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Awarding of the title of Honorary Doctor in Physics to

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Lectio Magistralis
The continuing need for "useless knowledge"

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I wish to thank the University of Parma, its Rector Professor Paolo Andrei and the Academic Authorities for honoring me with this degree and even more by enabling me, through it, to be linked to this wonderful institution. I also want to thank Professor Cristiano Viappiani, whose initiative and support help make today a reality.

Rector Andrei, faculty, students, and ladies and gentlemen: in 1939 *Harper's Magazine* published an article with the provocative title "The usefulness of useless knowledge" by the American educator and first director of the Princeton Institute for Advanced Study Abraham Flexner (*Harper's Magazine*, issue 179, pp. 544-552, 1939). By "useless knowledge" he meant information that did not have an immediate application, but was, in his words, "unexpectedly the source from which undreamed of utility is derived". His facetious use of the term "useless knowledge" highlighted a misunderstanding that continues to the present: that the most important scientific studies are the ones that are directed to addressing an immediate, real-world problem.

Flexner begins his essay by telling of a conversation he had with George Eastman, the founder of Eastman Kodak and a successful entrepreneur, about who was the world's most important scientist. Eastman chooses Guglielmo Marconi because of Marconi's invention of the radio and wireless. Flexner, however, disagrees, saying "Whatever pleasure we derive from the radio or however wireless and the radio may have added to human life, Marconi's share was practically negligible… [He] was inevitable. The real credit for everything that has been done in the field of wireless belongs… to Professor Clerk Maxwell [and] Heinrich Hertz". Clerk Maxwell and Hertz were the scientists whose development of our fundamental understanding of electromagnetic waves enabled the invention of radio, wireless, and much more. Although particular applications may be exceptionally useful, without an understanding of the fundamental science behind them, the "useless knowledge," they could not have been made. Both basic and applied research are necessary, since one underpins the other.

Indeed, all inventions build on a vast array of knowledge and discoveries made by many, mostly anonymous, people. An interesting infographic illustrating this point was made by the Quartsoft company (quartsoft.com/blog/201410/iphone-technology-history-infographic). The infographic shows the advances, both basic and applied, that were needed to produce the Apple iPhone with its battery, touch-screen, software, wi-fi, and display. The discoveries go back to 750 BCE (the oldest lens) and even earlier. A lot of "useless knowledge" is needed to make a single product.

We have all seen first-hand a more recent example of the importance of Flexner's "useless knowledge": the remarkable development of the mRNA vaccines that protected so many people and saved so many lives in the Covid-19 pandemic that we have just experienced. Decades of research in many labs produced the knowledge and techniques that allowed the virus to be isolated and studied and the vaccines to be made so quickly.

Many other discoveries initially seemed of little practical use, but later profoundly affected people's lives and health. In fact, for the past eleven years, the Golden Goose Award has been given in the United States for such research, specifically, 'scientific studies or research that may have seemed obscure, sounded "funny," or for which the results were totally unforeseen at the outset, but which ultimately led, often serendipitously, to major breakthroughs that have had significant societal impact' (https://www.goldengooseaward.org/). The award has been given, for example, to the maser, which led to lasers and all of the subsequent discoveries and applications that ensued, the discovery that coral is an excellent bone substitute for surgery, and studies on baby rats that showed the importance for contact for survival of premature babies.

Since basic research is essential for the development of future applications and medical advances, how is this new knowledge obtained? Some knowledge, of course, comes from the investigation of existing problems and testing hypotheses. The physicist Enrico Fermi, however, had a very different perspective saying, “If the result [of an experiment] confirms the hypothesis, then you’ve made a measurement. If the result is contrary to the hypothesis, then you’ve made a discovery”. As such he is pointing out how little we know and how much we need to learn, and how much we should be alert to these unexpected discoveries.

Numerous examples of momentous accidental discoveries can be seen among the research recognized by the Nobel Prizes. The research that led to a Nobel Prize in Physics to Robert W. Wilson and Arno Penzias resulted from difficulties they had calibrating the microwave telescope they wanted to use. These difficulties resulted in their discovering the background radiation in the cosmos, the first experimental evidence of the Big Bang. John O’Keefe’s discovery of place neurons in the brain, the basis of his Medicine/Physiology Nobel Prize, began with electrical recording of nerve cells from the wrong part of the brain. And the discovery of the green fluorescent protein (GFP) by Osamu Shimomura for which he received a Nobel Prize in Chemistry resulted from two accidental discoveries. The first discovery occurred when he tried to purify the bioluminescent protein, now called aequorin, from the jellyfish *Aequorea victoria* and failed until he threw samples away in a sink that had sea water, which had the calcium needed to trigger light production. This discovery allowed him to purify the protein. The purified protein, however, left him with another problem which led to another discovery: aequorin gave off a blue light, but the jellyfish produced a green light. This discrepancy led him to discover GFP as the source of the green light.

My own involvement with GFP resulted from a different type of accident. I learned about Shimomura's research during a lunchtime talk given by a guest speaker in my department 27 years after the work was published. At that time, I was using genetics to study nerve cell development and function in the nematode *C. elegans*. My lab had cloned several of the mutated genes, and we wanted to know which cells turned those genes on. Several methods existed to answer this question, but they all involved fixing and preparing the tissue, giving a static picture of gene expression. When I heard about GFP, I realized that it could be used to show us active genes in living tissues, giving us a dynamic view of gene expression. I was so excited about the possibilities that I fantasized about the experiments we could do for the remainder of the seminar.

How can we increase the chance of making discoveries? In part the answer is through institutional support and in part in our individual approach into how we conduct our research. Institutionally, we need to provide resources to enable discovery. In this regard, Abraham Flexner had an answer. He designed the Princeton Institute of Advanced Study to be "a paradise for scholars who, like poets and musicians, have won the right to do as they please and who have accomplished most when enabled to do so". Three institutes that embody this principle and have been the sites of amazing discoveries: Bell Labs in New Jersey fostered the work of many physics and chemistry Nobel laureates, the Medical Research Council Laboratory of Molecular Biology in Cambridge, England fostered a similar amount of groundbreaking research in chemistry and biology, and the Princeton Institute of Advanced Study encouraged the work of most of the mathematicians who have won the Fields Medal.

How do these institutes enable discovery? Put simply they do so by providing wonderful colleagues, supportive facilities, and the freedom to take a chance on a novel idea. I was fortunate to do my postdoctoral research at the Laboratory of Molecular Biology. We had all the equipment and supplies we could ever need (I once asked for a UV lamp and was chided for not saying what wavelength lamp I needed). Even more important than having access to equipment, supplies, and knowledgeable staff were the other researchers. These scientists were people one could learn from and discuss experiments with, and they all shared an enthusiasm for science. Being in such a supportive environment also meant that one had no excuse for getting on with the work. The onus was on us.

I also think that the way we approach our work can lead us to discoveries. Specifically, we need to ask questions (lots of questions) about the world around us and we need to question our assumptions about what we know. I have been struck by how many interesting questions seem to be hiding in plain sight. Some of these questions that came as surprises to me when I learned of them are 1) What makes some tissues, particularly the cornea and lens of the eye, transparent? 2) Why do the limbs of some trees grow upwards (Italian cypress), extend parallel to the ground (fir), or seem to fall toward the earth (weeping willow)? and 3) What makes the white meat and dark meat of the chicken so different. All of these problems have been investigated by researchers who realized their potential for scientific discovery.

In addition to being open to asking questions and to wonder about the world around us, we also need to question what we assume is true and why we believe what we do. My friend and former colleague Mu-ming Poo is one of the world’s most accomplished neurobiologists. One day several of us were talking about our experiments and someone asked Mu-ming where he got his ideas. He replied that he would read a text book (in his case the second edition of *Molecular Biology of the Cell*) and ask why a particular conclusion about nerve growth was accepted. Looking at the original research, he would often find that some conclusions were not as firmly grounded as people thought. He would then test the underlying idea using newer methods and either generate better supporting data or show that the previous conclusion needed to be modified. Using this method, which he called the "retrospective approach," he made many discoveries.

Although Flexner remarks about "useless knowledge" that it has "undreamed of utility", I do not want to end this essay leaving the impression that the importance of basic or fundamental research lies in its potential usefulness. Much more can be gained from the pursuit of "useless knowledge", importantly in understanding the world in which we live. I will end with two of my favorite quotes that say as much. The first is by the mathematician G.H. Hardy, who in his autobiography wrote:

> The case for my life... is this: that I have added something to knowledge, and helped others to add more; and that these somethings have a value which differs in degree only, and not in kind, from that of the creations of the great mathematicians, or of any of the other artists, great or small, who have left some kind of memorial behind them (*A Mathematician's Apology*).

My second quote comes from the congressional testimony of the physicist Robert R. Wilson, who was asked to justify building the Fermilab particle accelerator, the biggest at that time, by indicating in what respect it would help the national defense. He replied

It has only to do with the respect with which we regard one another, the dignity of men, our love of culture... [It] has to do with: Are we good painters, good sculptors, great poets? I mean all the things we really venerate in our country and are patriotic about. In that sense, this new knowledge has all to do with honor and country but it has nothing to do directly with defending the country except to make it worth defending (https://history.fnal.gov/historical/people/wilson_testimony.html).