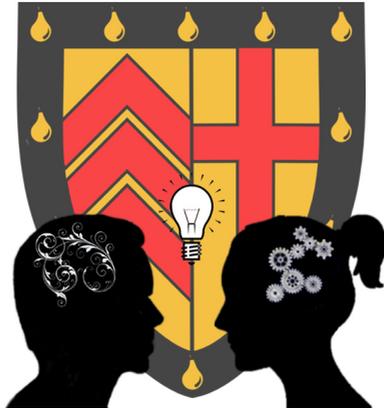


Clare College

Research Symposium

March 12th 2009



"Our purpose is that through their study and teaching at the university, they should discover and acquire the precious pearl of learning."

– Elizabeth de Burgh, Lady of Clare, 1359

Welcome to the second annual Clare College Research Symposium

The symposium showcases the research activities of college members at all levels, from undergraduate, through to graduate and research associate. Our aim is to encourage interdisciplinary learning and a free exchange of ideas between friends and colleagues.

This year's delegates will present their research on a wide range of topics in the Arts and Sciences, during several presentation sessions and a poster session.

We are also fortunate to have two extraordinary keynote speakers, Emeritus Master of Clare College, Professor Sir Bob Hepple representing the Arts and Dr John van Wyhe, a Darwinian Historian, representing the Sciences.

Funding for the symposium was generously provided by the College Research and Scholarship Fund, and the Clare Graduate Society (i.e. the MCR), to whom we are very grateful.

The organising committee,

Scott Newman
Robin McCaig
Mark Schenk

Timetable

The Clare Research Symposium will take place in the Gillespie Conference Centre, off Memorial Court. The poster session will be held in the MCR, Old Court.

09:00 - 09:15 Coffee & Registration

09:15 - 09:20 Opening Remarks

09:20 - 10:20 **Session 1 ~ Sciences**

Adrian Slusarczyk — Part III, Biochemistry

Owen Churches — PhD, Psychiatry

Hayley Thirkettle — PhD, Oncology

10:20 - 10:40 Coffee Break

10:40 - 11:40 **Session 2 ~ Arts**

Robin McCaig — PhD, Law

Candice Kent — PhD, English

Jim Blackstone — PhD, Divinity

11:40 - 12:30 **Arts Keynote Speaker**

Professor Sir Bob Hepple, QC FBA LLD

Emeritus Master of Clare College

12:30 - 13:30 Lunch

13:30 - 14:30 **Session 3 ~ Sciences**

Roheet Rao B — PhD, Oncology

Katie Siddle — MPhil, Biological Anthropology

Elizabeth Batty — PhD, Pathology

14:30 - 14:40 Break

14:40 - 15:40

Session 4 ~ Arts

Anna Tristram — PhD, Linguistics

Johanna Jonsdottir — PhD, International Studies

Rachel Bower — PhD, English Literature

15:40 - 16:00

Coffee Break

16:00 - 17:00

Session 5 ~ Sciences & Arts

Vincent Ho, PhD — Chemical Engineering

Jonathan Birch — MPhil, Philosophy of Science

Gary McDowell — PhD, Oncology

17:00 - 17:10

Break

17:10 - 18:00

Sciences Keynote Speaker

Dr John van Wyhe

Bye-Fellow of Christ's College, Cambridge

18:00 - 19:00

Poster Session & Wine Reception in the MCR

Chris Hindley — PhD, Oncology

Gary McDowell — PhD, Oncology

Lidia Duncan — CRA, Molecular Immunology

Mark Schenk — PhD, Structural Engineering

R. C. Wheeler — Alumnus

Richard Wallbank — PhD, Genetics

Scott Newman — PhD, Pathology

Sinead English — PhD, Behavioural Ecology (Zoology)

Session 1 ~ Sciences

Session Chair: Roheet Rao B (MCR President)

09:20-09:40 Adrian Slusarczyk — Part III, Biochemistry

Engineering New Genetic Codes for Synthetic Biology

The translation of genetic messages into proteins is mediated by one of the most ancient and complex biomolecular machineries, comprising ribosomes, transfer RNAs, and associated enzymes. Recently, it has become possible to alter the genetic code that assigns a chemical meaning to each genetic base triplet. To this end, the enzymes that charge transfer RNAs with specific amino acids for incorporation into new proteins are re-engineered by in vitro evolution.

The expanded chemical repertoire for protein engineering now comprises fluorescent probes, chemical crosslinkers, sugar units, and enzyme inhibitors. In addition to a technological toolkit for researchers, drugmakers and bioengineers, this research promises insights into the constraints which shaped some of the earliest stages of evolution of life on earth by probing the functionality and design of the genetic code.

But incorporating more than one unnatural amino acid at a time remains a daunting challenge, and often the unnatural protein can be obtained only in small quantities. Our laboratory has therefore embarked on an ambitious research programme to transcend these limitations and turn the ribosome into a general polymerization machine capable of synthesizing a wide range of unnatural proteins and biosimilar materials. This talk will explain the strategies used, reveal recent milestones, and look ahead to future goals and applications in biomedicine and biomanufacturing.

Seeing faces where there are none: An event-related potential study

While the face sensitive ERP component, the N170, is reliably larger to faces than other objects, it also varies in amplitude between non-face object categories. One account for this variance is that some objects are perceived as more 'face like' than others and that the N170 is a graded response associated with the subjective perception of an image as facelike.

Method: To test this hypothesis directly, 15 neurotypical adult participants were presented with a series of objects and asked to classify them as 'face like' or 'non-face like' while EEG was recorded. Actual faces were included in the series as a control. Waveforms were averaged separately according to each participant's classification.

Results: The N170 was largest (most negative) to images classified as actual faces and smallest to images classified as non-face like objects. In between these, and significantly different from both, was the N170 to objects classified as face like.

Conclusion: These data are consistent with the view that the N170 is a graded response associated with the subjective perception of facelikeness. The implications of a face processing network that differentiates between non-face objects based on how 'face like' they appear is discussed in terms of signal detection theory. That is, these results imply that the system measured by the N170 has high sensitivity to facelikeness but is not specific to actual faces. This paradigm will be used next with people with autism.

Waxing LYRICal about prostate cancer

Prostate cancer is the most common cancer in the UK and accounts for 1 in 4 diagnoses of cancer in men. Biomarkers are used as a tool to predict cancer risk, cancer progression or cancer outcome. PSA is the current biomarker used to diagnose prostate cancer and well as prostate cancer progression. However, PSA screening detects prostate cancer that would otherwise remain undetectable throughout life. Therefore there is a need for a biomarker that can identify those patients with an aggressive form of prostate which require treatment, from the patients that can live with their prostate cancer. We have shown that LYRIC is a putative marker for poor prognosis of prostate cancer. Human cells are divided into the nucleus which contains the cells DNA, and the cytoplasm where proteins are made. LYRIC location within the cell has been shown to predict the survival time for prostate cancer patients. Patients with LYRIC in the nucleus survive longer than those patients with no LYRIC in the nucleus. Hence, the regulation of LYRIC localisation is important in prostate cancer progression. The cell can direct proteins to different locations through a cellular postal system. Subcellular addresses can be found within a protein such as localisation signals, or proteins can be stamped for delivery to a compartment with a posttranslational modification. We have shown that LYRIC enters the nucleus through an internal nuclear localisation signal and is retained in the cytoplasm through posttranslational modification.

Session 2 ~Arts

Session Chair: Dr Patricia Fara (Senior Tutor)

10:40-11:00 Robin McCaig — PhD, Law

Deceived by False Colours: First World War Historians and the Law of Flags in Naval Warfare

In August 1914, in the opening days of the First World War, the German warship Goeben shelled Philippeville in French North Africa after approaching the town under a Russian flag. In October 1914 the German cruiser Emden entered Penang harbour to attack Allied ships by disguising itself as a British vessel and “flying a flag that was taken for the white ensign”. In August 1915 a Royal Navy decoy ship, HMS Baralong, disguised as an American tramp steamer sank the German submarine U-27; at the same time Allied merchant vessels and passenger liners (such as the Lusitania) were seeking to avoid and confuse the U-boats by displaying the flags of neutral states.

All these instances of the use of false colours have been condemned by certain historians of the 1914-18 War as breaches of the established laws of armed conflict. Allegations that the USA tolerated “unlawful” uses of its flag by Allied ships have also been cited as evidence that President Wilson’s government was biased against the Central Powers even before the declaration of war on Germany in 1917. During the Great War itself the Germans used the Allies’ “illegal” employment of false colours as one of the justifications for ordering the first phase of unrestricted submarine warfare from February 1915, and claimed that, because of the uncertainty resulting from the Allied policy, they could not be held responsible for the destruction of any neutral shipping “mistaken” for enemy merchant vessels.

This paper analyses the historians’ specific criticisms by describing the actual state of the law of flags in naval warfare in 1914 to discover whether a resort to false colours was a war crime or a legitimate ruse de guerre, and examines the relationship between the laws of war on land and at sea. It deals with the definition of perfidy in international law and touches upon wider questions of disguise and the use of enemy uniforms during war.

Intersecting Identities: hybrids in Virginia Woolf's *Mrs Dalloway* and David Garnett's *Lady Into Fox*

This talk examines human-animal hybridization as it appears implicitly in Virginia Woolf's *Mrs Dalloway* (1925) and more explicitly in David Garnett's *Lady into Fox* (1922). It argues that in *Mrs Dalloway* Woolf delivers a complex and equivocal engagement - after a prolonged period of incubation - with T. H. Huxley's *Evolution and Ethics* (1893), an essay in which Huxley highlights the tension between compassion, as human trait, and the animal competitiveness of natural selection. And it claims that Woolf's hybrid undermines simple conceptions of duality in human nature. Just as beastly human behaviour is disturbing, so animals which approach the borders of humanity cause discomfort. This is dramatized in David Garnett's *Lady into Fox* (1922), a novella in which the animal self is brought into uncomfortable proximity to the human self. The talk examines how Garnett makes rhetorical use of the hybrid as a device for generating sympathy for non-human creatures, and it interrogates the ways in which the hybrid is deployed to articulate possibilities of human-animal communion. Both texts reflect a process of simultaneous reaction to ideas from evolutionary theory and the animal welfare movement. Evolutionary theory undermines the mutual exclusivity of human and animal categories, emphasizing the animal within the human. And in counterpoint the animal welfare movement agitates for the recognition of the human within the animal by calling for the extension to animals of considerations previously reserved for humans.

Iconography and the body in the Orthodox theology of Gregory Palamas (1296-1359)

Gregory Palamas, monk of Mount Athos and later Archbishop of Thessalonika, defended particular methods of contemplation that centred on stillness or 'hesychia'. In constructing his defence, Palamas developed a distinction between essence and uncreated energies within God. This distinction allowed Palamas to maintain that a human being may participate in the uncreated energies of God whilst maintaining also that the essence of God is unknowable. The distinction continues to be controversial amongst philosophical theologians in the Western (or Latin) Christian traditions.

This paper takes a different perspective on Palamas's theology by engaging aesthetic categories. A brief visual presentation of fourteenth century iconography will precede analysis of Palamas's iconic interpretation of the Transfiguration event. It will be argued that an iconographic approach to Palamas offers an enriched understanding of his theological epistemology. More specifically, an iconographic approach elucidates the necessary role of the body in contemplative knowledge.

Arts Keynote Speaker - Professor Sir Bob Hepple

Introduced by Dr Patricia Fara

11:40-12:30 Professor Sir Bob Hepple, QC FBA LLD
Emeritus Master of Clare College

The Transformation of Labour Law in Europe 1945-2004

Session 3 ~ Sciences

Session Chair: Dr Anna Philpott

13:30-13:50 Roheet Rao B — PhD, Oncology

Alternative roles of adaptor proteins in prostate cancer

Adaptor proteins act as scaffolding factors for clathrin-mediated endocytosis which affects cell signalling. Akin to signalling enzymes, mutations and/or alterations in the expression of adaptor proteins may dysregulate cell proliferation and migration. One such adaptor, Huntingtin Interacting Protein 1 (HIP1) has been reported to be overexpressed in prostate cancer and a wide range of other tumours. Ectopic overexpression of HIP1 drove fibroblast transformation by perturbing growth factor receptor signalling; in HIP1 null background tumour progression was blocked in transgenic models of prostate cancer (TRAMP). We have previously shown that HIP1 translocates to the nucleus and acts as an androgen receptor (AR) coactivator. Effects on cancer progression may therefore be mediated in the nucleus or at membranes.

To explore the nuclear role of HIP1 we undertook a yeast two-hybrid screen. Two predominantly nuclear interacting partners of HIP1 were identified- an E3 SUMO ligase, PIASx α and a homologue of histone deacetylase 3 (HDAC3). Sumoylation is a post-translational modification which affects subcellular localisation, protein stability, gene transcription and has been described for nuclear as well as cytoplasmic proteins. In silico analyses highlighted eight putative sumoylation sites and two SUMO interacting motifs (SIMs) within the HIP1 sequence. Pulldowns with recombinant GST-tagged HIP1 domains (coiled coil and C-terminal domains each containing a SIM) showed that these regions interact with SUMO1. A number of high molecular weight species of the C-terminal ILWEQ domain of HIP1 were seen using an in vivo *E. coli* SUMOylation system. Whilst HIP1 is an AR coactivator in reporter assays, we found that this effect was abrogated by mutating the principal sumoylation sites within the AR (K386 and K520).

In conclusion we have found that HIP1 is both a SUMO binding protein and a SUMO substrate. The contribution of HIP1 to AR coactivation potentially requires AR sumoylation at K386 and K520. Ubc9 has previously been reported to be overexpressed in prostate cancer and to act as an AR coactivator. Daxx is a SUMO-binding protein which acts as an AR corepressor. Future research will focus on changes to the composition of AR transcription complexes when HIP1 expression and sumoylation status is altered.

Relict Populations or Recent Adaptations? Exploring Genetic Variation in the Philippine Negritos

The evolutionary history of the indigenous populations of Southeast Asia and Oceania remains among the most enigmatic topics in the debate surrounding the settlement and prehistory of this diverse region. The Negritos, indigenous peoples of Southeast Asia who share a particular set of phenotypic characteristics, have traditionally been understood to be relict populations whose ancestry traces back to the earliest period of human occupation of the region in the Late Pleistocene. The phenotypic similarities of these scattered, fragmented groups, both to each other, and to African populations, in addition to their foraging subsistence strategy, has led many to propose an ancient common origin of Southeast Asian Negritos. However, evidence from linguistics and classical polymorphisms have instead suggested that the Negritos are more closely related to neighbouring non-Negrito populations, raising the possibility of multiple instances of recent independent evolution of the Negrito phenotype in Southeast Asia. In light of these conflicting interpretations, I will present the results of ongoing research into genetic variation in Philippine Negritos asking to what extent this evidence can be understood to support, or refute, the traditional view of the Negritos as an ancient relict population.

Chromosome rearrangements in cancer

The chromosomes of cancer cells are often highly rearranged, and this has been shown to play an important role in the development of cancer. Amplification of certain regions of chromosomes 8 and 11 is a feature of many breast cancers, with the two regions often being co-amplified to form a complex, intermingled structure. Finding the exact nature of the rearrangements which lead to the complex amplified structure is difficult using traditional cytogenetic methods. The recent development of next-generation sequencing offers a new way to map these rearrangements, but brings new challenges in data analysis and verification.

We have taken a model breast cancer cell line, MDA-MB-134, which has an example of the complex amplification, and produced a library of genomic fragments which were used for high-throughput paired-end sequencing. We have aligned these short reads to a reference genome, and the reads which map as expected based on the genomic fragments were used to derive high-resolution copy number data. The reads which map to the reference genome in unexpected locations were used to characterize the chromosome rearrangements, including inversions, translocations, deletions and amplifications which occur within the amplicon.

Session 4 ~ Arts

Session Chair: Mr Robin McCaig

14:40-15:00 Anna Tristram — PhD, Linguistics

Variable agreement in French: some preliminary results

Agreement has been a topic of interest in various fields of linguistics for many years, in the past primarily as a means of investigating syntactic phenomena or of testing syntactic theories (to do with the structure of sentences), and also as means of shedding light on morpho-syntactic processes (to do with the internal structure of words as well as sentence structure). My research takes a slightly different approach again, in using agreement as a means of investigating sociolinguistic variation (i.e. how different groups of people in society use language in different ways, and what this tells us about them). I focus on agreement with a specific type of structure: collective nouns and quantifying expressions, which in many languages can vary between singular and plural agreement. For example in English:

"The team has/have had a good season this year."

"The government is/are undecided as to how to proceed on this issue."

In French, this variable agreement occurs with a variety of nouns denoting quantities, e.g.:

"La majorité des données a/ont provoqué peu de problèmes"

"Une partie des employés a/ont eu une augmentation de 4%"

This variation can be exploited in order to help understand patterns of sociolinguistic variation, and therefore social variation more generally: fundamentally, where there is a choice between two or more options, the (mostly unconscious) choices people make can be revealing in a number of ways, especially if any of these choices are prescriptively disallowed. It might tell us something about social class, for example, or about the differences between the ways men and women use language, and if we look at different age groups, we can start to understand the processes of language change, a major area of interest in linguistics.

This paper will present some results from a pilot study I have conducted over the last couple of months, which I am using to help me construct the methodology for my main fieldwork, to be conducted in France in the coming months.

Europeanisation of the Icelandic political system

Europeanisation studies generally focus on the impact of the European Union (EU) on domestic political systems or the adaptation of national structures, processes and policies in response to the demands of the EU. The EU's competences have greatly expanded over the years and empirical work on its member states has demonstrated that the EU can induce significant domestic change. Iceland is one of the few countries in Western Europe that has (until now) chosen to remain outside of the European Union. Nevertheless, it is closely linked to the Union through the European Economic Area (EEA) Agreement. Through this agreement Iceland has become a participant in the EU's policy process which has had a substantial impact on the content of public policy in Iceland as well as on the structure and behaviour of political and administrative organisations. In my PhD I take a qualitative case study approach in order to examine the Europeanisation of the Icelandic political system, both in terms of uploading, or Iceland's ability to project its policy preferences at the EU level, and downloading, i.e. the adoption of EU policy at the national level.

Epistolarity as formal and political intervention: examining the letter exchange in J. M. Coetzee's *Disgrace* (1999)

This paper is part of a wider research project which examines how the epistolary form is used in contemporary literature to forge new creative and humane spaces, in critical response to the contemporary theoretical emphasis on difference. In its persistent demand for communication across borders, and by simultaneously engaging with contact and separation, the epistolary form contests ideologies based on extreme separation or the systematic classification of difference, such as the apartheid regime or the so-called 'clash of civilisations.' More specifically, this paper will examine the single letter exchange in J. M. Coetzee's novel *Disgrace* (1999), and consider this as a formal literary intervention which engages with the wider political concerns of writing within post-apartheid South Africa. Although the epistolary form is not commonly associated with this novel, by focussing on the letter exchange I aim to open up a discussion of how epistolarity and dialogue might be useful in negotiating difficult political situations.

Session 5 ~ Sciences & Arts

Session Chair: Dr Maciej Dunajski (Graduate Tutor)

16:00-16:20 Vincent Ho — PhD, Chemical Engineering

Magnetic Targeting of Mammalian Cells for Bioengineering Applications

The ability to precisely locate mammalian cells offers great potential for numerous applications. One method for manipulating cells uses magnetic fields to position magnetically labelled cells. This technique is effective and substrate-independent. Current labelling techniques usually require cellular internalisation of magnetic materials, and this is hard to control actively and time-dependent. A simple and expedient labelling method was developed in which cell membrane proteins were first biotinylated and then bound to streptavidin paramagnetic particles. Characterisation studies were carried out to examine and analyse this labelling method. The results showed that the degree of magnetic labelling could be easily varied by adding different amounts of paramagnetic particles. The particles bound to the cell surface were internalised subsequently and studies showed this labelling method did not have any observable drastic effect on cell viability and proliferation. The magnetically labelled cells were seeded onto culture dishes and patterned using magnetic fields. Highly defined cell patterns were achieved using HeLa, TE671 cells and human monocytes. Spatially segregated HeLa and TE671 cells were also successfully co-cultured on the same plate using this technique. This cell labelling methodology can be adapted to any mammalian cell types. The labelled cells could then be patterned with high precision using magnetic fields. A variety of applications could be derived from this technology, such as cell assembly in tissue engineering. It could also benefit other related technologies such as cell-based therapies and magnetic resonance imaging.

Because without cause: how to explain without causal knowledge

There is a fairly common (and at first glance plausible) view in the philosophy of science that to give a scientific explanation of a phenomenon is to give some relevant information about its causal history. Why were you vomiting so forcefully? Because you got norovirus. Why do auroras occur? Because solar wind collides with atoms in the upper atmosphere. I consider cases in which this general schema appears to fail. In such cases, we are typically ignorant of the fine-grained causes of the phenomenon. The causal information we possess, taken by itself, lacks explanatory force. But we gain understanding by reasoning statistically to the conclusion that the phenomenon was “to be expected”. I discuss the case of statistical mechanics, but suggest applications of this form of explanation in economics and biology.

Cycling through the canons: Ubiquitination of NGN

The *Xenopus laevis* bHLH transcription factor Neurogenin (xNGN2, also known as xNGNR-1A) causes cell cycle exit and differentiation of neuroblasts into neurons through activation of a cascade of downstream targets including NeuroD. Our lab has shown that xNGN2 protein is stabilised by the presence of cdk inhibitors, using a function over and above their ability to block the cell cycle, and has prompted us to look at the mechanism of regulation of NGN2 protein stability.

Recent work looking at the ubiquitination and degradation of xNGN2 has highlighted unusual ubiquitination patterns. Ubiquitination of proteins commonly occurs on internal lysines but has been observed also through an N-terminal peptide linkage to ubiquitin in some proteins. Using mutated forms of xNGN2, we have investigated sites of ubiquitination and speed of protein degradation. We find that xNGN2 is, indeed, ubiquitinated on multiple internal lysines. In addition, ubiquitination occurs directly on the N-terminus of the protein. However, most surprisingly, we find that xNGN2 mutants, where all these canonical ubiquitination sites had been mutated or blocked, still undergoes ubiquitin-directed proteolysis.

Further biochemical analyses revealed that ubiquitination can also occur on cysteines via labile thioester linkages, and this highly unusual cysteine-dependent ubiquitination also occurs in the wild-type protein. Moreover, the importance of this cysteine ubiquitination is cell-cycle dependent. Finally, we also see that the homologous mouse NGN2 undergoes both canonical and non-canonical modes of ubiquitination in P19 embryonal carcinoma cells. Thus, we demonstrate that NGN2 is a highly unstable protein that exhibits very unusual patterns of ubiquitination. Regulation of NGN2 ubiquitination and degradation, resulting in its short half-life, are likely to play important roles in controlling the activity of this pivotal protein.

Science Keynote Speaker - Dr John van Wyhe

Introduced by Mr Scott Newman

17:10-18:00 Dr John van Wyhe

Bye-Fellow of Christ's College, Cambridge

Mind the gap: Did Charles Darwin really keep his theory a secret for 20 years?

Poster Session

Chris Hindley — PhD, Oncology

Loss of cdk Consensus Phosphorylation Sites Leads to Hyperactivity of Neurogenin

Gary McDowell — PhD, Oncology

Cycling Through the Canons: Ubiquitination of NGN

Lidia Duncan — CRA, Molecular Immunology

Regulation of Cell Surface MHC Class I Molecules by Ubiquitination

Mark Schenk — PhD, Structural Engineering

Folded Shell Structures

R. C. Wheeler — Alumnus

Maps of the Witham Fens

Richard Wallbank — PhD, Genetics

Decoding Gene Regulation and Patterning in the Drosophilidae

Scott Newman — PhD, Pathology

Early and Late Mutations in Breast Cancer

Sinead English — PhD, Behavioural Ecology (Zoology)

Personality and Helping in Meerkats

