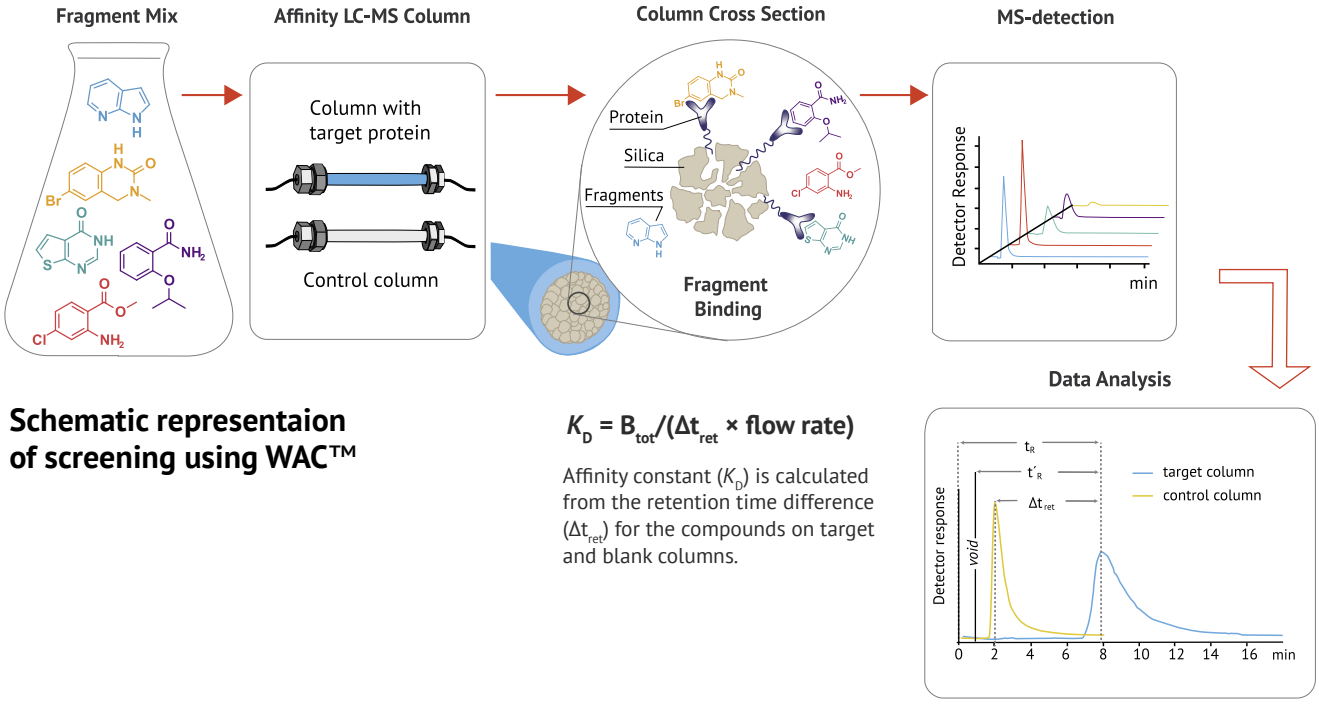
Fragment Screening in Lead Discovery by Weak Affinity Chromatography

WAC™
Weak Affinity Chromatography



Schematic representaion of screening using WAC™

$$K_D = B_{tot}/(\Delta t_{ret} \times \text{flow rate})$$

Affinity constant (K_D) is calculated from the retention time difference (Δt_{ret}) for the compounds on target and blank columns.

WAC™ Facts
- Screening and binding assay in one experiment
- Measure fragment affinity to immobilized protein
- Built-in quality control (MS)

WAC™ Key Advantages
- Robust and accurate (validated against NMR and X-ray)
- Quick set-up and workflow (3 weeks turnaround)
- High throughput (>5000 cmpds/week)
- Low material consumption (<5 mg protein)
- Find mM hits by screening fragments at low concentration (1-5 µM)
- Hit rates from 1% to 20%, (avg 6%)
- Output – High quality data for MedChem

WAC™ Applications
- Screen for novel chemical starting points
- Assess druggability of new targets
- Find differentiated backups in mature projects
- Rescue mode for challenging targets (PPI etc.)

WAC™ Fragment Screen
- In-house collection or client fragments
- Two step milestone process:
  1. Feasibility and set-up
  2. Full screen

Description
- Feasibility using client's reference cmpds
- Client supply protein or protein production included
- Preparation of column with immobilized protein
- Screening in duplicates
- Optional validation of hits using NMR or TSA

Deliverables
- List of hits sorted after Δt_{ret}
- Report with results

Follow-up Activities
Opportunity for rapid fragment hit expansion by accessing our integrated lead discovery platform (medicinal chemistry, computational chemistry, X-ray crystallography, biophysical validation, biochemical and cell-based screening, *in vitro* ADME etc.)

RED GLEAD

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