

# Exploring the bromodomain of SMARCA4 (BRG1) by Weak Affinity Chromatography (WAC™)

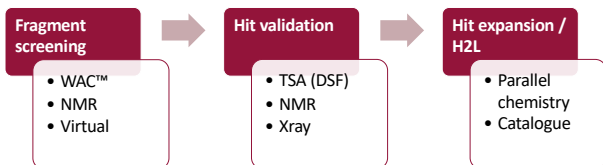
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<sup>1</sup>Red Glead Discovery, Lund, Sweden

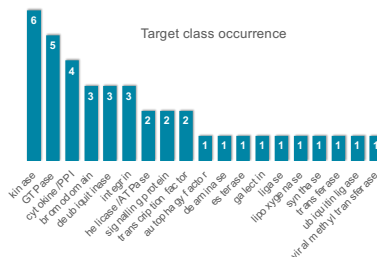
<sup>2</sup>SARomics Biostructures, Lund, Sweden



## Our FBLD platform and workflow

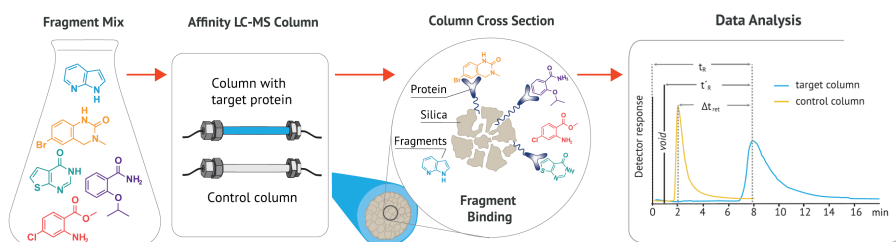


## Completed targets



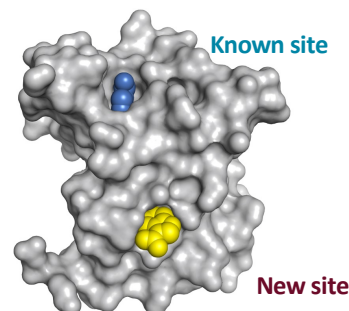
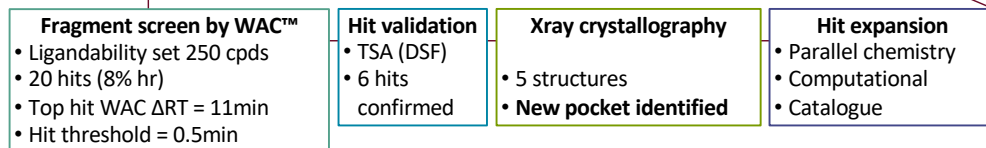
- > 50 FBLD projects over 5 years
- 20 distinct target classes
- Hit rates from 1% to 20%, avg 6%

## WAC™ screening

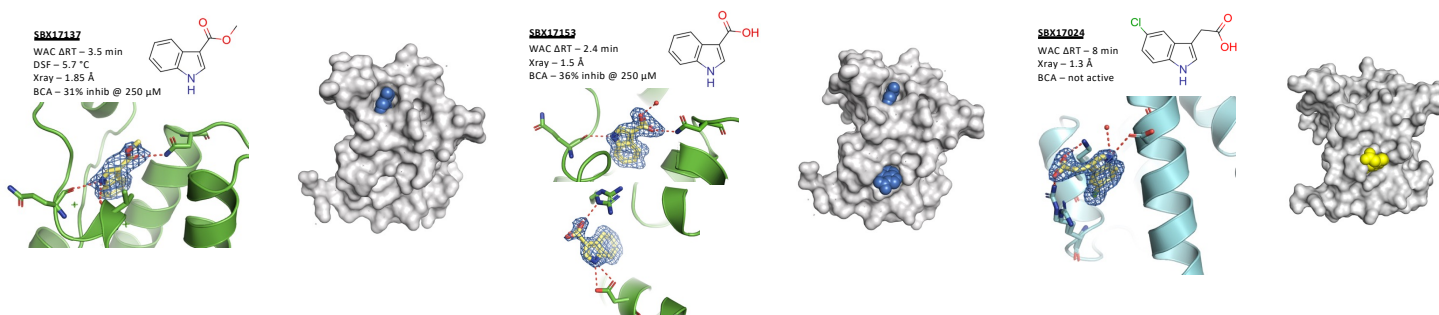


- Protein load – 2-5mg
- High throughput (> 5000cpds / week)
- Affinity range high nM to mM
- MS-detection, built-in QC
- $K_D = B_{tot}/(\Delta t_{ret} \times \text{flow rate})$
- Used along TSA, NMR, X-ray

## SMARCA4 FBLD Case Study



## Xray crystallography: binders to known site identified, new site discovered



## Hit expansion: analogue screening by WAC™, CC, parallel chemistry reveals SAR trends and site-selectivity patterns

ID										
WAC ΔRT (min)	2.4	3.5	6.1	2.1	5.6	?asap	8.2	10.7	3.6	4.2
Xray	Yes, P1&P2	Yes, P1	Yes, P2		Yes, P2		Yes, P2			
BCA %inhib	36% @ 250 μM	31% @ 250 μM							65% @ 250 μM	85% @ 250 μM