Institution: Newcastle University

Unit of Assessment: UoA 8: Chemistry

Title of case study: The provision of novel compounds for the healthcare industry via the Newcastle University based company NewChem

1. Summary of the impact (indicative maximum 100 words)

Newcastle research is the driving force behind NewChem, a Newcastle University spin-out company which provides creative molecular design and synthetic/analytical services for the pharmaceutical/chemical industry. During 2008-2013, NewChem assisted Shire, a global pharmaceutical company, in the quest for new drugs for treating a range of therapeutic indications, including pain, cardiovascular disorders, ADHD and Alzheimer’s disease. Since 2008, NewChem has provided employment for > 60 FTE’s and achieved sales exceeding £1 million per annum.

2. Underpinning research (indicative maximum 500 words)

The application of synthesis to the solution of problems in biology and medicine has been the central tenet of Newcastle University research led by Professor Golding (1983 to date – Professor of Organic Chemistry) in the period 1993-present as exemplified by over 160 research papers. Post-1993, a portfolio of powerful synthetic methodologies applicable to a range of therapeutic targets were developed [P1 – P4]. This work included the accumulation of expertise in selective isotopic labelling [P1], which was subsequently applied to the synthesis of specifically labelled drug metabolites. Studies of some of the most challenging problems in mechanistic enzymology [P1] underpinned key innovations in drug design, most notably leading to the development of the anticancer agent Rucaparib. These fundamental studies created a unique research environment from which emerged seminal discoveries relevant to the treatment of some of the most challenging medical conditions including cancers, cardiovascular diseases, dementias, attention deficit hyperactivity disorder (ADHD) and infections arising from Clostridium difficile. This invaluable experience derived from wide-ranging research achievements led to the creation of prodrugs that are structurally fine-tuned to release their parent drug under either chemical or enzymatic conditions.

Examples of Newcastle research in the context of drug development are:

- Knowledge derived from research requiring selective isotopic labelling [P1] applied to the synthesis of labelled drugs for metabolism studies.
- Fundamental research on the anagrelide metabolite 3-hydroxyanagrelide leading to new anagrelide analogues (e.g. 3,3-dimethylanagrelide, ‘Rafingrelide’) resistant to metabolism [P2] One critical aspect of this research was the application of X-ray crystallography at Newcastle to the identification of a previously unrecognised isomer of 3-hydroxyanagrelide.
- Extensive experience of the synthesis of prodrugs [P3] enabling an array of new prodrugs to be developed.
- Wide ranging nucleoside and nucleotide research [P4] underpinning the synthesis of complex nucleotides for medical detection devices.
- Diverse heterocyclic chemistry exemplified in > 50 research papers since 1993 [e.g. P5, P6].

Key Researchers

Daniele Ciceri (2000 to 2001 – Research Associate)
3. References to the research (Newcastle personnel are italicised)


[P4] *Munter, T; Cottrell, L; Hill, S; Kronber, L; Watson, WP; Golding, BT*, Identification of adducts derived from reactions of (1-chloroethenyl)oxirane with nucleosides and calf thymus DNA, *Chemical Research in Toxicology*, 2002, 15, 1549-1560 (DOI: 10.1021/tx020070e). Research that unravelled the complex adduct chemistry arising from the reactions of a chloroprene epoxide with 2c-deoxyguanosine, 2c-deoxyadenosine, 2c-deoxycytidine, thymidine and calf thymus DNA. First comprehensive study relevant to chloroprene mutagenesis and has been much cited in subsequent work on chloroprene.


* = 3 papers that best indicate the quality of the research

Selected grants


4. Details of the impact (indicative maximum 750 words)

The Newcastle University spin-out company NewChem Technologies, which was founded in 2002, is primarily a drug development company working in association with industrial partners. The company is the route by which the academic research of Golding and his group is commercialised. In 2008, as the result of steady growth, NewChem invested in new laboratories within the School of Chemistry which are adjacent to Golding’s research group, thus enabling continuous and fruitful exchange of information and expertise. In the period 2008-2013, NewChem has provided employment for high quality chemists (>60 FTE) and has achieved annual sales of greater than £1 million, thus making a significant contribution to employment in the North East region [E1].

The impacts of Newcastle University research through the vehicle of NewChem include contributions to the science of the drug anagrelide (Xagrid), a core product of Shire, as well as development of prodrugs of several therapeutic agents [e.g. galanthamine (Alzheimer’s disease), guanfacine (ADHD), meptazinol and oxycodone (pain) [E2, E3]. NewChem developed several customised release mechanisms for prodrugs that aimed to resolve disadvantageous drug properties, e.g. poor intestinal absorption, poor bioavailability due to extensive 1st pass metabolism, high abuse potential, local GI toxicity, colonic delivery etc. According to the Former Head of New Product Discovery (Small molecules) at Shire: “The positive impact of that relationship [NewChem and Shire] on the research output of Shire cannot be overstated and singularly contributed to the development of over 40 patents on potential new drug products” [E3].

Anagrelide (Xagrid or Agyrlin®) which is used to treat the myeloproliferative disorder called essential thrombocythemia (ET) has annual peak sales of $97 million [E4]. Individuals with raised platelet counts have a higher risk of adverse thrombotic and haemorrhagic events. Previous investigations identified a metabolite 3-hydroxyanagrelide, derived from oxidation of anagrelide. Whilst anagrelide and 3-hydroxyanagrelide are similarly potent against ET, the metabolite is nearly 40-fold more potent against phosphodiesterase-III (PDE-III), which causes severe cardiovascular side-effects. Based on prior Newcastle research a synthetic route to 3-hydroxyanagrelide was devised [P2] which made this biologically potent molecule reliably available for the first time and enabled a full determination of its pharmacological profile. An analogue of anagrelide was developed (3,3-dimethylanagrelide, ‘Rafingrelide’) [E4], which retains potency against ET, but has much reduced activity against PDE-III. This compound “has completed phase 2 clinical testing…current estimates of its market potential in the anti-thrombotic market exceed $500 million” [E3 Former Head of New Product Discovery (Small molecules) at Shire]. Phase 2 clinical trials represent an average of $19,300 per patient investment into the drug [E6].

During 2008-2012, a major contribution has been made to the Shire drug guanfacine which is used to treat attention deficit hyperactivity disorder (ADHD) [E1]. Children with ADHD are deficient in normal social skills and lack the ability to focus on tasks. Current sales for the established ADHD drug Vyvanse approach $1030 million per annum [E4]. The alternative ADHD drug guanfacine has been converted into a novel carbamate prodrug. Shire recently invested substantial effort via NewChem in research for new prodrugs for alleviating pain. This has resulted in the development of carbamate prodrugs of meptazinol and oxycodone, which were produced by the synthetic methodologies analogous to those described [P3]. NewChem studies for Shire have also created novel prodrugs of the anti-Alzheimer drug galanthamine [E2]. Shire has requested that the details of these prodrugs be kept confidential but we can disclose “that three compounds (not to be named) that…[NewChem researchers] worked on were nominated for IND [Investigational New Drug] studies (2009-2012) and two of these went into man [phase 1 trials in humans]” [E5, Senior Director Exploratory Projects, Shire]. Phase 1 trials represent on average an investment per patient of $15700 (USD) [E6].

During 2012/2013 NewChem has provided invaluable assistance to two SMEs. This assistance included the synthesis of key intermediates and products that could not be sourced elsewhere. A key step in the synthesis of complex nucleotides for the company QuantuMDX was accomplished.
based on Golding’s knowledge of protecting group chemistry arising from his Newcastle research on nucleosides and nucleotides [P3]. QuantuMDx have “…secured £1.4 million from the Technology Strategy Board ‘biomedical catalyst fund’ for developing a handheld device for rapid tumour profiling…and … a £3.5 million EU FP7 grant for developing a handheld diagnostic test for Malaria…” [E7, Chief Operating Officer, QuantuMDx Group Limited]. In another notable achievement, Golding’s Newcastle research has also assisted the company Glythera in the synthesis of heterocyclic derivatives that are the basis of therapeutic applications. “Based on the success of these studies Glythera has…secured its second tranche of funding of £700,000 from its investors” [E8, Chief Operating Officer, Glythera Ltd.

In all of the projects described above prior Newcastle research on prodrugs, protecting groups, heterocyclic chemistry, nucleosides and reaction mechanisms was critical to success.

5. Sources to corroborate the impact (indicative maximum of 10 references)

[E1] Corroborating contact: Newchem Managing Director


[E3] Testimonial from the Former Head of New Product Discovery (Small molecules) at Shire


[E5] Email from the Senior Director Exploratory Projects, Shire


[E7] Testimonial from the Chief Operating Officer, QuantuMDx Group Ltd.

[E8] Testimonial from the Chief Operating Officer, Glythera Ltd.