

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

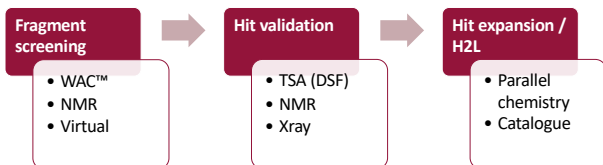
Kirill Popov¹, Stella Timpka¹, Krister Henriksson¹, Martin Welin², Carl Diehl², Kenth Hallberg², Ricardo Ferreira¹, Johan Evenäs¹, Björn Walse²

¹Red Glead Discovery, Lund, Sweden

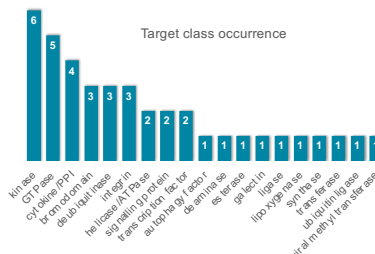
²SARomics Biostructures, Lund, Sweden



Our FBLD platform and workflow

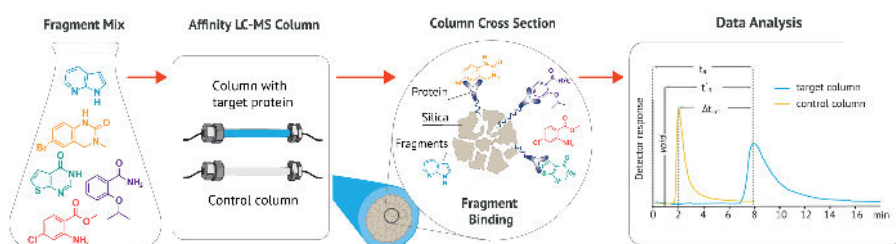


Completed targets



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

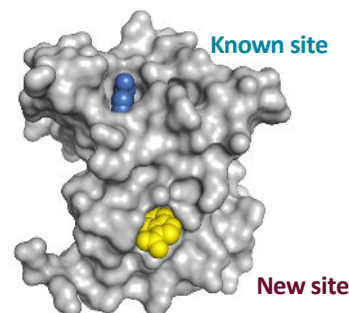
WAC™ screening



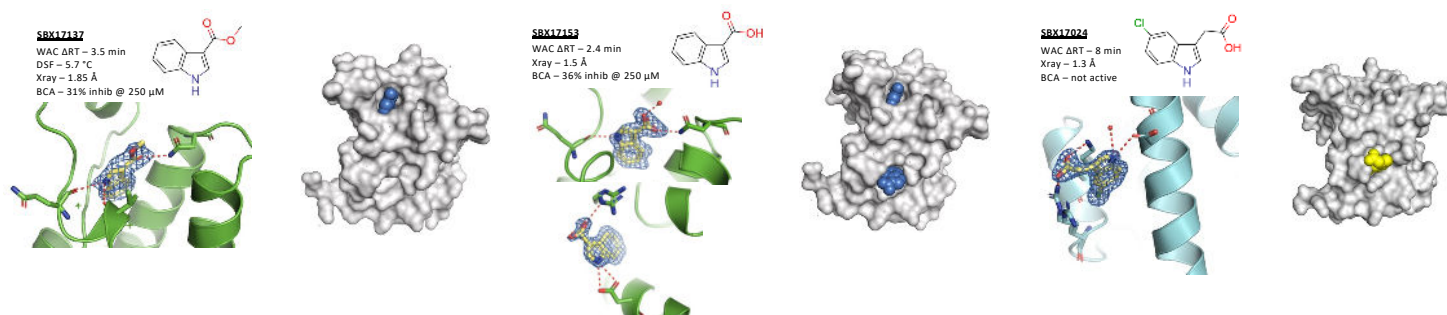
- Protein load – 2-5mg
- High throughput (> 5000cpds / week)
- Affinity range high nM to mM
- MS-detection, built-in QC
- $K_D = B_{tot}/(\Delta t_{ret} \times \text{flow rate})$
- Used along TSA, NMR, X-ray

SMARCA4 FBLD Case Study

Fragment screen by WAC™ <ul style="list-style-type: none"> Ligandability set 250 cpds 20 hits (8% hr) Top hit WAC ΔRT = 11min Hit threshold = 0.5min 	Hit validation <ul style="list-style-type: none"> TSA (DSF) 6 hits confirmed 	Xray crystallography <ul style="list-style-type: none"> 5 structures New pocket identified 	Hit expansion <ul style="list-style-type: none"> Parallel chemistry Computational Catalogue
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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