

# **TURN ON THE LIGHTS! FUNDAMENTAL SCIENCE LEADS TO SCIENTIFIC PROGRESS: A PERSPECTIVE FROM DEVELOPMENTAL BIOLOGY**

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## **ABSTRACT**

Many of the ways in which we interact with the world around us have been shaped by the dual efforts of fundamental and applied sciences. Generally speaking, fundamental science generates knowledge about how things work at a fundamental level, and applied science employs this body of knowledge to create a new product or overcome an existing challenge. Developmental biology is a classic example of fundamental science that drives several avenues of applied science. For example, understanding how cells, tissues, and organs develop, and are coordinated within a functioning organism can form the basis for diagnosing medical conditions and exploring treatments. As a developmental biology lab researching bone and cartilage in birds and fish, we are acutely aware of the disparity in financial support between fundamental and applied

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science research in Canada. Funding cutting-edge applied research with immediate impacts on society is attractive and more easily justifiable to tax payers. However, funding grassroots fundamental science research is equally important but receives significantly less attention and support because the impacts are harder to predict and are longer-term. This commentary addresses this inequity in science funding and highlights the dire need to improve supports for early career scientists.

Keywords: Fundamental science, developmental biology, students, Canada, science funding

## INTRODUCTION

Both fundamental science research and applied science research involve critical thinking and developing international and national collaborations. In Canada, there are many funding initiatives to support applied science research, however, the importance of fundamental science is often overlooked yet underlies the advancement of society (Naylor *et al.* 2017). The ripple effects of fundamental science are a major driver of economic growth. Unfortunately, as noted in the Naylor report (Page 19, xix) in 2017, the Canadian government continues to fund applied science research over fundamental science. There are major federal funding sources for fundamental science (e.g., the Natural Sciences and Engineering Research Council of Canada, NSERC, Discovery Grants program) but they are limited. In contrast there are numerous funding opportunities for applied research (NSERC alliance grants, Canadian Institutes of Health – CIHR grants, MITACs grants, New Frontiers Grants, etc.). This article describes why fundamental science deserves more attention and needs more federal and institutional support. We also highlight the impact that under-funding has had on the well-being of scientists.

## THE SCIENTIFIC PROCESS

All science research, whether applied or fundamental follows the same scientific process. This is an iterative process, which involves a series of steps that start with a thorough understanding of the knowledge that has previously been gained in the specific research area. With this basis, scientists develop the study objectives, a hypothesis and the methodology and approach (Atkamis & Ergin 2008). Controlled experiments with measurable results ARE validated by

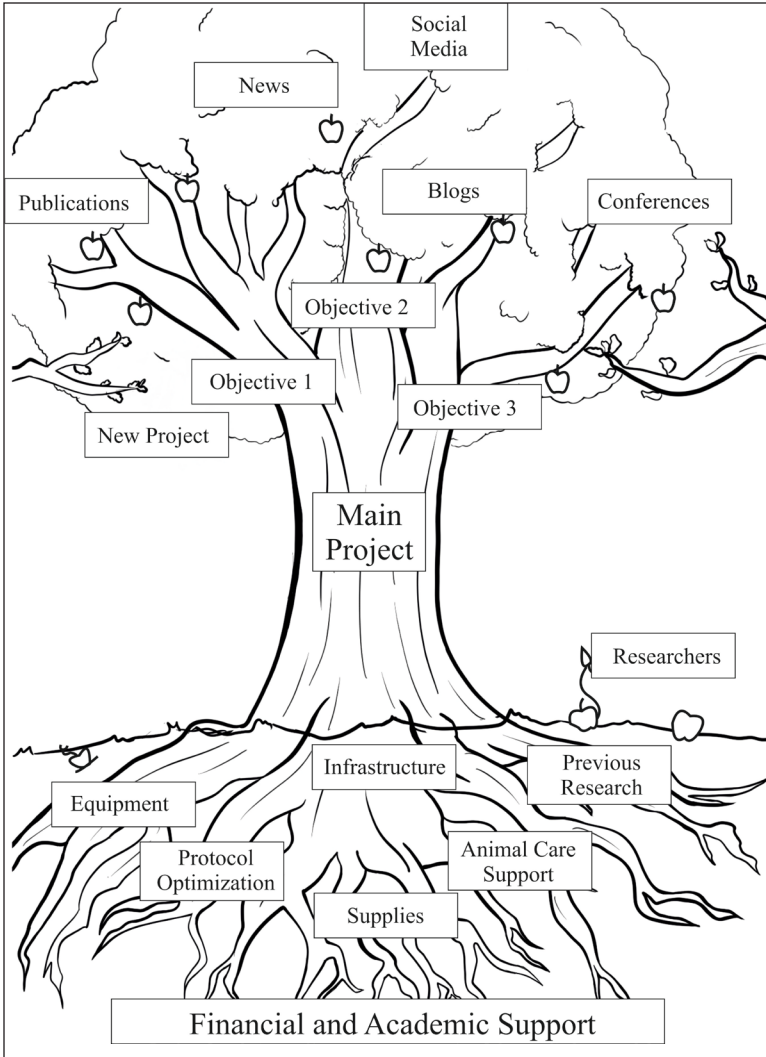
appropriate statistical analyses AND are essential for scientific discovery.

Skilled people are required to design and execute a study. A well-designed project requires including people with different experiences and perspectives during the design phases (Powell 2018). The output of science in terms of published research papers is often considered the most important aspect of one's research, and this aspect is primarily judged during grant reviews. However, the people that are trained during a research study are also of great importance – they are not only essential to obtain results but they are also the future knowledge holders in terms of expertise and scientific research approaches. The more scientifically literate Canada is, the better we are able to make informed decisions about our health and environment.

Another aspect of the scientific process that is often not recognized is that even if a study does not lead to a major new understanding, the process of conducting that study is nevertheless valuable. For example, the protocols and procedures of how to conduct an experiment that are developed and optimized during a study are valuable assets to future research. While scientific studies always include a methods section, these are becoming more and more abbreviated such that studies can not be repeated based on these sections alone. It is only in the last three decades that journals, which solely publish protocols or methods, have been established. Thus, the benefits of science funding are more than just the actual scientific output (i.e., the publication or the product). These added benefits apply to both fundamental and applied scientific studies. Fig 1 highlights some of the hidden and obscured aspects of science, and the important role that trainees play in science research endeavours.

## **THE IMPORTANCE OF FUNDAMENTAL SCIENCE**

The scientific discoveries made within Nova Scotia are numerous. Well-known inventions include the Silver Dart, designed by Graham Bell, which was the first aircraft to make a controlled powered flight in Canada and the British Commonwealth in 1909. A lesser-known example was the invention of modern paper by Charles Fenerty in Halifax, NS in 1844. He was the first to use wood pulp for paper, which revolutionized world paper production. A more recent invention was the bionic knee brace that was developed by Spring Loaded



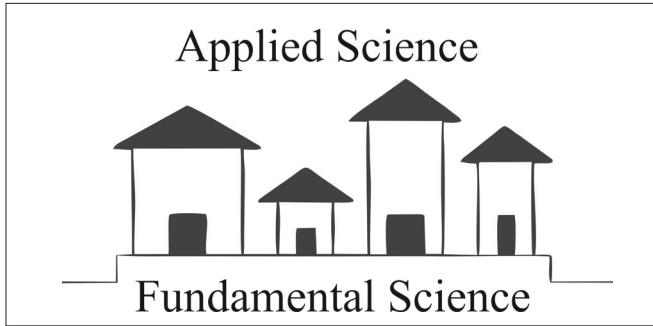
**Fig 1** A depiction of a typical research project represented by an apple tree. The research that is visible to the public is above ground whereas the research that is hidden from the public is below ground. For example, results of scientific studies are often shared at conferences, in publications and on social media. Below ground, this research is supported by the purchase of equipment and supplies, by previous research and by establishing optimized protocols. Importantly, the researchers (i.e., trainees, students) conducting the science research (represented by apples), are often obscured, they may drop off the project and start their own research group, or they may leave science all together. Principal investigators design the project and ensure its success.

Technology in Dartmouth, NS in 2016. These examples have been mentioned in the proceedings of the Nova Scotian Institute of Science published since 1864. These examples are of applied research leading to a product and they were made possible by existing fundamental knowledge. An understanding of developmental biology and the anatomy of how tissues interact underpins the knee brace invention, cellular chemistry underpins the paper invention and the invention of powered flight was not possible without an understanding of the physics of air flow, metallurgy and the chemistry of oil and combustion. Thus, years of fundamental science research preceded these inventions.

Throughout history, global crises lead to pivotal points for life-changing innovations and discoveries. A recent crisis is the COVID-19 pandemic, which rapidly had an impact on the lives of millions of people. The development of the COVID-19 vaccines was the result of previous scientific knowledge which enabled the rapid development of vaccines in response to this pandemic (Kashte *et al.* 2021). Researchers had to look for a solution to provide protection against this strain of COVID, and to understand it, they had to investigate where it came from, how it enters and impacts the body, and finally, how it can be managed. These questions were answered by investigating RNA viruses, testing a multitude of techniques, and developing solutions and vaccines. Under the pressure of a worldwide crisis scientists needed to produce a fast response and this was achieved with the help of governments who provided significant funding. This all contributed to the rapid development of COVID-19 vaccines with many scientists around the world collaborating. Without fundamental knowledge, however, it would have taken much longer to design the strategies required to address the COVID-19 pandemic. Scientific discoveries are the result of a solid fundamental research base that is continually reinforced and expanded by scientists (Fig 2).

## **WHY DEVELOPMENTAL BIOLOGY IS IMPORTANT**

Developmental biology is one of the oldest fields in biology and dates back 500 years when the focus was centred on anatomy and the comparative morphology of organisms (Schoenwolf 2002). Today, it is one of the core fields of vertebrate biology. Filled with

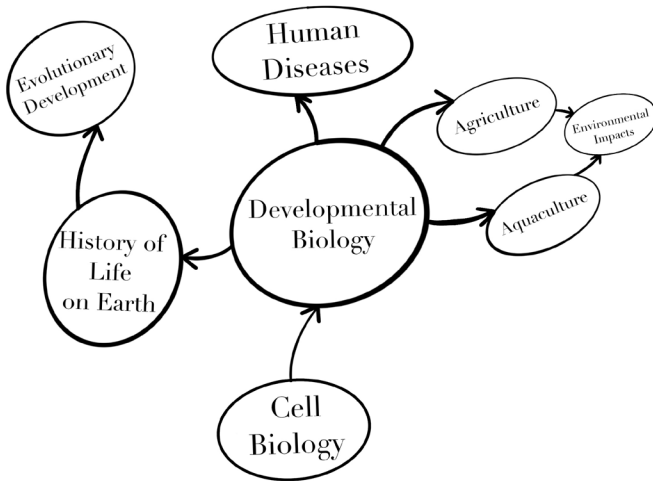


**Fig 2** Metaphorical representation showing that fundamental science is the foundation on which all applied research projects are built, regardless of the field.

wonder for the diversity of animals, scientists turned to understand how this diversity arose by studying the embryos of animals. The field now known as developmental biology studies the development and growth of both plants and animals.

With the advancement of genetic and molecular biology techniques in the last century, these descriptive studies have been complemented by experimental embryology studies, which assess how organisms develop at the cellular and tissue level. Developmental biology research is incredibly useful in that it spans the gap between the cellular and molecular levels, and the systems and organismal levels. Developmental biology generates knowledge for other fields of research, such as anatomy, stem cell research, genetics, neurobiology, cancer biology, and evolutionary biology (Fig 3, Gilbert 2017). Understanding how organisms normally develop helps to provide information on the progression of diseases that may arise during development (i.e., congenital disorders) or those that arise later in life (e.g., osteoporosis). This understanding helps to explain, for example, why some animals are able to heal wounds and regenerate certain body parts, and also provides insights into the causes of birth defects in human populations.

More recently, developmental biologists have turned to the history of organisms to answer some of their questions in a “new” field called evolutionary developmental biology (Müller 2007). This field studies developmental processes over evolutionary time. For example, why are some birds flightless and why do snakes have no legs? Biology helps us to understand more about the world around us. It is



**Fig 3** A flow chart detailing the interconnected nature of some common fields of biological science, and how these fields are connected to developmental biology.

the inter-connectedness of many fields of biological research that has led to progress in fundamental research, and ultimately to progress in our society (Naylor *et al.* 2017).

### SKELETAL BIOLOGY RESEARCH

Our research group conducts fundamental science research to understand the development and growth of bones and cartilages of vertebrates. Because studying the cells of human embryos is difficult, scientists often turn to animal models. What we learn about bone and cartilage development from our work is important for applied research (e.g., to understand congenital birth defects, environmental effects on the skeleton, space biology, etc.)

We utilise two model organisms to answer different research questions. One of the traditional developmental biology animal models is the chicken (*Gallus gallus*). Eggs are easily obtainable and embryos are large (e.g., Stern 2005, Burt 2007). These embryos are also easy to access, manipulate, and observe. Chickens are one of many bird species that have ocular skeletons. These are bones and cartilages within the eyeballs that support the retina. Ocular skeletons have a long evolutionary history among vertebrates. Our research over the

last decade and a half has explored how bones and cartilages develop in birds as well as in bony fish. The other model organism we use is the common zebrafish (*Danio rerio*). This fish offers advantages, such as ease of reproduction and rapid development (Mariotti *et al.* 2015). We use this organism to study environmental impacts on the growth of the skeleton since the entire lifespan or life cycle of zebrafish can be studied in the laboratory.

A key aspect of development of the skeleton is ossification. Ossification is the series of processes that occur during the formation of bones and can be broadly split into one of two categories: intramembranous ossification and endochondral ossification (Hall 2015). Intramembranous ossification results in the formation of bone directly from the surrounding tissue without the need for a pre-existing template (e.g., development of the skull roof). Cells intercommunicate to form an aggregation or cluster of cells, which then directly differentiate into bone cells (i.e., osteoblasts and osteocytes). In contrast, endochondral ossification first requires the formation of a cartilaginous template, which is later replaced by bone (e.g., long bones in arms, wings and fins). As part of the replacement process, the cartilage must be broken down and resorbed to make room for bone tissue to form. There are still many large gaps in our understanding of bone formation and resorption – what mechanisms are used to direct cell aggregation and differentiation into bone cells, and what changes need to occur in cartilage tissue prior to resorption? Whereas these fundamental questions still remain, their answers have massive impacts on our understanding of the overall development, growth, and maintenance of the skeleton. This knowledge is critically important if we want to understand and treat human skeletal disorders. In our research group, we have uncovered some of the key signaling pathways in the earliest stages of bone development and how these genes interact (e.g., Duench and Franz-Odendaal 2012, Jourdeuil and Franz-Odendaal 2016, Giffin and Franz-Odendaal 2020).

One of the problems facing human civilization is how to survive extreme environments. We highlight our research as an example of the research in this field taking place in Nova Scotia. We focus our research on the effects of vibrations and microgravity. After a space trip, astronauts face several health issues, but one of the main problems is a substantial loss of bone mineral density recorded at an alarming rate, about 1.5% per month in long duration spaceflights



(Iwamoto *et al.* 2005, Sibonga *et al.* 2015). The loss of bone density imposes a high health risk in astronauts as it reduces their fitness, and increases the risk of fractures and body support (Sibonga *et al.* 2015). We use zebrafish and/or their scales in a random positioning machine or on a vibration platform to understand the effects of these environmental stressors on the skeleton. Zebrafish have scales composed of a thin layer of bone and we can use these scales as an *in vivo* way to study the responses of adult bone tissues. Larval fish can be placed into the random positioning machine or on the vibration platforms to determine the effects this has on their skeletal growth. We have the tools and methods to study these effects, through fluorescence microscopes, as well as to study changes in bone morphology, disruption of tissues and organs, and changes in gene expression in the tissue (e.g., Duench and Franz-Odenaal 2012, Giffin and Franz-Odenaal 2020). These results will generate a basis for future research in the use of developing organisms on board the International Space Station. Understanding developmental biology should enable scientists and engineers to design methods to circumvent environmental stressors such as zero-gravity and vibrations.

### **INEQUITIES OF SCIENCE FUNDING IN CANADA**

Many important discoveries in science have been incredibly serendipitous: take for example the discovery of penicillin by Sir Alexander Flemming (Hare 1970, Ligon 2004). Many other important discoveries in science have been the result of chance encounters – showing that science is non-linear, and it is often unknown where a given project will lead. While many perceive scientific research as an objective study of the universe that is free from outside influence, it is critical that we recognize the effects that biased funding decisions have on scientific progress. A poignant example of this is the impact of the sugar industry on health research in the 1970s (Kearns *et al.* 2015). Here, scientists were influenced by funding sources from within the sugar industry to favour the publication of studies that suggested that a low-fat, high-sugar diet was healthier to consume (e.g., Larsen and Dougall 2017). This led to a massive increase in sugar sales, at the overall expense of societal health. In contrast, cultures that support and encourage scientific research often are responsible for massive advances in their fields; for a period

of 500 years, the Arabic-Islamic world led a golden age of science due to the religious emphasis on research and scholarship (Faruqi 2006). The impacts of this golden age are still felt today and it is clear that society can have massive impacts on science outcomes.

One would think that an equal opportunity would be given to funding scientific research for each and every scientifically sound project. While this may be how it appears to the public, the bias in scientific funding is apparent to those within the science sector. The outcome of grant applications often reflects how a project is marketed and its short-term impact rather than the value that the research may bring to society decades in the future. In Canada, the federal government funds research through three main funding bodies: The Natural Science and Engineering Research Council of Canada (NSERC), The Canadian Institute of Health Research (CIHR), and the Social Sciences and Humanities Research Council (SSHRC). These three agencies (known collectively as the Tri-Council) are responsible for funding much of the research that occurs in public institutions. When looking at the size of the grants that fund science from each agency (NSERC Discovery Grants, CIHR Project Grants, and SSHRC Insight Grants), it is clear where the priorities of the Federal Government lie. The average CIHR Project Grant is valued at \$174,320, the average SSHRC Insight Grant is valued at \$158,074, and the average NSERC Discovery Grant is valued at \$36,516 (CIHR 2021, NSERC 2021, SSHRC 2021). Only the latter grant type funds fundamental science research and a researcher can only hold one of these grants at any one time. This is in stark contrast to applied science research, in which a researcher can hold any number of these grants concurrently, and often with higher funding envelopes. Clearly, with this structure, the progress in fundamental science research in Canada will be at a much slower pace than that in applied science projects.

One particularly important group that is disproportionately impacted by the current funding system is graduate students (Graddy-Reed *et al.* 2021). These students typically begin their graduate studies shortly after finishing their undergraduate degree; meaning that these students typically haven't had access to well-paying employment to save a meaningful amount of money to help cover expenses (e.g., rent, utilities and essentials, medical expenses, etc.) during their studies. Thankfully, many programs guarantee stipends for each student,

with the idea that graduate students should be able to commit fully to their research without the need to worry about their financial situation. Often the research students involved also work as Teaching Assistants, which provides financial support, but reduces the time available to do the required research. Despite the availability of stipends, institutions still fail to provide adequate financial security for their graduate students.

The graduate school experience is one that can often be characterized by scathing self-criticism, anxiety, and overwork. A quick internet search turns up countless discussions concerning these issues and how graduate students can suffer damage to self-image and physical health (Okoro *et al.* 2022). Graduate school is inherently stressful because of the nature of a thesis and is made significantly more stressful by financial worries. Much of the mentoring and bench-level work conducted in academic labs is done by graduate students, and therefore the stress experienced by graduate students has cascading effects across the academic system. Without adequate support for graduate students, it is very difficult for research groups to produce high quality, grant-winning research. Principal investigators are also pressured to train more graduate students in order to successfully secure funding, which is then not adequate to support these students. Clearly, more investments must be made to improve the well-being of graduate students, in addition to a dire need to increase the funding that supports these students. This is particularly true for those students conducting fundamental science research and who are dependant on NSERC for funding.

## CONCLUSIONS

Our intent with this article is to shed light on overlooked aspects of conducting scientific research and the critical need for significant increases in the recognition of the importance of fundamental science that fuels the success of applied science projects. In Canada, there is a dire need to significantly increase funding to support trainees (students and postdoctoral fellows) within research groups. The huge discrepancy in funding dollars for fundamental science compared to applied research must be addressed, as previously highlighted in the Naylor report (Naylor *et al.* 2017). We need to avoid elitist funding where a few researchers get millions of dollars while others

have to make do with very modest and often inadequate amounts. Fundamental science is the driver of applied research and should be recognised as such by funding bodies and society in general. It is time to reassess the funding of science in Canada to be more equitable across disciplines and research areas.

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