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History of molecular biology work in the Graham Kerr Building (1996-2024)

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John Graham Kerr's zoology was in a pre-molecular age: his 1917 lectures on *Amoeba* (this volume) indicate scepticism over the value of chemical investigation of how living organisms work. For genetics, this changed in the 1950s with the discovery of DNA's structure and the basis of genetic coding for proteins. Soon, Nobel Laureate Peter Medawar (1965) was able to suggest that although ecologists might not have to engage with molecular biology, good ecologists would. By the 1990s, the increasing availability of DNA sequencing methods at cheaper and cheaper costs generated a huge range of new possibilities for evolutionary biologists and ecologists. However, until the late 1990s, research at the molecular and biochemical levels was concentrated in other areas of the Institute of Biomedical and Life Sciences, such as the Division of Biochemistry and Molecular Biology (DBMB). Integration of DNA techniques with ecology reached Glasgow Zoology in 1996 with the appointment of Richard Griffiths. Griffiths, working at Oxford University, had identified a gene on the W/Z sex chromosomes in birds (equivalent to X/Y in mammals) that had sufficient differences between males and females to provide the basis for a bird-sexing test. The sexes of over 50% of adult bird species and nearly all juveniles are not distinguishable visually. This is a serious problem for conservation programmes where it is important to know the sexes of individuals used in captive breeding and is also a major limit on research into sex allocation in wild populations. Once at Glasgow, Griffiths established a new molecular laboratory staffed by himself, post-doc Bob Dawson and technical assistant Kate Orr (later Griffiths). They quickly developed and published (Griffiths *et al*., 1998) a rapid, cheap PCR-based test that allowed birds to be sexed from a single drop of blood or piece of feather (Fig. 1). Working with another core technician (Aileen Adam) and a Natural Environment Research Council (NERC) fellow (Iain Barber), they also extended the technique to fish (Griffiths *et al.*, 2000). Given the strengths in ornithology and fish biology, the Molecular Ecology unit was established in the "roof labs" (the floor built on top of the Zoology museum), as a cost recovery-based service primarily for molecular sexing to support other researchers in DEEB but also external partners (for example, from the Centre for Hydrology and Ecology).

Fig. 1. Sexing gull chicks as part of a study on resource allocation, Walney Island, Cumbria, England. (A) Kate Griffiths carrying a chick to the laboratory. (B) Kate Griffiths in the field molecular laboratory in 2007. (Photos: (A) N. Verboven; (B) R. Griffiths)

This service-based model was continued for nearly 20 years after Griffiths left in 2002; it finally came to an end when the COVID-19 pandemic limited access to the laboratories in 2020.

The other "big" field that was growing in the 1990s was molecular systematics, which was facilitated both by continuing advances in sequencing technology and in computing power. Known as an innovator in this emerging field, at least partly based on his seminal books on molecular evolution from a phylogenetics perspective (Page & Holmes, 1998) and very widely used programme for visualising phylogenetic trees (Treeview: Page, 1996; cited >13,000 times!), Rod Page was appointed as Reader of Taxonomy in 2001. His initial research in the GKB used phylogenetic approaches to uncover host-parasite coevolution (Page, 2003), but the work was fundamentally about understanding molecular evolutionary processes rather than just using molecular markers as tools for ecology. By the late 2000s Rod had switched his focus more towards biodiversity informatics (Page, 2008) rather than taxon-specific generation of molecular data but the innovation here was to achieve better integration of data from disparate sources.

The next molecular-based researcher to be appointed in the GKB, Lukas Keller, was in Glasgow for only two years (2002-2004) but he formed a critical bridge between the ornithologists in Zoology (which was then the Division of Ecology and Environmental, Biology, DEEB) and parasitologists in the Wellcome Centre for Parasitology (WCP). His primary research interests were in determining the molecular basis of inbreeding depression for conservation, with one of his most cited papers on this topic being published during his time in the GKB (Keller & Waller, 2002). Working with a postdoctoral researcher with expertise in molecular ecology who has remained in the Graham Kerr on various positions until now (Paul Johnson), Andy Tait (WCP) and the NERC biomolecular analysis facility in Sheffield, he also developed new molecular approaches (microsatellite markers) for investigating population

genetics of parasitic nematodes in order to understand the impacts of anthelmintic use on red grouse management (Johnson *et al.*, 2006). This work also involved a collaboration with Bill Mullen, a long-term research associate working with Alan Crozier, whose research used innovative approaches to investigate plant hormones and plant products for nutrition. Although he was based in DMDB he moved his laboratory (and his equipment) to the GKB after the Bower building fire in 2001. Together, they used high performance liquid chromatography (HPLC) for metabolite profiling to quantify how much of the drugs the grouse had taken up in order to explain why resistance was not developing as quickly in the bird parasites as occurred when the drugs were used on livestock (Adam *et al.*, 2011).

Integration between molecular evolution, molecular ecology, conservation genetics and host-pathogen interactions was continued when Barbara Mable joined the department, on a Natural Environment Research Council (NERC) advanced research fellowship in 2004. Her original training was in molecular systematics (Hillis *et al*., 1996) but her postdoctoral research shifted to population and evolutionary genetics. Her main interests focused on molecular evolution of gene families associated with recognition processes, such as host-pathogen interactions in plants and animals and mating system evolution in plants. Prior to coming to Glasgow she had worked on the evolution of whole genome duplication (polyploidy) in microbes (Mable & Otto, 2001), plants (Mable *et al*., 2004) and amphibians (Mable & Roberts, 1997). However, as the only geneticist in DEEB she became involved with multiple projects on a range of animals, including birds (Neves *et al*., 2010), fish (Le Vin *et al*., 2011) and mammals (Marsden *et al*., 2009), largely through helping PhD students to develop new molecular approaches. Other researchers also continued to use molecular markers as tools to address a range of questions. In collaboration with colleagues in the Division of Infection and Immunity (DII), Douglas Neil, whose research was originally focused on the neurophysiology of crustaceans, developed diagnostic markers to identify pathogens of important aquaculture species (Small *et al.*, 2006). In collaboration with research fellows (François Criscuolo and Pierre Bize) and Kate Griffiths, Pat Monaghan was involved in developing a quantitative PCR (qPCR) assay to quantify variation in telomere lengths in birds, as a marker of senescence (Criscuolo *et al*., 2009), which transformed the field and led to the establishment of a second molecular biology laboratory in the GKB.

The late 2000s also saw an increase in molecular expertise related to host-pathogen dynamics and epidemiology. In collaboration with the Pirbright Institute, Dan Haydon, a theoretical ecologist and epidemiologist, used whole genome sequencing to make inferences about viral pathogen transmission dynamics, such as tracing the 2001 foot and mouth disease epidemic (Cottam *et al*., 2006). However, it was not until Roman Biek was appointed in 2007 (funded by a University of Glasgow Kelvin Smith Fellowship in Biodiversity Management) that the expertise for pathogen sequencing became integrated into the GKB. His work lies at the interface of disease ecology and conservation; for example, using phylogenetic approaches to trace transmission dynamics of viruses in wild mammals (Biek & Real, 2010). At Glasgow, initially through collaborative PhD studentships, he also became involved in applied problems related to bacterial pathogens, including bovine tuberculosis (Trewby *et al*., 2016) and *Borrelia* (causing Lyme disease; Millins *et al*., 2017), while retaining interests in conservation (Muir *et al*., 2013). He was also integral to establishing world-leading strengths in rabies virus research when Sarah Cleaveland and Tanzania Lembo (both wildlife veterinarians) moved from Edinburgh to Glasgow in 2008, followed by Katie Hampson in 2009 and Daniel Streicker in 2013 (both of the latter originally supported by Sir Henry Dale Wellcome fellowships but now permanent members of staff). Led by a PhD student who subsequently has been retained on fellowships (Kirstyn Brunker) the team have made innovations in real-time diagnosis of rabies in the field using whole genome sequencing by developing a "lab in a suitcase" approach, opening up new possibilities for diagnostics and transmission tracing (Brunker *et al.*, 2020), and have made important contributions to understanding transmission dynamic networks for both dog (Lushasi *et al*., 2023) and bat viruses (Jacquot *et al.*, 2022).

During the restructuring of the Faculty of Biomedical and Life Sciences in 2010, DEEB became the Institute of Biodiversity, Animal Health & Comparative Medicine (IBAHCM), integrating veterinary research with ecology and evolution. This involved incorporation of researchers based on the Garscube campus, many of whom were focused on molecular parasitology. However, the restructuring also provided more investment in growth, including vast expansion of molecular capacity. In 2013 the appointment of Colin Selman complemented strengths in life history of ageing by bringing in perspectives from molecular physiology (Mulvey *et al*., 2014). Strengths in genomic approaches to conservation-related problems were enhanced when Kathryn Elmer and Kevin Parsons were both appointed in 2012. They shared interests in ecological speciation of fish (Elmer, 2016; Parsons *et al*., 2015) but also had complementary expertise in developing methods for using reduced representation genomic approaches to investigating population genetics (Recknagel *et al*., 2015) and quantitative genetics related to evolution and development (Parsons & Albertson, 2013). They added capacity to ecological research by the Scottish Centre for Ecology and the Environment (SCENE) director Colin Adams (Crotti *et al.*, 2021) and affiliate Colin Bean (Campbell *et al*., 2017) but also expanded the breadth of questions addressed - Parsons in adaptation to thermal stress (Smith *et al.*, 2024) and Elmer in complex trait evolution in amphibians (Burgon *et al*., 2020) and reptiles (Recknagel *et al*., 2021). A more applied focus to aquatic genomics was brought in with the appointment of Martin Llewellyn in 2015. He developed an artificial system for assessing the impacts of different diets on microbial communities

(Kazlauskaite *et al*., 2021), as well as developing innovative approaches for pathogen surveillance in aquaculture settings based on DNA metabarcoding (Peters *et al*., 2018) and genomic approaches for population genetics of parasites (Hernandez-Castro *et al.*, 2017).

The institute also attracted an increasing number of research fellows, many of whom have stayed on for permanent appointments. For example, Francesco Baldini, who initially came on a short-term Italian Leadership fellowship from Perugia University, Italy in 2013, strengthened molecular capacity in the vector ecology group, led by ecologist Heather Ferguson, and developed a novel technological approach for aging mosquitoes based on infrared microscopy (Siria *et al.*, 2022). Expansion of the molecular capacity of the malaria team was supported by the move of Lisa Ranford-Cartwright from the Institute of Infection, Immunity and Inflammation (III) to IBAHCM in 2018 (Mwangi & Ranford-Cartwright, 2013). Additional cutting-edge technological advances have also been brought in by other independent research fellows. For example, another Sir Henry Dale Wellcome fellow, Virginia Howick, introduced single cell sequencing to develop a malarial cell atlas, allowing spatial interpretation of changes in gene expression (Howick *et al.*, 2019). There have been ongoing contributions from a wealth of subsequent research fellows, across a range of subject areas funded by the Wellcome Trust, NERC, the Royal Society, the European Research Council (ERC) and the Natural Sciences Engineering Council of Canada (NSERC). As of 2024, nearly all of the fellows in the GKB have molecular approaches as core to their research and from the modest start in the 1990s, at least 23 members of staff in the GKB now use molecular approaches. This rapid expansion has been due largely to increasing technological developments in the scale and power of whole-genome sequencing, but also due to the highly collaborative nature of research within the GKB, enabling combined expertise from the molecular through to the organismal and population levels.

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