

## Limitations for Biotechnology Innovations in Brazil

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### Abstract

Four years ago I and others have published an Ebook for Bentham E Books: Opportunities and Limitations for Biotechnology Innovation in Brazil. Since 2011 I have contribute to the Bioentrepreneur Tradeseecrets blog of Nature: <http://blogs.nature.com/tradeseecrets/author/lbarreto>. To date thirty one contributions for the blog were produced mostly dealing with Biotechnology. The context move so fast that I feel stimulated to review the subject to analyze if Biotechnology Innovation in Brazil has progressed lately. We can start with the statement that Brazil has built intelligence in Biotechnology during the last half of century. In the seventies Brazil contributed with 0, 4% of the global scientific output. Today this contribution jumped to 2.6%. Nothing has been multiplied by six in Brazil during four decades and more important, this happened challenging political diversity that normally caused alternation in scientific policies for ideological reasons. As a National Secretary in Research and Development working for the Ministry of Science and Technology for fifteen years I experienced lack of continuity in our programs because new Ministers always wanted to introduce new ideas. It will be difficult for our Sc & Tech to survive if the selection of SC & T Ministers is not technical but political. Why this scientific intelligence has not been taken to industry? What limits yet this transfer? This is object of this Mini Review, that will summarize my latest Opinon Papers and contributions to the Bioentrepreneur Trade Secrets blog mentioned above I will try to demonstrate that not one but in fact many reasons contributed to this context.

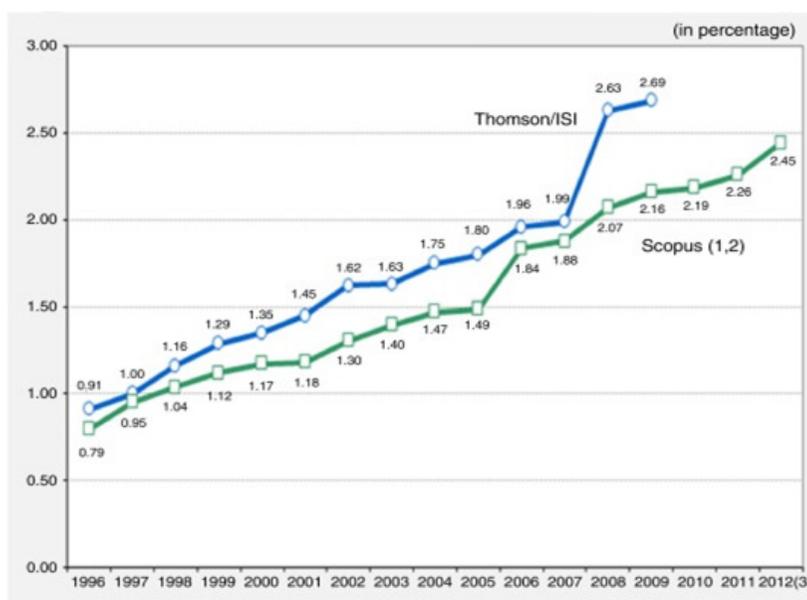
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### Background

Biology has been extremely rich in new discoveries in the last decade since RNAi [1], several versions of Gene editing particularly the one that uses Crispr Cas9 [2] and trascriptome mining [3]. Some countries even under developed ones like Uganda have progressed utilizing these techniques (Julius Ecuru Personal Communication). I feel stimulated to review the subject to analyze if Biotechnology Innovation in Brazil has progressed lately. We can start as I said in the Abstract with the statement that Brazil has built intelligence in Biotechnology during the last four decades. In the seventies Brazil contributed with 0, 4% of the global scientific output. Today this contribution jumped to 2.6%. This scientific intelligence is not taken to industry for reasons I will mention in this Article

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**Figure1:** World scientific output in Brazil. Source: [www.mct.gov.br/indicadores](http://www.mct.gov.br/indicadores)

Biotechnology has not progressed in the area of Pharmaceuticals. We do not innovate we have never registered a block buster in FDA. Pharmaceutical companies funded nationally import formulate and sell. We do not have GMP facilities, do not scale up gene expression in bacteria, yeast and mammalian cell. The SUS (Unique Health System) linked to the Ministry of Health is in the hands of the Big Pharma. They do not invest in Brazil but have offices in São Paulo. Constitutionally they area Brazilian companies.

Import monoclonal antibodies for cancer therapy and sell to SUS as previously said. Competition is very difficult for technical and financial reasons unless we change paradigms expressing genes in plants which has not been attractive to nationally funded pharmaceutical companies so far. The Big Pharma of course does not want to switch from the technologies they exercise and invested for decades. The situation is not the same in agriculture Biotechnology as we will demonstrate later in this Article. Society has access to the advances in terms of products coming from the Big Pharma using legal mechanisms that oblige the SUS system to offer said products to users.

### Public and Private Investments in Science and Technology

Brazil invest less than it should in the area of science and technology. Science and technology are not a priorities in Brazil and worse, when budgets are cut, science and technology comes first, even if reduction of investments in Sc & T do not contribute for the global economical demands of the Country. In 2017 the budget cut in science and technology in Brazil was 44% and the SC&T budget in 2018 will be less than the budget this year

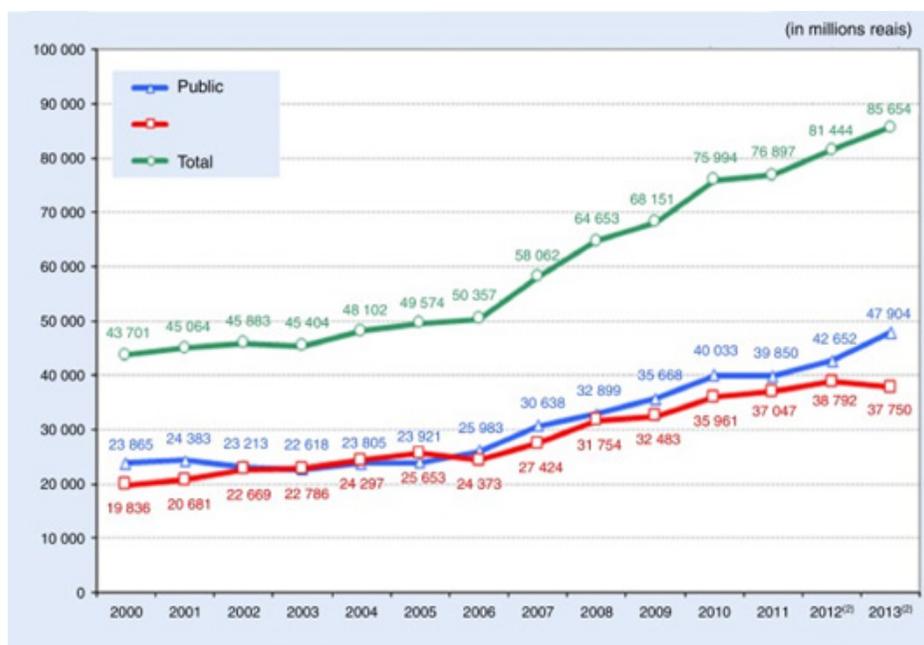
In an Opinion Paper in press [4] I called attention for the fact that Brazil invested recently, roughly 25 billion US \$ in science and technology and should invest at least twice as much. I concluded that after comparing our investment to the investment in the US that is 16 times over what we invest in Brazil the National Growth Income in the US is 8 times bigger than the NGI in Brazil not 16 times bigger. Comparison with other Countries can be worse. The NGI of Brazil and Canada are comparable but Canada invests ten times more [5] in science and technology than Brazil. If the private sector invested in science and technology in Brazil twice as much the investment of the public sector as in most developed countries our investment would be comparable to said countries.

**Why the private sector does not invest more in science and technology in Brazil?**

Brazil as well known is going thru a political crisis that had strong effects in our economy. The economical crisis in Brazil is probably the worst in our history and at the root of it we have corruption. An operation called “car wash” (lava a jato) sent to prison hundreds but it is not over. We impeached one President and may impeach another one. The Supreme Court is very active to support a strong effort to reduce corruption but this whole scenario had a devastating effect in the investment in science and technology already below what should be as demonstrated above.

Money from the private sector that could be invested in Sc & Tech is feeding corruption. Of course we could not expect that the private sector would increase the investment in Sc & Tech during this crisis but the worst part is that even the investments from the public sector is plunging. Public funds for Science and Technology this year is 13, 5 billion US\$, [op. cited]. The consequence is that many scientists are leaving Brazil to work abroad.

One cannot however conclude that the historical lack of investments in Sc & T from the private is due to the recent political crisis. It has happened systematically during the last decades. The reason is that when one could buy governmental bonds that paid high due to the so called Selic rate, the investment had no “risk” and paid way above inflation after one year. Selic rate is being reduced during this decade and will be less than 7.0% by the end of 2017. This will certainly attract private investments to science particularly if the political crisis comes to an end in 2018 with new elections. The second limitation is that Brazil has no venture capital compared with other Countries. In the US Venture Capital is in the magnitude of 40 billion US \$ [op. cited]. In addition the US invests 5 billion US \$ /year in the SBIR program that is governmental and stimulates the small business. We do not have a program of this magnitude in Brazil.



**Figure 2:** Brazilian investment in Sc & T: Public = publico, Private = Empresarial. 3.2 reais = 1 USD  
 Source: www.mct.gov.br/indicadores.

It is important to verify that public investments by most countries are no much above 1.0% of the National Gross Income [Figure 3] but private investments are sometimes two to three times higher than public up to five times higher as it is in Japan. This happen because develop countries succeeded to transfer science and technology to industry which we have not to date. Even though it is important to consider that investments in Sc & T are plunging lately in most countries even developed ones which stimulated the Marches for Sciences in most countries since February of 2017.

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This tendency is markedly prevalent in developing countries. Marches for Sciences have not taken place in Brazil. Our scientific “army” is too small to succeed this way. We have other efforts most of them linked to amendments to the Constitution in the Legislative (PEC). In September 2017, Deputy Roberto Freire entered the legislative with PEC 359. The goal is to add 1% of the GNP to Science and Technology. Compared to India where what is postulated is 3.0% of the GNP PEC 359 is a good efforts because even if the GNP of India is larger than the Brazilian GNP the population of India is six times larger than the Brazilian population.

Additionally we are trying to convince the mayors of two hundred counties that house universities to invest 1% of the taxes received by the county in the universities they lodge. The name of this project is Save the University and may be included in the agenda of the Brazilian Society for the Advancement of Science.

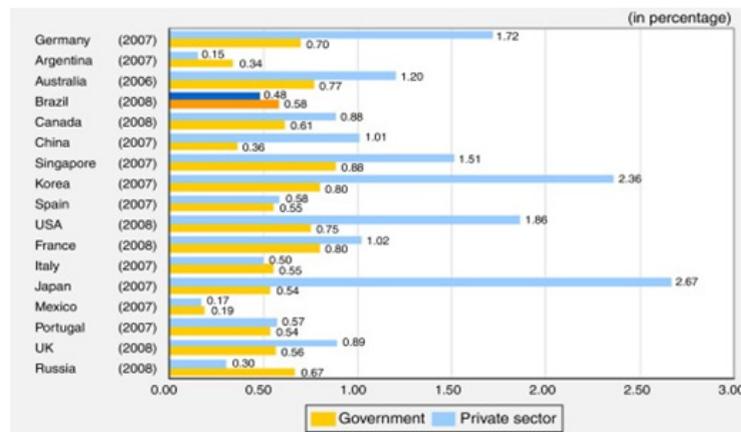


Figure 3: Investments in Sc & T from several Countries. Yellow: Government, Blue: Private Sector. Source: [www.mct.gov.br/indicadores](http://www.mct.gov.br/indicadores).

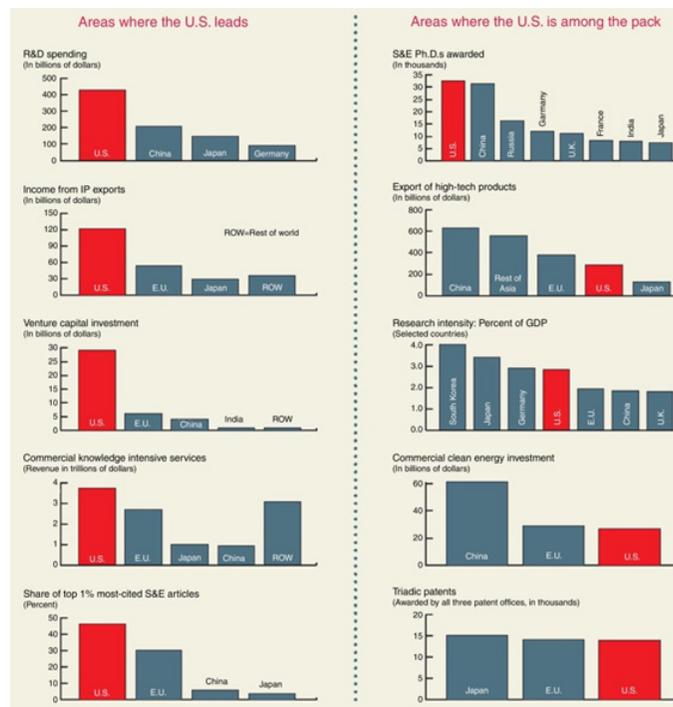


Figure 4: Where US leads and where it lags.

Source: Reprinted with permission from *The American Association for the Advancement of Science* (Mervis, 2014).

**Why investments in SC & T are decreasing lately worldwide?**

Science is not popular. Most people do not know much about the importance of science. They do not know that if not for science we would be dying before 40 years old out of flu. The worst part is that the Legislative does not know much about science either. When they receive a proposal from the Executive cutting scientific budgets as it is happening now during the Trump administration they end up approving reductions in scientific areas that are essential for society life quality. I see no satisfactory effort to make science popular.

When the Legislative cut science budgets the voice of society that should be heard stay silent the bad part is that since the investment in science and technology is not more than 1, 5% of the NGI, the global economy does not benefit from these cuts as said previously. Two important examples can be presented to illustrate this statement the history of vaccine development started in China in the 10<sup>th</sup> century [6] with smallpox by the precarious inoculation of the virus.

The history of vaccine development is a continuous battle that lasts more than a thousand years with pending results such as the lack of a vaccine for malaria that claimed the lives of millions in history particularly in developing Countries. In addition to date there is no vaccine for cancer despite of recent efforts with neo antigens that contain multiple mutated proteins, that are specific to an individual patient's tumor. Giving patients a dose of their tumor neoantigens, which look foreign to the immune system, should help activate immune cells called T cells to attack the cancer cells [7].

The second generation of vaccines was introduced by Louis Pasteur in the 1880s who developed vaccines for chicken cholera and anthrax [op. cited]. During the nineties vaccines became a matter of national prestige in Brazil and compulsory vaccination laws were passed [op. cited] Vaccination despite of the laws were not accepted by society easily in the past and even today. Oswaldo Cruz a medical doctor, microbiologist and scientist was born in São Paulo-Brazil in 1872. In 1897 he studied two years in France. Back to Brazil during the early nineties his challenge to control smallpox, bubonic plague and yellow fever were huge. He attempted to control vectors of these diseases and was strongly opposed by Brazilian medical doctors.

The rise of smallpox in 1904 prompted his campaign to massively vaccinate the population. He had strong support of Rodrigues Alves, President of Brazil that by decree forced vaccination. The reaction of society against vaccination was strong and even the media, the Congress and the Army reacted against vaccination. A League was created against mass vaccination this was known in Brazil as the "vaccine revolt". The Government had to defeat the revolt that lasted for a week in Rio de Janeiro but Cruz had his life and the lives of his family menaced by ignorance.

In 1907 yellow fever was eradicated in Brazil and when small pox became epidemic in 1908 the population asked to be vaccinated. Oswaldo Cruz resigned some years later and died young with 44 years in Petropolis. Yellow fever is native to Africa and was spread in the Americas with the slave trade. Even if considered eradicated in Brazil by Cruz in 1907 it is in fact endemic in the Country. From December 2016 to May of 2017 792 cases were confirmed. [8].

Advances in immunology during the twentieth century turned vaccines much safer reducing side effects. It is surprisingly then that in the 21<sup>st</sup> century important Countries like Italy and France had to make several vaccines mandatory for children. Both countries are facing measles in recent years. The Italian Parliament last July 28<sup>th</sup> voted 296-92 in favor of a new law that will require parents to provide proof of vaccination against measles and nine other diseases. Thirty % of the Parliament voted against compulsory vaccination. In France Prime Minister Edouard Philippe announced to the French Parliament last July 4<sup>th</sup> that childhood vaccines will be mandatory in 2018.

He said to Le Parisien previously that vaccination against 11 diseases were going to be demanded. Amongst 66 countries consulted the degree of confidence in vaccines pointed that France had the highest concern about vaccine safety. There are parents in Countries mentioned previously that are hesitant or decidedly against vaccinating their children [9].

The revolution in Medicine due to antibiotics started in the 20<sup>th</sup> century. Despite of many initial discoveries that led to the discover of antibiotics the major advance came with Alexander Fleming in 1928 when he identified penicillin from the mold *Penicillium chrisogenum*. His Nobel Prize came only in 1945 after he partnered with the chemists Chain and Florey who shared the prize with him. Together with vaccines and antibiotics nearly eradicated many diseases such as tuberculosis in the developed world and polio almost everywhere.

Different from vaccines however that were many times rejected antibiotics were overused. The World Health Organization classified antimicrobial resistance as a serious threat that is happening in every region of the world and affect anyone of any age in any country [6] The threat may have come to an end after Dale Boger in the Scripps Research Institute found a super Vancomycin, an advance that could eliminate the threat of antibiotic-resistant infections for years to come.

“Doctors could use this modified form of vancomycin without fear of resistance emerging,” said Boger. In addition punching holes in the Vancomycin molecule, gives vancomycin a 1,000-fold increase in activity, meaning doctors would need to use less of the antibiotic to fight infection. [10]

### The Regulatory Context

The Biosafety legislations were paramount for the development of Biotechnology in Brazil. I elaborated the Biosafety Guidelines for the PADCT/Biotechnology\*\* that became effective in 1986, very much using subsidies that were available in the Guidelines produced by the NIH after the Asilomar Conference during the seventies. We had no Biosafety Law in Brazil until the Law 8974 [11] was enacted in January of 1995.

The law called for the establishment of CTNBio – Technical National Commission of Biosafety. As National Secretary for Research and Development at the Ministry of Science and Technology I established the first CTNBio team and was President of the Commission from 1996 till 1999. During this period Brazil approved in 1998 the first genetically modified plant, the soybean RR presented by the Monsanto Company.

After this approval Brazil experienced the most aggressive campaign against GMOS that brought together NGOs like the Greenpeace to team with the Judiciary. That culminated with a decision to ban GMOs for eight years by a Judge called Prudente that sentenced that: GMOs utilize alien genes that will give rise to populations that will compromise the future generations in the Planet. Until 2005 Brazil could not legally deliver any GM plant but soybean RR entered illegally in the Country from Argentina and were largely cultivated in the border State of Rio Grande do Sul. More than one million hectares were soon cultivated with soybean RR from Argentina.

Those that were against GMOs wanted to burn these cultivations. President Lula da Silva prevented this and demanded a review of the legislation. He approved in March of the same year, the law 11.105 [12] that strengthened the power of CTNBio and created the Ministerial Council of Biosafety as the last resort for the decisions of the CTNBio. The Council never opposed technically decisions of the Technical Commission but accepted demands of other nature.

The decisions of the Council were final. Unquestionably during twenty years of the history of Biosafety in Brazil the Country went thru difficulties particularly until the law 11.105 was enacted. The most aggressive campaign was named: For a Country free of GMOS. During the last twelve years although many still oppose to GMOs no judicial attempts were made.

\*\*PADCT means: Program to Support the Development of SC & Technology See the World Bank

After more than fifty years dealing with Biology I have never found a technology that has been more regulated than the so called Recombinant DNA. Since the Asilomar Conference in 1973 many scientist considered that these regulations were needed to avoid any undesirable impacts of the technology to human health and to the environment. In 1973 I was a PhD student at UC Davis and remember clearly that the most concern that the scientists had about the technology in San Diego was related to its use to gene therapy in humans.

United States declared a moratorium until NIH regulations that followed, and were adopted by most Countries. NIH rules were responsible for the fact that to date very few (2 in the area of gene therapy) undesirable consequences of the use of recombinant DNA technology occurred. Even though GMOs face an unbelievable opposition in many Countries particularly in Europe. Many examples can be presented to illustrate this opinion. I will mention a couple.

Four hundred protesters invaded IRRI in the Philippines and uprooted the genetically modified rice plants growing inside experimentally. This happened in July of 2013. The rice plants were endowed with a gene from corn and another from a bacterium, making it the only variety in existence to produce beta carotene, the source of vitamin A. Its developers Ingo Potrykus and Peter Beyer called it "Golden Rice." [13].

The destruction of the field trial, and the reasons given for it, touched a nerve among scientists around the world, spurring them to counter assertions of the technology's health and environmental risks. On a petition supporting Golden Rice circulated among scientists and signed by several thousand, many vented a simmering frustration with activist organizations like Greenpeace, which they saw as playing on misplaced fears of genetic engineering in both the developing and the developed worlds.

Lack of Vitamin A causes blindness in a quarter-million to a half-million children each year. It affects millions of people in Asia and Africa and so weakens the immune system that some two million die each year of diseases they would otherwise survive. In this case, many more millions will needlessly suffer blindness and death because Golden Rice is still not available to them. No group, regardless of its intentions, has the right to condemn a technology without evidence. It is an unconscionable criminal act to destroy a field trial conducted in accordance to international safety norms, stated a petition put together by Neidenbach. [14].

In 1992 Aquabounty approached the Food and Drug Administration about selling a genetically modified salmon that grew faster than normal fish. In 1995, Aqua Bounty formally applied for approval. More than 17 years later, the public comment period, one of the last steps in the approval process, was finally supposed to conclude. The AquAdvantage salmon is an Atlantic salmon that carries two foreign genes: a growth hormone gene from the Chinook salmon that is under the control of a genetic "switch" from the ocean pout, an eel-like fish that lives in the chilly deep and feeds normally during the winter.

Atlantic salmon produce growth hormone only in the warm summer months, but these genetic adjustments let the fish churn it out year round. As a result, the AquAdvantage salmon typically reach their adult size in a year and a half, rather than three years. Sources within the government of Barak Obama say that the White House debated the political implications of approving the GM salmon, and said this would likely to infuriate a portion of its base. Many years ago I published an Article saying that science and politics should never mix.

Recently I published this finding in the Bioentrepreneur blog at Nature [15] combing two important examples. Taking from the blog I said that GM salmon in the FDA constitutes the longest case in history of a GM organism attempting to be cleared anywhere in the world. The United States has a role as leader in the subject of commercializing GM plants as food. I wrote a letter to President Obama. Others have, as well. In mine, I essentially said that science and politics do not mix.

In the last century Stalin following Lisenko a young geneticist denied the Russian people the right to study in the schools the modern genetics of Thomas Hunt Morgan. Morgan won the Nobel Prize in Physiology in 1933 and established a Division of Biology at Caltech that yielded seven other Nobel Prizes. Russia today imports grains, a lot of it from Brazil, where the genetics of Morgan was fortunately widely disseminated amongst our geneticists. Finally in August 4<sup>th</sup> twenty five years later Aquabounty announced that the first GM salmon was sold in Canada [16] this is the first animal genetically modified to be used as food. It is clear that since 1973 when Herbert Boyer first expressed the insulin gene in *E. Coli* and despite of the fact that the responsible and safe use of this technology over more than forty four years resulted in few impacts caused by gene therapy as the only negative effects of what now we call GMOs, the technology is not popular as in fact science in general is not popular [op. cited].

There is a myth that transgenic organisms are bad for you, even after many decades lacking scientific evidence to support this. At CENARGEN/EMBRAPA (Carlos Bloch personal communication) peptides could be genetically inserted into cocoa to prevent “witches’ broom”, a devastating crop disease. The cocoa industry did not accept this solution because the peptide was derived from the genome of a frog. We have a long-standing partnership with Elizabeth Maga at U C Davis to introduce by genetic engineering insulin and lactoferrin into dairy milk to reduce infant diarrhea that claims the lives of millions particularly in Africa but also thousands in the Northeast of Brazil.

The dairy industry, at least in Brazil (I cannot speak about Europe, where it may be worse), will never accept it because they believe that people will not consume a genetically engineered milk. One company in Brazil told me to produce insulin by my method and purify it, and said the company would then add it to the milk but would not say the method used was genetic engineering. This persists for many decades despite of a lack of scientific evidence as mentioned before. I think this will not change, and what is worse is that industry and some regulatory agencies will not accept GMOs.

The Golden Rice has never reached the market, while millions die due to the lack of Vitamin A. Even the GM sterile mosquito produced by Oxitec is waiting for approval at FDA that only recently cleared a genetically modified animal. Fortunately the same mosquito was released by CTNBIO in Brazil where the dengue fever affects hundreds of thousands of people. It was not however released by AN-VISA (equivalent to FDA) so far.

Brazil is second to the United States in the cultivation of genetically modified plants. In 2016 Brazil retained this position with 49.1million hectares of biotech crops planted, representing 27% of the global world cultivation of 185.1 million hectares [17] Brazil’s total biotech crop of 49.14 million hectares is an increase of 11%, from 2015. This 4.9 million hectare increase was by far the highest increase in any country worldwide in 2016 making Brazil the engine of growth in biotech crops worldwide.

Biotech crops planted include: 32.7 million hectares of biotech soybean; 15.7 million hectares of biotech maize (summer and winter maize); and 0.8 million hectares of biotech cotton. The total planted area of these three crops in Brazil was estimated at 52.6 million hectares of which 49.14 million hectares or 93.4% was biotech. From 2003 to 2016, Brazil has approved 57 events for food, feed processing and cultivation including 33 maize events, 12 cotton events, 10 soybean events, one bean event and one eucalyptus.

In 2017 the first genetically modified sugarcane resistant to herbicide was approved by CTNBio. Brazilian, multinational seed companies and the public sector research institutions are working on the development of various biotech crops. Currently, there are a number of biotech crops in the pipeline waiting for commercial approval, of which the most important are beans, sugarcane, potatoes, papaya, rice and citrus. Except for beans and sugarcane, most of these crops are in the early stages of development and approvals are not expected within the next five years.

My opinion is that we could have approved more than 57 events at CTNBio if the costs one has to pay to release an event for commercial use were not so high. These costs are easily affordable by multinational companies but not for the majority of the public institutions. Amongst the 57 events released by CTNBio only bean resistant to the Golden Mosaic was produced by EMBRAPA the largest public company working in science and technology for agriculture. Not one University in Brazil could pay for these costs.

I am not criticizing the presence of multinationals seed companies in Brazil. Since 1960 Brazil doubled its grain production that was 30 million tons in 1960. We expect to produce 240 million tons of grain in 2020. These results are due largely to the presence of EMBRAPA that was created in 1973 and the adoption of Brazil for investments by the multinationals after we passed a law deciding to produce seed by private and not by public institutions in 1965.

However even admitting that I was largely responsible for these regulations early in the eighties we have to simplify the process to release events at CTNBio because the history demonstrated that the technology is safe and no impacts to human health and to the

environment occurred. Biology is complex and we were careful to do no mistakes The history of the biosafety in Brazil is getting close to ¼ of a century. We have to review the law and reduce costs to stimulate public companies to come aboard. One example is comparability studies that are expensive.

Biology like I said is complex and extremely rich in new discoveries that may turn recombinant DNA a technology of the past. I am specifically calling attention to the gene editing and CRISPR Cas 9 new technology that is being used largely to answer the majority of the questions in Biology. So far they have not faced regulatory hurdles because they are not transgenic. The regulatory agencies will now work to determine if rules are needed. Certainly this will be the case if human embryos are intended to be targeted with gene editing, but possibly not for plants and other animals.

The decision is not out yet. This may end up being the democratization of genetic engineering because the technology is in the hands of everybody. I discussed this issue in the Blog Bioentrepreneur published by Nature [18] unfortunately considering how agencies behave I am not optimistic. Biology is so rich that gene editing may not be the end of recombinant DNA because now we can express metabolic pathways [19] for biodiversity rich countries like Brazil this may be the technology of the future

### Why invest in science and technology?

Twenty five years ago when the Christian Democrat President of Chile Eduardo Frei Ruiz-Tagle invited authorities of the most prominent institutions in the world to visit Chile, or, as he called it, the end of the world. In the agenda one simple question: can less developed countries (LDC) perform long-term science at the same level that developed countries do? Most people attended from the World Bank, AAAs, Japanese and Korean authorities. Almost all relevant institutions were there.

The President of Brazil then was Fernando Henrique Cardoso. The Minister of Science and Technology was Israel Vargas and I was his Secretary for Research and Development. He included me in his team. The unanimous answer of representatives from developed countries was positive. The route was to invest more in science and technology. Implicit in this answer was the fact that in LDCs, science and technology was not a priority in LDCs. as already stated.

When Representatives answered to President Frey that investments in Sc & T pay back is because they know that there is a link between these investments and income per capita. Laplane from University of Campinas proposed to double the income per capita in Brazil in fifteen years increasing investments in Sc & T. He showed that developed Countries invest at least 2% of GNP (some countries invest 4%). Compared these investments to show that the number of scientists and engineers/million people in these Countries were consequently very high. Technological development depend of these scientists and engineers particularly in the private sector; not a tendency in developing countries.

Other studies corroborate this relations. Albuquerque., *et al.* (2006) from the CEDEPLAR/UFMG showed that there is a correlation between GDP/capita and technological development (Log 10 P). (Figure 6) In the same Article we clearly identify three classes of Countries when we compare scientific production (A) and technology development (P). In the first group scientific output is too low to stimulate technological development. This group includes very poor countries (squares) the line representing these countries is horizontal.

A second group were Brazil is included scientific production is higher and stimulate some technological development, (represented by triangles). The slope of line representing these countries is slightly inclined Finally a group of developed countries were scientific production is very high and also technology development and it is the main determinant of economic growth The line representing these countries is more inclined (represented by losenges) The authors suggest more investments in SC&T for countries in group 2 to reach group 3.

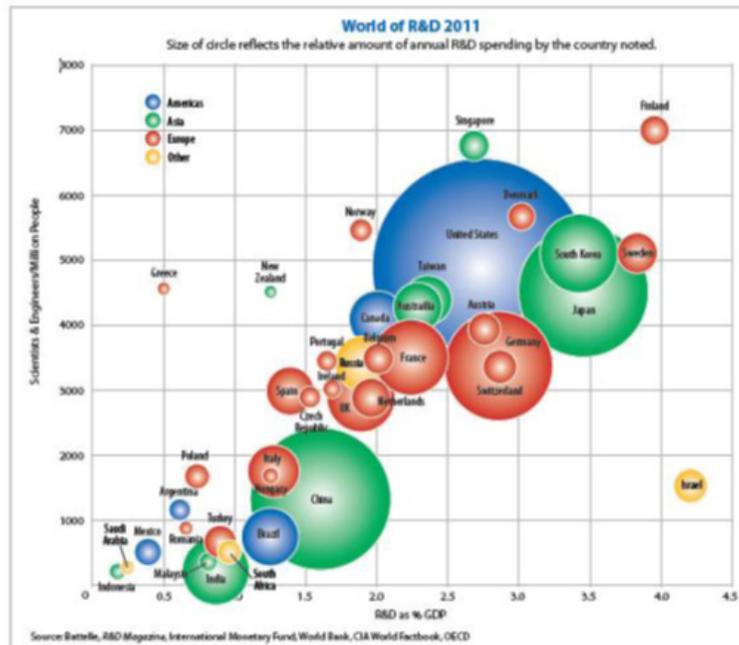


Figure 5: Correlation between scientific output and technology development.

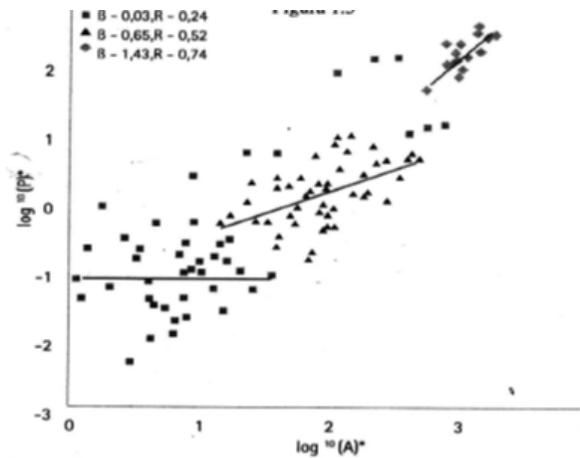


Figure 6: Correlation between GDP/capita and technology development.

### Conclusions

I follow Biotechnology since its onset when Herbert Boyer expressed a gene coding for Insulin in *E. coli* in California. I was a PhD student at U C Davis then. We all saw that Biology was going to change dramatically. Brazil was not far from this advances. Scientists in Brazil repeated the Boyer experiment almost at the same time. Nevertheless after more than four decades Biotechnology has not innovated in Brazil particularly in the pharmaceutical industry.

The first reason is that we invest less in SC & T than we should. In addition we do not invest in Venture Capital and in programs like the SBIR that fund the small business initiative. In the same issue the private sector in Brazil does not invest in technology development like we see in developed countries. The third reason is that bureaucrats of the financial area in Brazil do not trust that SC&T is important to society.

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There is a difference of procedure between developed and developing countries. Developed countries protect SC & T budgets. Cuts are rejected in Congress. Developing countries do the opposite. They cut SC & T budgets and considering the size of these budgets cuts make no difference to the overall budget of the Governments. Bureaucrats cut as said because they do not trust SC&T is critical for the countries.

The bureaucrats of the Finance and Planning Ministry in Brazil believe that science is good for nothing. They do not know that when they cut the budgets of Sc & T they are destroying the intelligence of the country. They know nothing about Sc & T. Cutting Sc & T budgets is like eating foundation seed instead of planting it. Developing countries suffer from another syndrome: alternation of political power as we said when dealing with the increase of scientific output in Brazil and will emphasize here again.

New Presidents, new Governors, new Ministers interrupt long term projects. I was Secretary for Research and Development at the Ministry of Science and Technology for fifteen years. I worked with five different Presidents and four different Ministries. They do not know what Sc & T mean for the Country. The Legislative does not know that either and unfortunately the population does not know how important Sc & T is for their survival. Finally the Regulatory Frame Work is not reliable. This includes intellectual property, biodiversity and biosafety. Investments need a trustful regulatory framework.

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