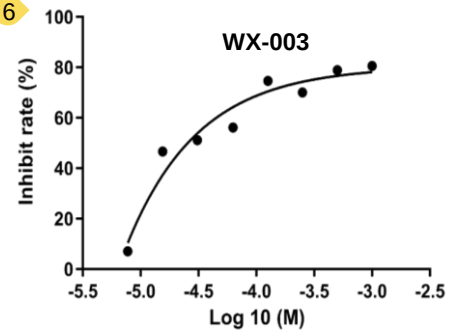
◆ nanoDSF analysis of a confirmed hit

5



◆ Dose-response measurement of a confirmed hit using ASMS

6



◆ Glucose uptake assay conducted for a confirmed hit

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ALIS

Automatically high-quality but elongated separation

Suitable for the most of targets and widely used in the industry

What Makes Our ASMS Service Ideal for You

- ✓ No available assay format required
- ✓ Silent binder identification
- ✓ Tag-free screening
- ✓ Scalable by pooling compound strategy
- ✓ Suitable for exploring possibilities for any challenging target

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