

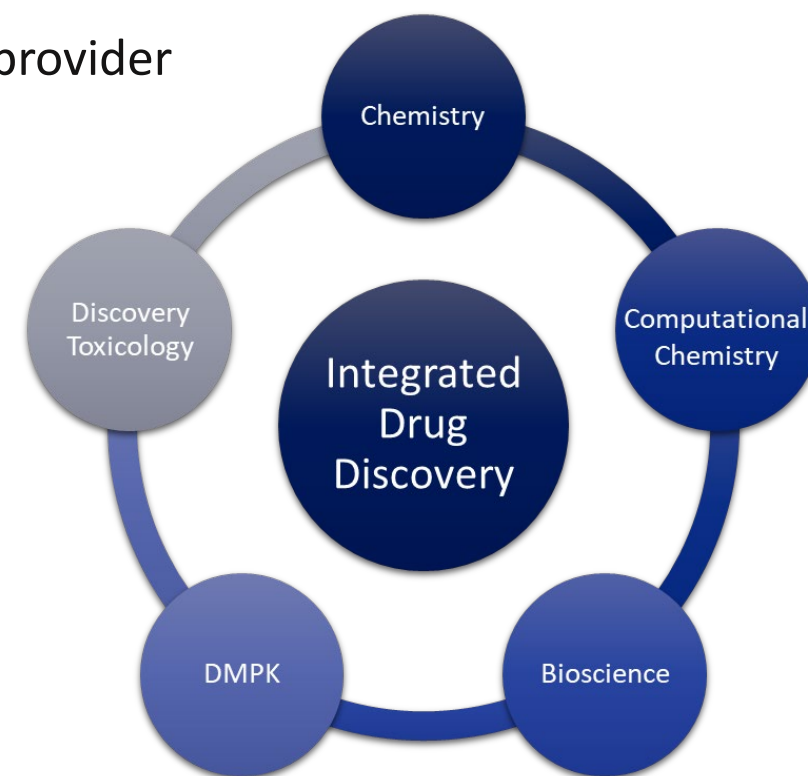
Efficient fragment library screening at Sygnature Discovery by SPR and MST

Dr Chris Tomlinson



Company overview

- Leading independent drug discovery and pre-clinical services provider
- Sygnature founded in 2004 in BioCity Nottingham
- 240 staff
 - 80% of Sygnature's scientists have PhDs
 - Considerable pharmaceutical industry R&D experience
- Private equity-backed company since September 2017
 - Financially stable
 - Investment funding expansion of capabilities and capacity
 - Ambitious future growth plans
- 14 Compounds in the clinic (Phases I and II) since 2011
- 13 Compounds in pre-clinical development (excluding clinical compounds.)



Biophysics Platforms

800MHz NMR

Automated and Cryoprobe equipped



Solution based Fragment screening

Biacore 8K

Multi-channel SPR Reader



Rapid Fragment screening
Binding kinetics and Hit validation

Biacore T200

SPR Reader



Fragment screening
Binding kinetics
Hit validation

Nanotemper Monolith

Automated MST reader



Fragment/MTS library screening
Binding affinities
Hit validation

Nanotemper Monolith Pico

Manual MST reader



Compound profiling
Binding affinities
Hit validation

Biorad CFX384

Thermal shift



FTSA (DSF)
Hit validation

Viscotek

DLS reader



Aggregation
(compound or protein)
Hit validation

MicroCal PEAQ

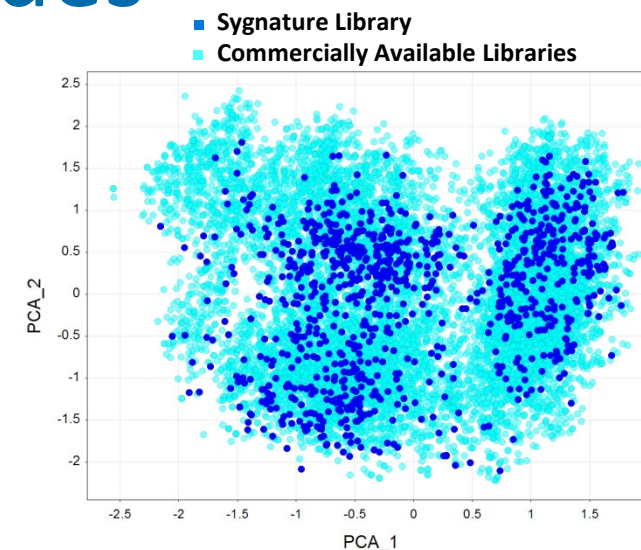
ITC reader



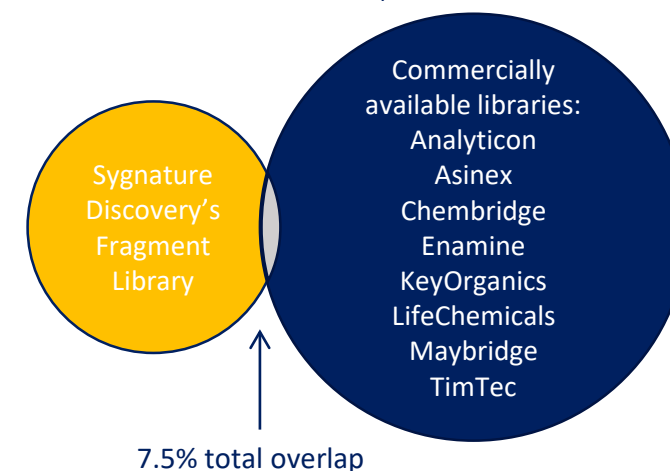
Binding thermodynamics
Binding kinetics
Hit validation

Robust fragment screening cascades

- Proprietary library of >1000 well-designed fragments
- Explore chemical space more efficiently than HTS/MTS
 - Sygnature's fragments combine good physio-chemical properties with feasibility for elaboration
 - 'Clean screened' against 3 diverse targets to remove non-specific binders
 - Library screened successfully against range of targets
- Biophysical techniques at Sygnature for screening at high fragment concentrations to interrogate target
 - Surface plasmon resonance (SPR)
 - Microscale thermophoresis (MST)
 - Thermal shift (FTSA)
 - Ligand-observed NMR
 - Isothermal calorimetry (ITC)
 - Crystallography via Peak Proteins



Representative fragments provide good coverage of chemical space



Come find us!

- Stand E2
 - Dr Scott Pollack (Associate Director of Biophysics and Enzymology)
 - Dr Emily Eaton (Business Development Director)
 - Dr Kris Clark
 - Dr Chris Tomlinson
 - Dr Alec O' Keeffe
 - Dr Jamie Patient (Scientist, DMPK and Physical Sciences)
- } Senior Bioscientists



Enabling Success

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