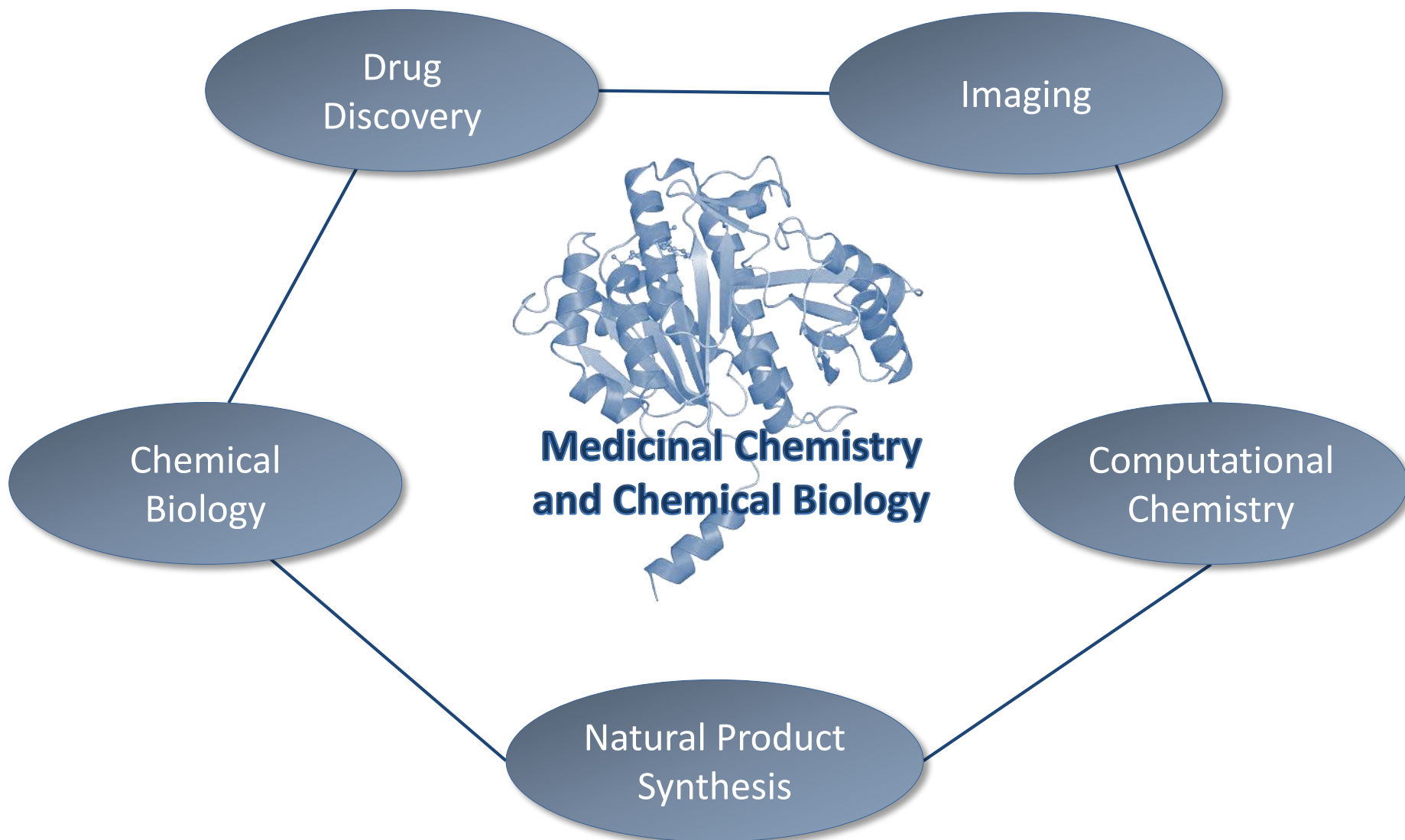


Medicinal Chemistry and Chemical Biology





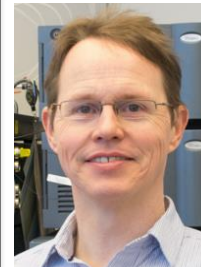
Current Staff



Mike Waring
*Professor of Medicinal
Chemistry*



Bernard Golding
*Senior Research
Investigator*



Ian Hardcastle
*Reader in Medicinal
Chemistry*



Celine Cano
*Senior Lecturer in
Medicinal Chemistry*



Mike Carroll
*Senior Lecturer in
Radiochemistry*



Michael Hall
*Senior Lecturer in
Organic Chemistry*



Agnieszka
Bronowska
*Lecturer in
Computational Medicinal
Chemistry*



Danny Cole
*Lecturer in
Computational Medicinal
Chemistry*

Drug Discovery at Newcastle



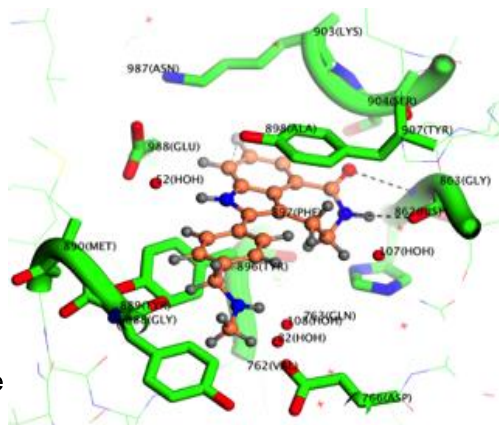
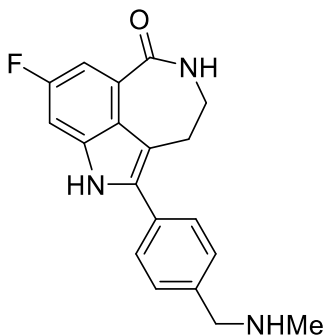
Drug discovery established in 1990

Co-directed by Roger Griffin

Funded by the North of England Cancer Research Campaign, followed by the Cancer Research Campaign and then Cancer Research UK from 2002

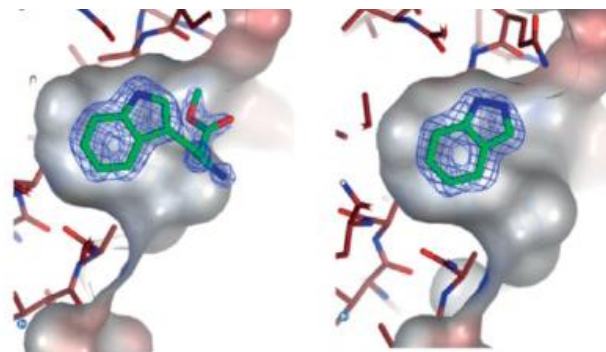
Identified **clinically efficacious compounds**

Rucaparib



- Oral, small molecule inhibitor of PARP1, PARP2 and PARP3 developed for advanced ovarian cancer
- US FDA approval Dec 2016
- REF2014 4* impact case

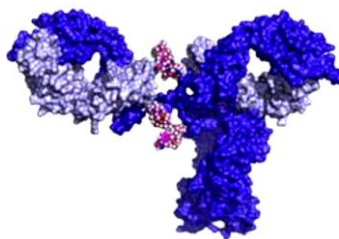
Drug Discovery - Next 5 Years...



- Embedded in CRUK drug discovery network – 1 of 4 CRUK drug discovery centres
- **CR UK Programme:** £5M, 5 years, 2015-20
- **Five year Alliance with Astex Pharmaceuticals**
- Portfolio of 5-7 projects
- **Structure-guided fragment-based**
 - Crystallographic (in-house)
 - Biophysical screening (in-house)
 - NMR (excellent collaborations and growing in-house capability)
- **Additional industrial partnerships** currently being explored

Selective targeting of tumour cells

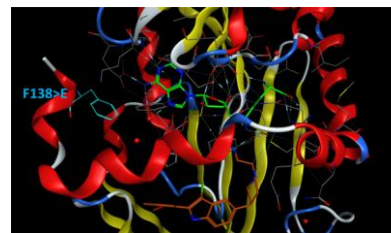
- New warheads for antibody-drug conjugates
- Small molecule targeting approaches



Waring

Chemical probe discovery

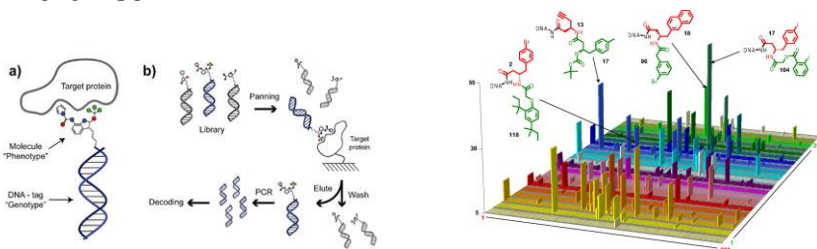
- Chemical tools for novel targets
- Target validation for methyltransferases



Cano, Hardcastle
Golding, Waring

New methods of hit generation

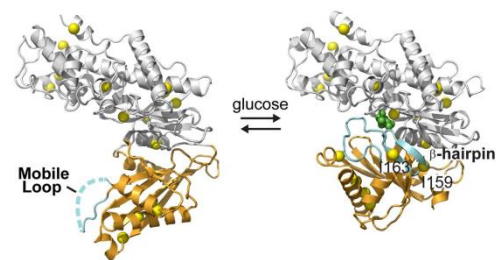
- New approaches to DNA-encoded chemical libraries



Waring

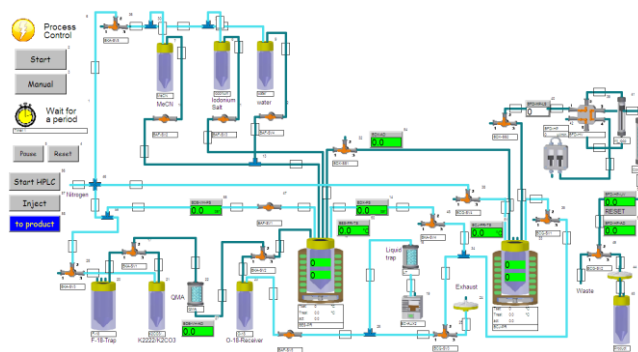
Drug discovery outside oncology

- Probe metabolites for recreational drugs
- Type II diabetes
- Dementia
- Parkinson's disease
- Anti-infectives



Cano, Carroll, Hall,
Hardcastle, Waring, Bronowska

- Multiple automated reaction platforms – batch/microfluidic
- [^{18}F]FDG, [^{18}F]FEC, [^{18}F]MPPF, [^{18}F]FBA, [^{18}F]SFB and new methods
- GMP facility, clean room, MHRA licence application underway

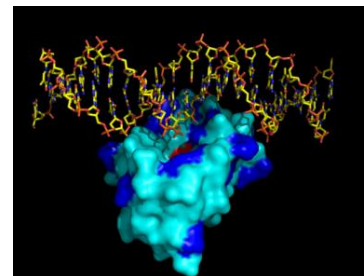
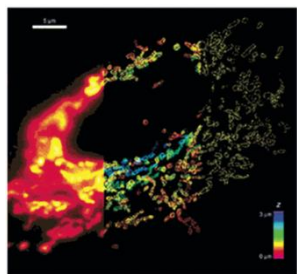


Current activities

- Dementia Platforms UK (network)
- Neuromuscular Diseases
- New methodology - hypervalent iodine precursors to [^{18}F]fluoroarenes

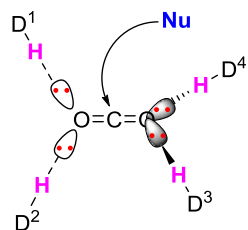
Future plans

- New PET facility at the Campus for Ageing and Vitality
 - 2nd cyclotron (adds ^{11}C), also ^{64}Cu , ^{68}Ga , ^{89}Zr , 18 hot cells/chemistry/QC
- New pre-clinical PET-MR scanner and autoradiography



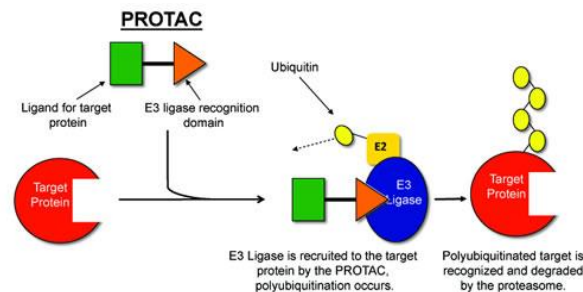
- **Fluorophores** for super res bioimaging
- **Novel antibiotic** natural products: biosynthesis, semi-/total-synthesis and synthetic biology approaches
- Enzymes for **biofilm** disruption
- Chemical modification of **bacterial cell walls**

Hall



- Modelling extant biology – bifurcated hydrogen bonds and application to catalysis and med chem

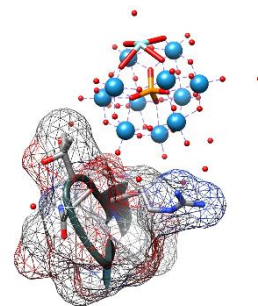
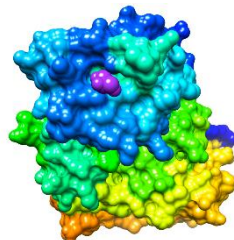
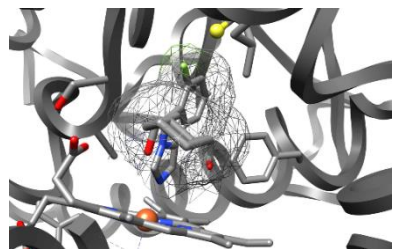
Golding



- New approaches to protein downregulation for target validation

Cano, Hardcastle, Golding, Waring

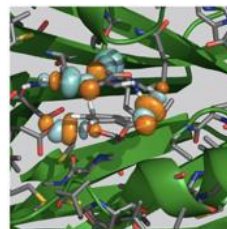
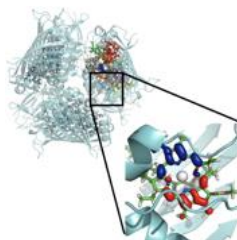
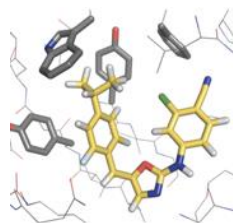
New targets, capabilities and applications:



- IDO1 inhibitors for treatment of dementia
- AHR antagonists
- C3LP
- IDPs as drug targets
- Transient binding pockets
- Halogen bonding in ligand design
- New approaches to irreversible inhibitors
- Biocompatible materials for implantable devices

Bronowska

Application of linear-scale quantum mechanical methods to biological problems:



- Protein specific force field parameterisation for drug discovery
- Optical spectroscopy in a light harvesting protein
- Transition state searching in enzymes
- Protein-ligand binding in metalloproteins

Cole

Potential Synergies Across University



- Expand **oncology** drug discovery programme with NICR (FMS)
 - Deliver CRUK / Astex / Newcastle Alliance portfolio but also develop new industrial partnerships
 - Expand capability in hit finding
- Establish Newcastle as a Centre of Excellence for **Biomedical Imaging** (NHS, FMS)
- Develop programmes in **other disease areas** in collaboration with
 - FMS (Institute of Neuroscience, Institute of Cellular Medicine, School of Pharmacy)
 - SAgE (School of Agriculture, School of Biology)
- Expand activities in **chemical biology** with Centre for Synthetic Biology
- Establish research programme in **computational** medicinal chemistry
- Bid for EPSRC Med Chem Doctoral Training Award



The Newcastle upon Tyne Hospitals



NHS Foundation Trust