Genetics Needs Non-geneticists

Citation for published version:
Ponting, CP 2020, 'Genetics Needs Non-geneticists', *Trends in Genetics*.
https://doi.org/10.1016/j.tig.2020.06.015

Digital Object Identifier (DOI):
10.1016/j.tig.2020.06.015

Published In:
Trends in Genetics

Trends in Genetics

CellPress
REVIEWS

Scientific Life

Genetics Needs Non-geneticists

Chris P. Ponting[1,*,@]

Answering genetics' big data questions often needs an interdisciplinary team whose members freely share their diverse expertise in analysis, statistics, and computation. Sharing requires mutual trust and open acknowledgement of strengths and weaknesses, including those of established geneticists. Only then will newcomers to genetics contribute far beyond their entry-level expectations.

I came into the 1990s as a physicist and left them as a computational biologist. This was less a career plan and more a series of fortuitous events. The Human Genome Project was then culminating, so genetics had an immediate need for numerate scientists with some grasp of biology. The new human DNA sequence posed a gigantic set of interlocking puzzles that fascinate even now. Migrants from other disciplines were also attracted to make their own career journeys, bringing with them tools and expertise that are helping to solve these puzzles.

Genetics has always drawn heavily from other disciplines. Earlier in its history, chemists took the first X-ray diffraction pictures of DNA and produced the first molecular sequence database. Physicists proposed the intron–exon structure of genes and determined protein structures showing how transcription is initiated and regulated. Mathematicians developed statistical approaches underlying population genetics and sequence database searching. This has been no one-way flow, because genetics has greatly influenced other disciplines from archaeology and human history, to forensic science, epidemiology, ecology, and more.

It was challenging to come to genetics later than most. Foremost was my feeling of inferiority: I would never acquire the intricate knowledge of career geneticists. There were just too many conceptual and procedural details to be learnt; too much jargon and lore; too great a distance to biology's leading edge. Eventually, however, I discovered that these feelings are common too among 'card-carrying' geneticists although more rarely admitted.

As latecomers to genetics we often face a false presumption that our interest is only in technical or analytical aspects. Pigeon-holing us solely on the basis of our entry-level skills overlooks later hard-won expertise and knowledge. Nevertheless, we can also employ labels for advantage, for example, by coaxing a valuable big picture perspective from both career geneticists ('Start at the beginning: I'm only a physicist') and physicists ('Start at the beginning: I moved from physics long ago').

Our first conversation with an established scientist can be a minefield. We walk into their area of expertise blindfolded by our meagre genetics knowledge, carrying only our intellectual toolkit and the hope that it contains a crucial device that defuses the situation, allowing us to safely traverse the field together. A successful meeting is unfortunately rare. It can blow up because of our lack of a relevant skill or knowledge, or because either misjudges the scientific opportunities. It also can fail because the more senior scientist pulls rank, making demands that benefit them only. By contrast, success can ensue when expertise, motivation and trust are appreciated fully by both parties.

The allure of genetics continues to be strong. In my university, we have received hundreds of applications to a 4-year fellowship programme that trains early career researchers to become leaders in genetics and molecular medicine. The fellows are postdoctoral researchers wishing to transition from diverse fields such as artificial intelligence, astronomy, particle physics, or pure mathematics. They bring with them an abundance of analytical and often computational expertise, and a strong motivation to be as adept at addressing biomedical questions experimentally as analytically. Fellows spend the first of their 4 years trialling various projects and immersing themselves in the local science environment, taking courses and attending lectures and tutorials before plunging into their own crossdisciplinary project.

As Director of this programme I have learnt the following four lessons. (i) Fellows initially could be attracted to one question, only later to become obsessed by another. So it is foolhardy to expect genetics novices to know *a priori* what scientific questions will ultimately appeal to them most. Choice of future research path is optimised by trial and error. (ii) Not all research or research groups can accommodate fellows or their crossdisciplinary research because of limitations either in available data or high-throughput techniques, or in the host group's enthusiasm to spare some portion of their chosen research field within which the fellow's future career can then be cultivated. (iii) The best questions are the most fundamental, and yet these are the least likely to be asked. Fellows need to feel sufficiently secure to ask such questions if they are to acquire new knowledge rapidly. (iv) The most effective crossdisciplinary collaborations are those in which researchers are trusted partners who bring complementary skills and knowhow into their team.

In the 2020s, as genetics research scales up its big data projects to the population scale (~10^6 people or single cells), team working continues to be essential. To be

CellPress REVIEWS

effective, teams need to recruit experts from across disciplines including data and software engineering, analysis, and statistics. Additionally, all team members should understand others' jargon, concepts, limitations, and expertise, and should have tacit permission to ask basic as well as critical questions. Many questions remaining in genetics will not be answered by a single narrow discipline but by interdisciplinary teams who actively welcome diverse ideas, skills, and backgrounds. Established geneticists should actively recruit, support, and mentor scientists whose paths into genetics differ greatly from theirs.

[1]MRC Human Genetics Unit, Institute of Genetics and Molecular Medicine, University of Edinburgh, Edinburgh EH4 2XU, UK

*Correspondence:
Chris.Ponting@igmm.ed.ac.uk (C.P. Ponting).
[@]Twitter: @CGATist (C.P. Ponting).

https://doi.org/10.1016/j.tig.2020.06.015