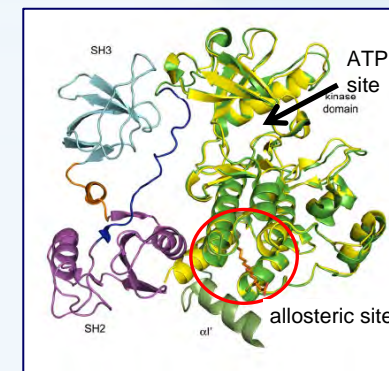


P05 Impact of sp^3 -richer fragments on improving Intracellular activity in c-Abl kinase activation

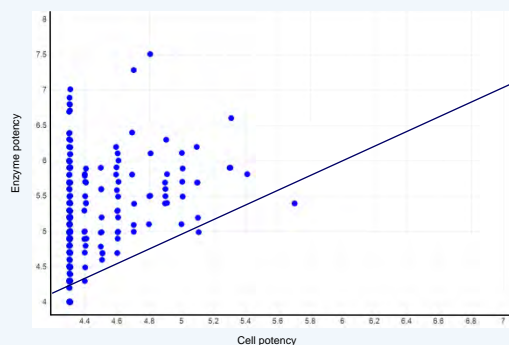
Sophie Bertrand



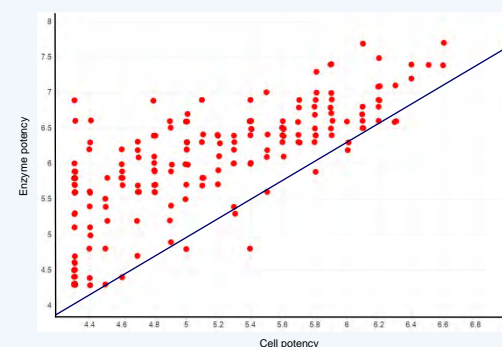
- | **Allosteric direct activation** of the c-Abl protein kinase
 - | **Novel approach** to modulate signalling pathway
- | **Fragment screening** breathed new life into existing sp^2 -rich series and allowed **discovery of sp^3 -richer fragments**
- | **Focus on physicochemical properties** enabled discovery of activators with increased solubility and cellular activity



Initial HTS series



Fragment series



Moderate cell activity: up to **5.7**
High cell drop-off: **> 100 fold**
Poor Solubility – sp^2 character
Flat molecule

Good cell activity: up to **7.0**
Low cell drop-off: **~ 10 fold**
Lower chromlogD
Increased solubility – sp^3 character,
Break crystal packing