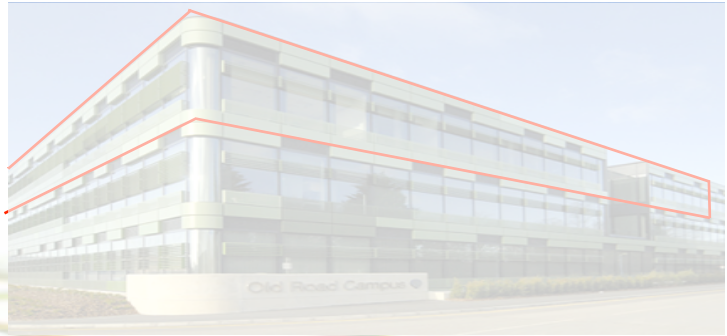
XChem follow-up meeting

Anthony Bradley
Project Leader, Ox XChem
Chemistry and SGC Oxford, Diamond



This meeting

– Go through existing projects – update on progres (Anthony)
  - Focus on NUDT7 progress

– Target (Alice)

– Priorities
  - Computational work
  - Chemistry
  - Screening

Ox XChem Summary

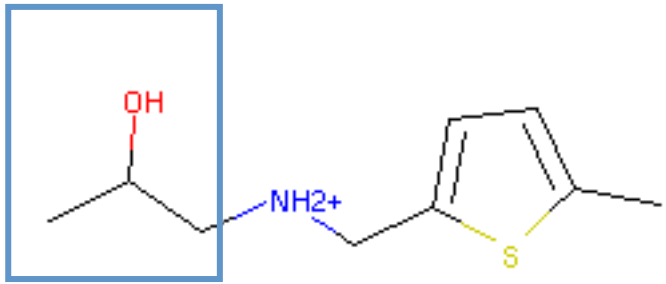
Target	# screened?	Max potency	Active series	# being acq'd	Total cost (£K)
DCP2	40	3.72	3	140	5.0
NUDT7	0	2	5	100	0.0
SHH	20	5.2	2	5	0.5
OXA10	20	2	1	3	0.0
VIM2	20	3.5	1	10	0.0

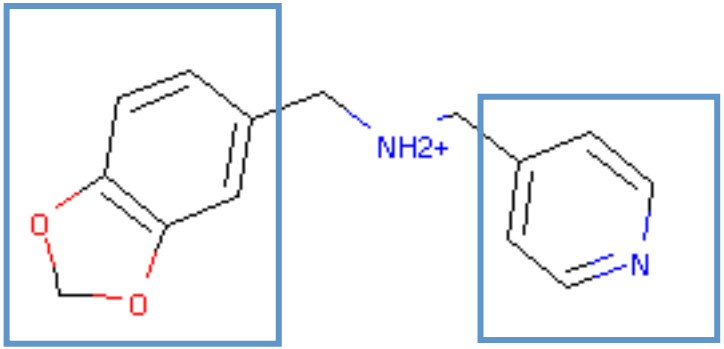
Chemistry Timeline

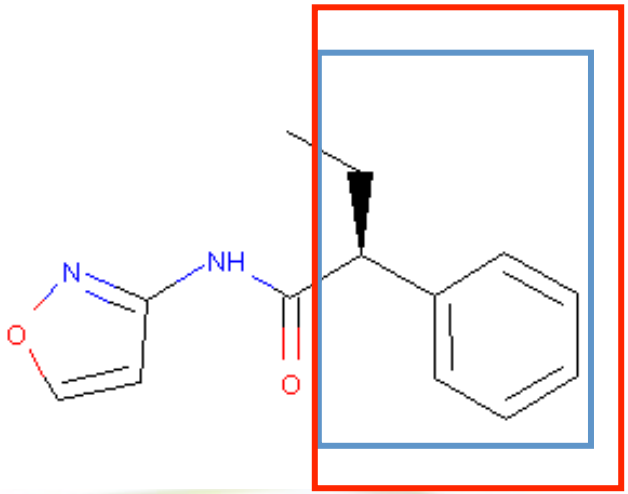
Target	Chemist	22	24	26	28	30	32	34	36	38	40	42	44	46	48	50	52
DCP2	Fudan (24)			L													
	Catalogue (50)			L													
	Enamine (100)					L											
NUDT7	Paul (~50)						L										
	Catalogue (70)					L											
	Ox XChem Cupboard (100)			L													
	Nelson (30)									L							
	Spencer (TBD)						L										
SHH	Tony (5)				Le												
OXA10	Tony (TBD)																
VIM2	Dixon Cupboard (15)				J												
	Tony (TBD)																

CompChem
Meeting
Acquire
Screen

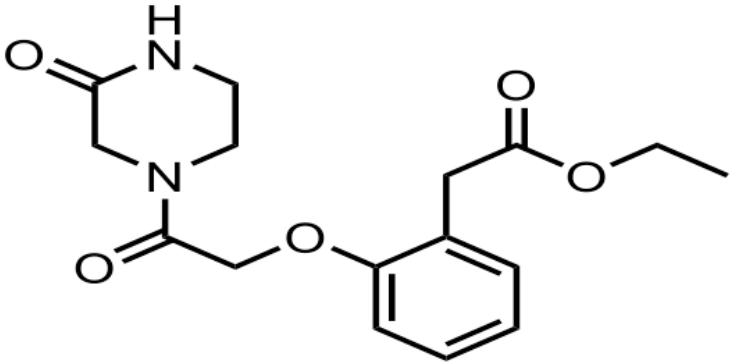
NUDT7 – 2D Exploration

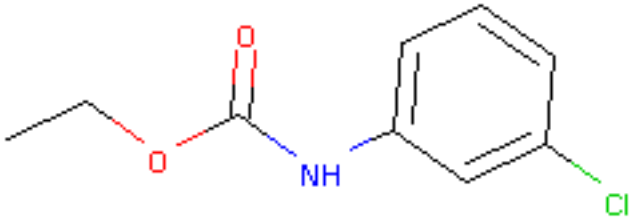


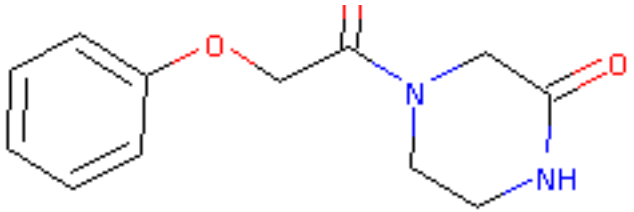


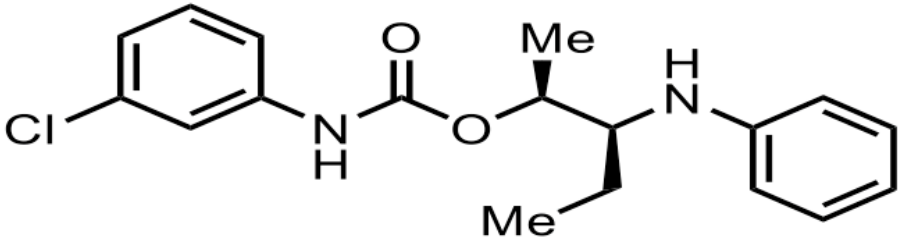


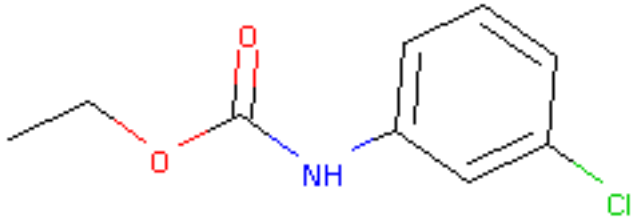
NUDT7 – 2D Linking

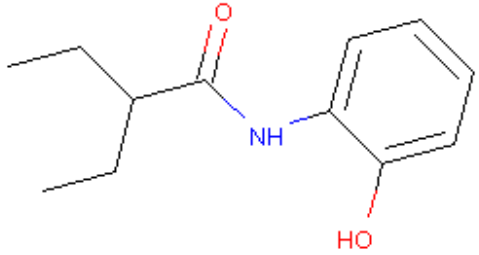








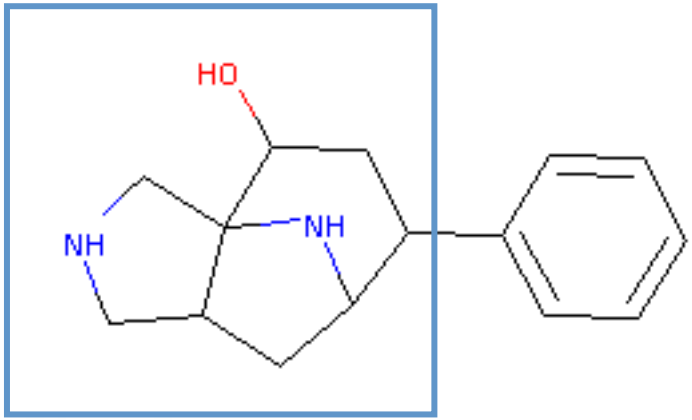




2D - External collabs

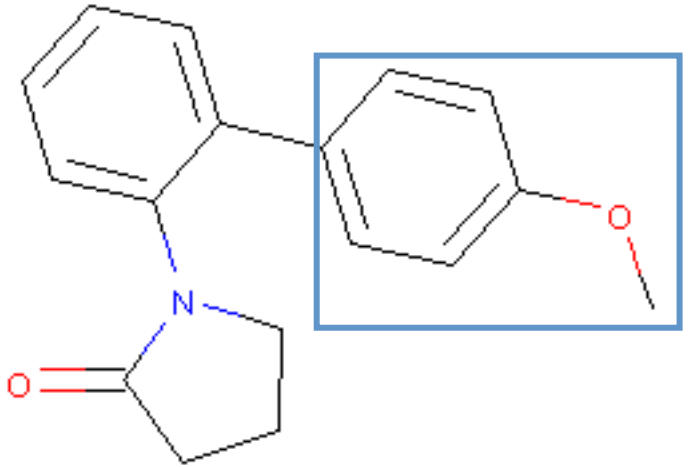
Adam Nelson

- 3D Scaffold – rearrangements – optimize H-bonding

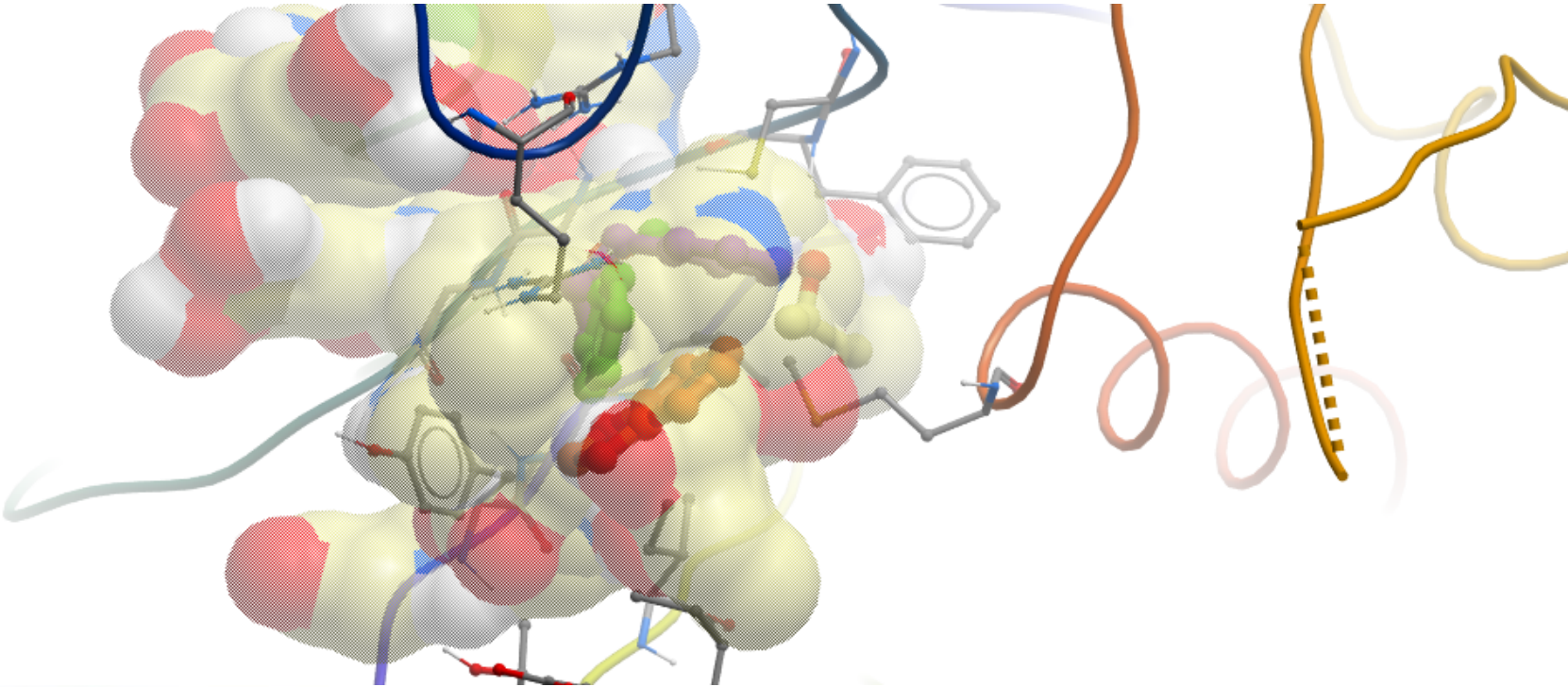


John Spencer

- Novel chemistry – makes methoxy aryl poised



NUDT7 – 3D exploration



Alice

Prioritise

- Remove waters / sidechains for hybrid docking of merged ligands. Put together two molecules. Test on NUDT7 data.
- Automated queries for close analogues of original hits - followed by Docking into all sites
- Fragment merging and joining detection. And library searching for close analogues - pip repo.
- Fragalysis pip repo - just to do pharma, water, residue and site clustering - output as data to be inserted into a database (e.g. JSON) - in the front-end
- Lydia scripted version.
- Script to annotate molecules on Proasis interactions / rank them
- What's the optimal number of items to have to make a good decision. e.g. compound discovery.
- Enrichment factor vs cost to make vs cost to compute plot
- Generic X-Y joiner in SQUONK.Work on fragalysis repo - how would be integratedSwissDrugDesign - add to SQUONK.
- Registering web services. As command line tools. Docker and AWS.