Team Science Research Careers

UHR Showcasing Good Practice – 23 November 2020

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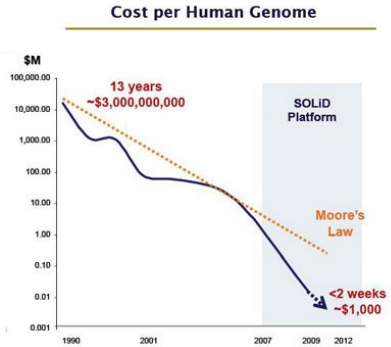
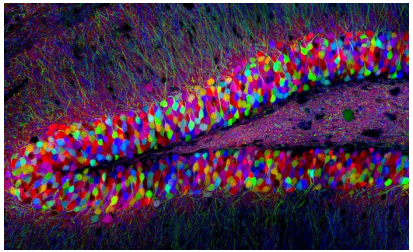
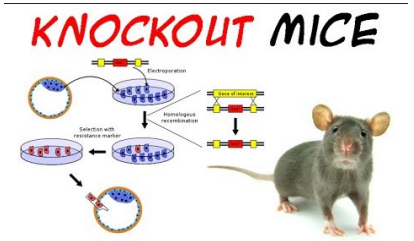
Team Science

‘Team science’ is becoming increasingly common across all fields of research. Teams spanning different specialties and geographical centres are often needed to tackle contemporary research questions in biomedical science.







You can’t be an expert in everything!

Team Science

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AGGREGATION OF PREDATORS AND INSECT PARASITES AND ITS EFFECT ON STABILITY

By M. P. HASSELL and R. M. MAY*

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INTRODUCTION

Searching animals, such as predators and insect parasites,† usually spend more time where their requisites are more plentiful, a behaviour that has an obvious selective advantage. Despite this, it is only from relatively recent work that aggregative responses to uneven prey distributions have been adequately quantified in terms of predator numbers, or the time spent by a predator, per unit areas of different prey density. This in turn is reflected in the relatively few predator–prey models that have allowed for such aggregative behaviour (Royama 1971; Hassell & Rogers 1972; Hassell & May 1973; Murdoch & Oaten 1974). These are in contrast to the many models (e.g. Lotka 1925; Volterra 1928; Thompson 1924; Nicholson & Bailey 1935; Watt 1959; Hassell & Varley 1969) where search is random, which effectively implies an even distribution of predators throughout the whole prey area and makes the particular types of prey distribution irrelevant to the model outcome.

In an attempt to show how predator aggregation could affect stability, Hassell & May (1973) considered a simple modification of the Nicholson–Bailey model in which the prey survival was given by

* The order of authorship was determined from a twenty-five-game croquet series held at Imperial College Field Station during summer 1973.

predators are distributed. To make a general stability analysis easier, the prey population was divided between the n unit areas with a single area of high density and the remainder of equal low density. The distribution of predators was achieved by a single parameter characterization (μ) such that

$$\beta_i = c\alpha_i^{\mu} \qquad (2)$$

where c is a normalization constant and μ is the 'relative aggregation index'.

Eqn (2) was not intended to be a realistic description of how predators aggregate. It was chosen for its simplicity and because it conveniently spans the behaviours of random search ($\mu = 0$) to complete aggregation in the highest density area, making the remainder effective prey refuges ($\mu \rightarrow \infty$). The predators were also taken to respond only to the *proportion* of prey in each area and not to the *number* per unit area. Moreover, the particular distribution of prey was chosen to make a general stability analysis easier and not to represent accurately prey distributions in the field. This model did, however,

* The order of authorship was determined from a twenty-five-game croquet series held at Imperial College Field Station during summer 1973.

† Henceforth, we refer to both as 'predators' unless otherwise stated.

ARTICLE

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Decoding human fetal liver haematopoiesis

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Definitive haematopoiesis in the fetal liver supports self-renewal and differentiation of haematopoietic stem cells and multipotent progenitors (HSC/MPPs) but remains poorly defined in humans. Here, using single-cell transcriptome profiling of approximately 140,000 liver and 74,000 skin, kidney and yolk sac cells, we identify the repertoire of human blood and immune cells during development. We infer differentiation trajectories from HSC/MPPs and evaluate the influence of the tissue microenvironment on blood and immune cell development. We reveal physiological erythropoiesis in fetal skin and the presence of mast cells, natural killer and innate lymphoid cell precursors in the yolk sac. We demonstrate a shift in the haemopoietic composition of fetal liver during gestation away from being predominantly erythroid, accompanied by a parallel change in differentiation potential of HSC/MPPs, which we functionally validate. Our integrated map of fetal liver haematopoiesis provides a blueprint for the study of paediatric blood and immune disorders, and a reference for harnessing the therapeutic potential of HSC/MPPs.

The blood and immune systems develop during early embryogenesis. Our understanding of this process derives from mouse and in vitro model systems, as human fetal tissue is scarce. Although haematopoietic development is conserved across vertebrates[1], there are notable differences between mouse and human[2,3]. Comprehensive interrogation of human tissue to understand the molecular and cellular landscape of early haematopoiesis has implications beyond life in utero, as it provides a blueprint for understanding immunodeficiencies, childhood leukaemias and anaemias and generates insights into HSC/MPP propagation to inform stem cell technologies.

The earliest blood and immune cells originate outside the embryo, arising from the yolk sac between 2 and 3 weeks after conception. At 3–4 post-conception weeks (PCW), intra-embryonic progenitors from the aorta–gonad–mesonephros (AGM) develop[4]. Yolk sac and AGM progenitors colonize fetal tissues such as the liver, which remains the major organ of haematopoiesis until the middle of the second trimester. Fetal bone marrow is colonized around 11 PCW and becomes the dominant site of haematopoiesis after 20 PCW in humans[4]. Yolk sac-, AGM-, fetal liver- and bone marrow-derived immune cells seed peripheral tissues including non-lymphoid tissues (NLTs), where they undergo specific maturation programs that are both intrinsically determined and extrinsically nurtured by the tissue microenvironment[5,6].

In this study, we use single-cell transcriptomics to map the molecular states of human fetal liver cells between 7 and 17 PCW, when the liver is the predominant site of human fetal haematopoiesis. We integrate results from imaging mass cytometry, flow cytometry and cellular morphology to validate the transcriptome-based cellular profiles. We construct the functional organization of the developing immune network by comparative analysis of immune cells in fetal liver with those in yolk sac, and skin and kidney as representative NLTs.

Single-cell transcriptome of fetal liver

To investigate blood and immune cell development in the fetal liver, we generated single-cell suspensions from embryonic and fetal livers between 7 and 17 PCW. We used fluorescence-activated cell sorting (FACS) to isolate $CD45^+$ and $CD45^-$ cells using adjoining gates for comprehensive capture (Fig. 1a, Extended Data Fig. 9a) for single-cell RNA-sequencing (scRNA-seq) (both 10x Genomics platform and Smart-seq2) (Fig. 1 and Supplementary Table 1). To enable parallel evaluation of blood and immune cell topography in NLT and the yolk

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Academic career paths

1) Teaching only

2) Research only

3) Teaching and research

4) Neither teaching nor research

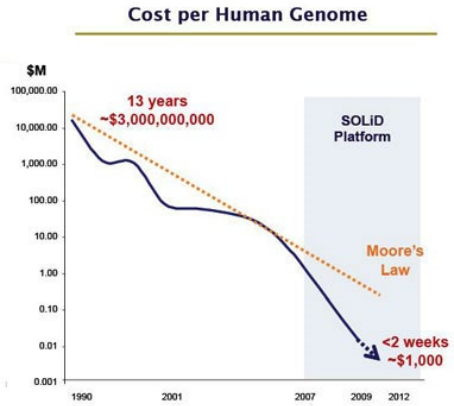
Grade 6: New post doc
Grade 7: Experience post doc
Grade 8: Independent Fellow or Lecturer
Grade 9: Senior Lecturer/Reader
Grade 10: Professor

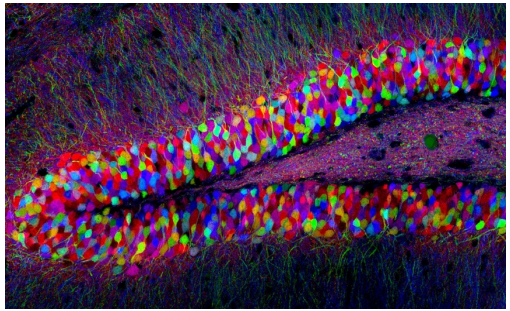
Movement between these families is possible but can cause problems!

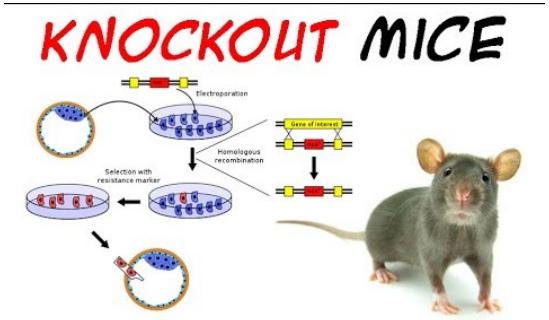
But is this fit for purpose in the 21st Century?

Problem 1

Research Scientists who play pivotal roles in research and outputs may not fit the current criteria for promotion!







A problem of evaluation

Smith, R; Murphy P; Stewart, L; Jones, N; Bryant, D; MacLeod, K; **Burton, H.** (2019) The relationship between chemokines and the cost of a pint of beer. ***J. Well Fancy That.,*** **12,** 345-349.

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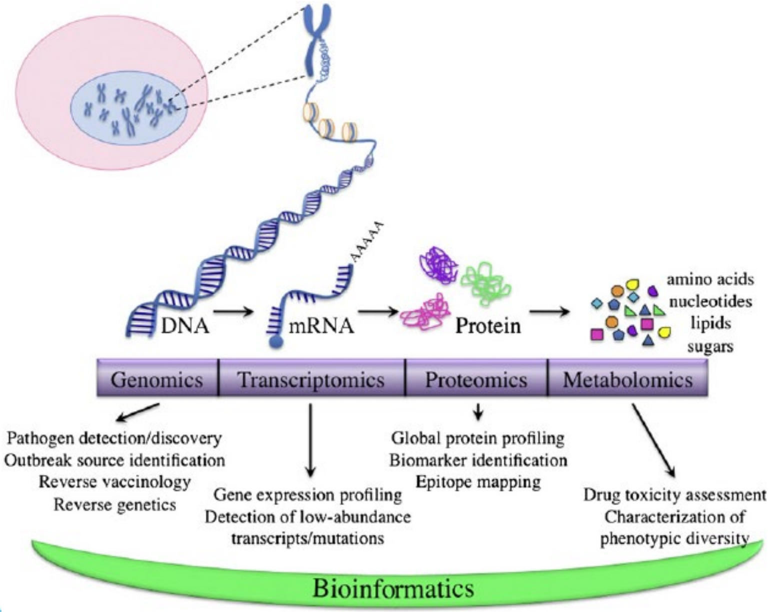
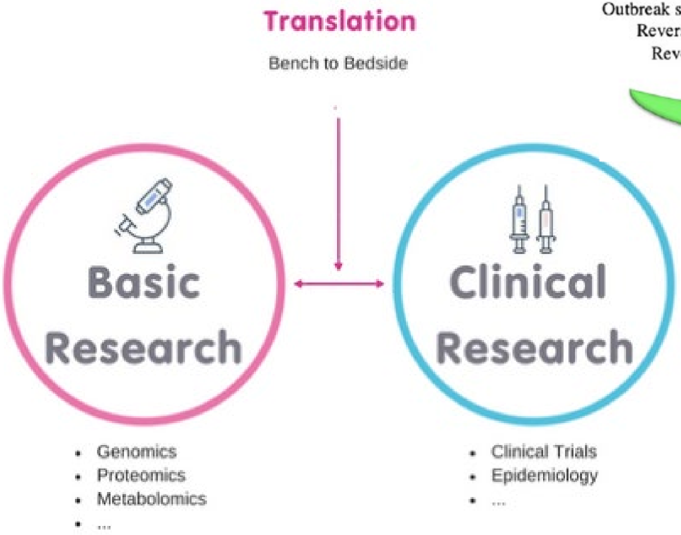
So, how do we assess and reward these distinct contributions?

Current performance review systems are inadequate.

Statistics
organization
scientific
descriptive
analysis
samples
collection
interpretation
data
statistical
Inference
probability
theory
experiments
science
mathematical
mathematics
provides
parameters
design
discipline
pertaining
called



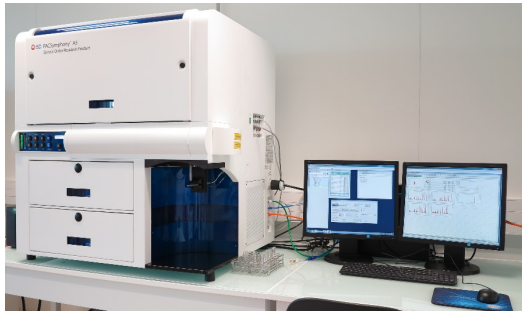
DNA
mRNA
Protein
amino acids
nucleotides
lipids
sugars
Genomics
Transcriptomics
Proteomics
Metabolomics
Pathogen detection/discovery
Outbreak source identification
Reverse vaccinology
Reverse genetics
Gene expression profiling
Detection of low-abundance
transcripts/mutations
Global protein profiling
Biomarker identification
Epitope mapping
Drug toxicity assessment
Characterization of
phenotypic diversity
Bioinformatics

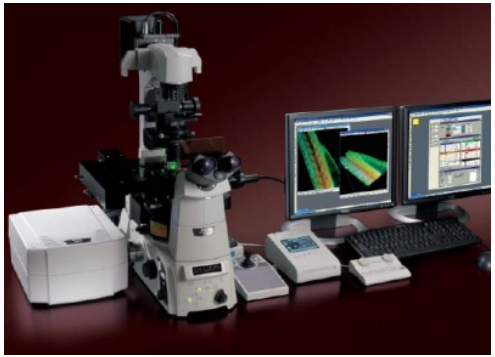


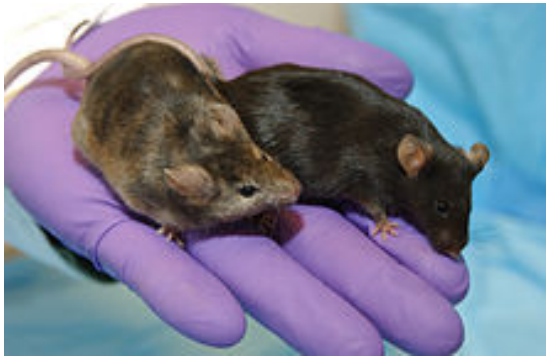
Translation
Bench to Bedside
Basic Research
Clinical Research
Genomics
Proteomics
Metabolomics
...
Clinical Trials
Epidemiology
...

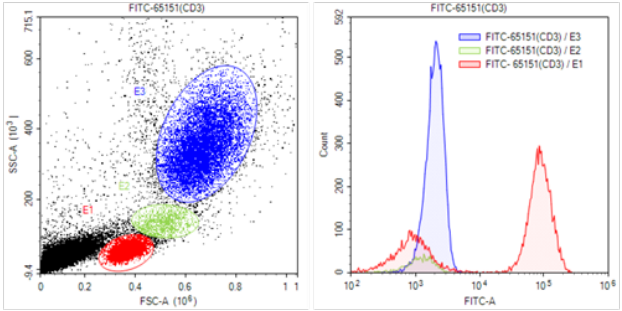
Problem 2

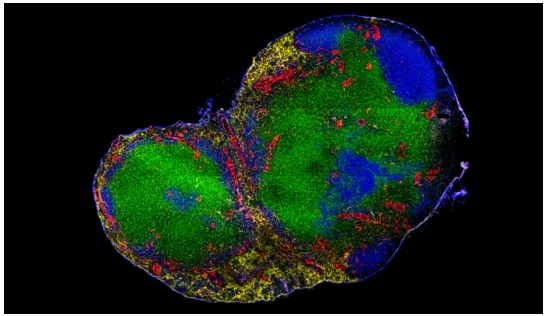
Technicians/technologists running complex facilities or with distinct high level technical expertise do not have a ‘fit for purpose’ career path.











Technicians/technologists may not have published outputs

Conceptualization
Data curation
Formal Analysis
Funding acquisition
Investigation
Methodology
Project administration
Resources
Software
Supervision
Validation
Visualization
Writing – original draft
Writing – review & editing

CRediT Guidelines

The challenge

Increased need for high level core expertise in e.g. statistics, bioinformatics, ‘omics’ analysis etc.

Increased centralisation of complex facilities.

Distinct contributions from classical academic job family staff.

Need to recognise and reward performance.

Recruitment, retention and promotion support for this new category of researcher.

University career pathways

- Traditional academic pathways well understood, e.g. HESA definitions

1	Academic contract that is teaching only
2	Academic contract that is research only
3	Academic contract that is both teaching and research
4	Not an academic contract
9	Academic contract that is neither teaching nor research

- Career pathway descriptors and metrics over past 20 years
- Non-traditional role fit and identity?

Performance review systems

- Cross-sector – increased measurement at HEI/unit/theme levels
- Staff appraisal – including performance rating systems
- Pay and promotion systems – metrics and standard criteria
- What counts? Recognising the norms vs special/non-traditional?

Research Scientists & Technologists - 2016

- **Research Scientist** https://www.gla.ac.uk/media/Media_498056_smxx.pdf
  - Variant on Research-only – up to SL equivalent
  - Academic contribution remains at heart of role

- **Technologist** https://www.gla.ac.uk/media/media_506090_en.pdf
  - Extended Technical & Specialist job family – up to SL equivalent
  - For technical experts and facility leaders

- **Academic Clinician** also introduced – medical, dental and veterinary

Flexible career pathways

The solution

The Research Scientist career track

Grade 6: New post doc
Grade 7: Experience post doc
Grade 8: Independent Fellow or Lecturer
Grade 9: Senior Lecturer/Reader
Grade 10: Professor

A record of scholarly output/A record of contributing to scholarly output.
Participation in external engagement/provision of advice, transfer of knowledge and methodologies
Principle Investigator on grants/subject specific lead or key contributor on grants
Leadership and coordination of research project/leadership and coordination of research or specialist project

The solution

The Technologist career track

Grade 6: New post doc
Grade 7: Experience post doc
Grade 8: Independent Fellow or Lecturer
Grade 9: Senior Lecturer/Reader
Grade 10: Professor

Technical & Specialist job family extended to grades 8 and 9.

The solution

The Academic Clinician career track

Grade 6: New post doc
Grade 7: Experience post doc
Grade 8: Independent Fellow or Lecturer
Grade 9: Senior Lecturer/Reader
Grade 10: Professor

Recognition of clinical activities
Supervision of interns/residents
Clinical postgraduate qualification recognition
Leadership/management of clinical group/services

Implementation

1) Identifying staff to transition to the new pathways
2) Ensuring that these pathways are equally valued
3) Ensuring that these pathways are not perceived as easier
4) Managing expectations
5) Managing promotions

The future

- Creating community – need to join up experiences across the sector
- Funding models – HEI level and research funder recognition
- Long term career pathways – recognised routes and role models
- Can we envisage a ‘middle management’ structure in academic research?
- Seniority – typical expectations, e.g. professorial level?
- Mobility – national and internationally, incl immigration system recognition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