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Practical paper

The GMO-crop potential for more, and more nutritious food is blocked by unjustified regulation

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ABSTRACT

This article is about the need for more and more nutritious food, the potential genetic engineering technology has to contribute to a solution, the fact that this potential is blocked by regulation, which to my understanding is totally unjustified.

El potencial de la cosecha de OMG para más, y más alimentos nutricionales es bloqueado por un reglamento no justificado

Palabras clave:
Hambre
Organismos genéticamente modificados (OGMs)
Tecnología de ingeniería genética
Arroz Dorado

RESUMEN

Este artículo trata sobre la necesidad de alimentos cada vez más nutritivos, el potencial de la tecnología de la ingeniería genética que debe contribuir a ser una solución, el hecho de que este potencial esté bloqueado por la regulación, que a mi entender es totalmente injustificada.

Shortage of food has two facets: The term 'hunger' describes the situation if somebody does not have enough calories. I assume that most of you may have experienced the unpleasant feeling in your stomach which is the consequence of short-term calorie shortage. Our body gives us a clear warning and there is no negative effect, if we return to a state with sufficient calories. However, long-term shortage of calories has severe consequences on the physical development of our body, which are the more serious the younger we are. To date there are ca. 800 million human beings that suffer from long-term hunger, and this is unacceptable.

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But far more important than hunger is a lack of 'nutritious' food and which means lack of micronutrients such as minerals (iron, zinc, iodine), vitamins, and essential amino acids). And lack of micronutrients it is a far larger problems than lack of calories. And this is something science has discovered only a few decades ago, it is not that long, and the term 'hidden hunger' is very perfect because you do not realise that you are lacking micronutrients until the medical consequences are becoming serious. And I want to talk to you about the potential of the new technology, which you call genetic engineering, on reducing 'hidden hunger'.

As some kind of introduction, I want you to explain some previous ideas.

(1) Genetic engineering technology has substantial potential to contribute to both "food security" (sufficient calories) and "nutrition security" (sufficient micronutrients). The need for both is urgent, especially to alleviate nutritional insecurity ("hidden hunger") in poor populations in developing countries.
(2) The responsibility for the poor is primarily with the public, not the private sector. However, virtually all GMO[1]-plant products in the global market have been developed and deployed for profit by the private sector. The private sector has, of course, economic interests and no direct responsibility for food/nutrition security of the poor.
(3) Despite this situation, there have been well-documented benefits from GMO-crops for the poor, but these are essentially fortuitous "spin-off" effects derived from industrial GMO-crop projects.
(4) From the authors point of view the public sector – not the private one – has responsibility to develop GMO-crop projects specifically targeted at the needs of the poor. Ideally the outcome should enable the poor to help themselves in dignity and sustainably, and with respect for their independence. So far there is an apparent lack of public sector contributions on the market place.
(5) An example is "Golden Rice" designed to target vitamin A deficiency, the most important cause of child mortality, as well as childhood blindness, globally. This public sector project started in 1991; the science was completed in 1999. However, to date and 17 years later a product is still not in the hands of the needy.
(6) The history of this public sector project demonstrates that the "lack of contributions of the public sector" has two major causes: (a) the rules and regulations established world-wide for work with transgenic plants and (b) an ideology-based radical opposition – both heavily promoted by Greenpeace.
(7) Without these two significant burdens we would witness numerous public sector GMO-projects for the benefit of the poor – and several of them would already have improved health and saved the lives of millions.

"**Food security**" is the scientific term for enough calories, "**nutrition security**" is a scientific term for sufficient micronutrients to live a healthy and productive life. There is an urgent need for action because about eight hundred million people do not have enough calories and more than 2.4 billion people do not have enough micro-nutrients. I very often hear in the discussion that people opposed to GMO technology claim that the biotechnology industry is not really working for the poor. Of course not. Each industry is working for profits. That is the normal situation in the liberal economy we enjoy to live in. The responsibility for taking care of the poor is with the "**public sector**", which is universities, public institutions, governments, not the industry. So it does not make any sense to blame the industry for not taking care of the problems of the poor. That is our responsibility. Transgenic plants have been in use for nearly twenty years now and there are many well documented cases, where poor people have benefited. But these benefits for poor people were "**spin-off**" effects from industrial projects. None of those transgenic plants which are in the marketplace, have been designed with the primary goal to help poor people. All these are from industrial projects designed to bring a financial return to the companies. But, fortunately, they had also a beneficial effect on poor people.

A morally correct situation, from my understanding, would be that the public sector responds to his responsibility and designs projects which are specifically designed to help poor people. And these projects ideally should end up in products which allow poor people to help themselves in dignity and sustainability and in respect for their independence. If you look around in the fields, there is not a single such product. Obviously, there is an apparent lack of contribution from the public sector.

You know that I will write about our 'Golden Rice' project and you may have also asked yourself that, having heard for many years about Golden Rice, why it is not in use yet. What happened to Golden Rice? For you to understand the politics around Golden Rice I have to tell you about its history.

Golden Rice represents both the power and drawbacks of GMO-based solutions

I started this project in 1991. The science part was completed in 1999. It was a very complicated project and I had the collaboration of a fantastic partner from Germany, Peter Beyer. However, despite the science being completed in 1999 up to date there is no Golden Rice in the hands of the farmers or the needy. And the topic of my presentation is to tell you why this is so, and what responsibility in a negative terms, Greenpeace and other opponents to GMOs have. In the entire Golden Rice project there is no profit to anybody involved. Nobody who has been working on Golden Rice or is continuing on Golden Rice has any financial return. We all invest our lifetime and our energy, resources from public funding but nobody expects a financial return. The only beneficiaries are the poor.

There are two major hurdles for Golden Rice. The first is the rules and regulations established worldwide for transgenic plants, and I will give you examples of what this means. And, secondly, an ideology based on radical opposition. And both of those are heavily promoted and, in part, initiated by Greenpeace. So it is not a problem that Greenpeace is occasionally disturbing or destroying a test field. The responsibility of Greenpeace goes far deeper and it goes further back

[1] Genetically modified organism.

in history. Without these two burdens you would witness numerous public sector projects for the benefit of the poor and several of them would have already saved the lives of millions. I know of a number of public projects in Spain which would have an enormous benefit on the wellbeing of poor people if they could end up in a product which could be used.

I often have been asked why I have used genetic engineering to produce Golden Rice, knowing that this was a problematic technology. Why have we not used other technology? Well, there is no alternative. If you want rice which has provitamin A in the endosperm, there is no choice. The amazing situation is that when we started to work on vitamin A and rice, nobody talked about '**bio-fortification**'. Bio-fortification means to use the power of genetics to enhance the micronutrients of crop plants. We worked for nearly 7 years until somebody coined that term bio-fortification. So the Golden Rice is, without any doubt, the first example towards biofortification. But it is a GMO project.

When we were nearly ready, other scientists started to use the potential of traditional breeding for biofortification and in 2016, **World Food Prize** has been awarded to the HarvestPlus project, which started ten years later, but could go to the field directly. It is possible to avoid genetic engineering technology if the trait you want to use (e.g. provitamin A) is available, but to low in expression. But you cannot use traditional breeding if the crop plant does not contain the trait. For many important traits or characters like vitamin A, iron, high-quality protein, other vitamins like folic acid or vitamin B6... where the trait is lacking or to weakly expressed you have to use genetic engineering and, without any doubt, for Golden Rice we had to use genetic engineering.

What is the progress with Golden Rice to date?

The technology is stable, reproducible, free of charge for the trade because we have established a "**humanitarian project**", applicable to all rice varieties tested so far, and provides sufficient provitamin A from half a cup of rice to prevent vitamin A deficiency. We have received free licenses for all technology involved. Therefore, farmers do not pay a cent for the trait. Compared to traditional interventions, Golden Rice is highly cost-effective and sustainable, and optimised varieties are under development in the Philippines, in Bangladesh, in India, Vietnam, Indonesia and China.

What are the challenges?

Besides the 'normal' GM-challenges such as fierce opposition, vandalism, anti GM-propaganda, 'liability' concerns, no permission for working in the field, variety development without field data, there are specific challenges such as all breeding to be based on one lead event, selection of the lead event without agronomic data, availability of the lead event to all partners, timely provision of the lead event to further target countries with high VAD and rice consumption such as Myanmar, Laos, Cambodia, and countries in Africa and Latin America – and epidemiological studies on efficacy. It is a tragedy that despite the fact that we have the technology and could use it, those countries, which have the highest level of vitamin A malnutrition, like Myanmar, Laos and Cambodia, all have about 40% vitamin A malnutrition, have not yet received the technology. And also in countries in Africa and Latin America.

Vitamin A-deficiency – a public health problem in 156 countries

- 190 million children & 19 million pregnant women affected globally.
- 1–2.5 million deaths per year through immune response suppression.
- 500,000 per year blinded.
- 600,000 women die annually from VAD related causes at childbirth.

So, a lot of unnecessary deaths and suffering because the technology is here, to compare to present public health problems, I give you years in data: global mortality from malaria 715,000, from tuberculosis 1.4 million, from HIV-AIDS 1.7 million, from vitamin A deficiency 2.4 million, and from micronutrients deficiency 8.5 million. I am sure you have heard a lot about AIDS, and have heard from malaria, and the billions of support going into projects to reduce these maladies. I am sure not many of you have heard of micronutrient malnutrition until today. The consequences if you are vitamin A-deficient: it impairs vision up to complete blindness. It impairs epithelium integrity against infections and you die from normal infectious diseases like measles or other simple childhood diseases. It affects immune response, haematopoiesis, skeletal growth, iron absorption, brain development and cognitive and mental capacity. These are not only health problems that affect our wellbeing but they also really affect our cognitive development and cerebral capacity.

What are traditional intervention's

Distribution of vitamin A in capsules, encouragement for diversified diet, encouragement for support for plants rich in provitamin A. These interventions are all effective but the figures that I have shown you are on top of these traditional interventions so it is obvious that we need more powerful interventions.

The concept for a complementing intervention

Now let's talk about "biofortification". Biofortification is the term for a scientific approach to use the power of genetics of crop plants to improve their micronutrient content. This is a perfectly "green" approach, because you use genetics, a biological technology, and you use this technology to change the genetic makeup of crop plants.

An approach with the largest possible impact

Why did I work on rice? Because I wanted to have the largest possible impact and no other crop plant is as important for humankind as rice. Rice feeds nearly half of the world

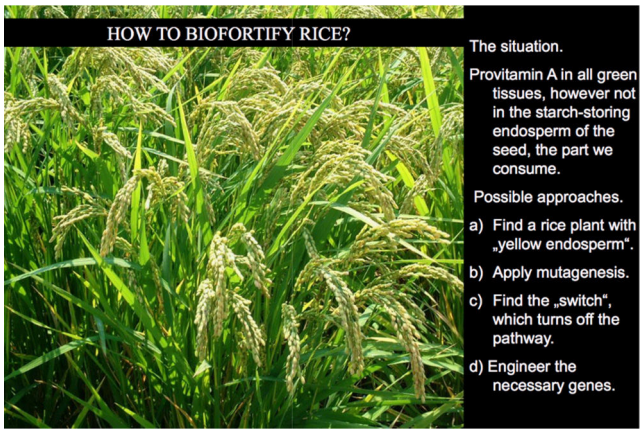

Fig. 1 – The four alternative approaches to biofortification of rice.

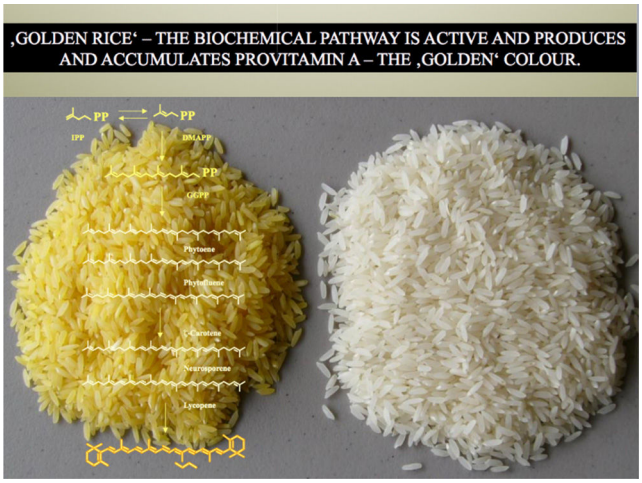

Fig. 2 – Golden Rice and its counterpart, normal white rice.

population. Rice provides up to 80% of the food. It is a perfect source for calories and it contains some protein and fat but is very poor in iron, zinc and it totally lacks provitamin A. Technical fortification is not possible and, therefore, rice was the ideal target to test not only the science of a biofortification approach but also the practical implication (Fig. 1).

How to biofortify rice?

What can you do if you want to biofortify rice? You have four alternative possibilities. Actually provitamin A is in all green tissues of the rice plant. All green colour you see represents provitamin A. But we do not eat rice leaves, we eat rice endosperm. Endosperm is white which means there is no provitamin A. From the fact that we have provitamin A in the green tissue and not in the endosperm we can conclude, that there must be a switch which turns off the pathway in the endosperm.

Therefore, the most logic approach would be to try to find this switch and when we proposed our project of genetic engineering to the Rockefeller Foundation, the scientific advisory board proposed to invest into finding this switch and they financed a laboratory in the US to find this switch. And this was 1992 and every scientifically knowledgeable person believed this would be the most promising way to go. Well, the switch has not been found until today.

You can try mutagenesis, induced random changes of the genome. There are lots of technical possibilities and they all have been tried extensively, but no mutant has been found which produces provitamin A in the endosperm.

You can look for national variation. Again, this has been done extensively for many years and rice breeders looked at 80,000 different accessions of rice and rice relatives, but there is no yellow endosperm in the rice or rice relatives. Therefore, plant breeding could not be used to solve the problem.

The only remaining alternative was **genetic engineering**. It took eight years and it was a very complicated effort. We had to account for eight genes to isolate and to re-introduce with endosperm-specific regulation, to bring them to work together, in membranes, assembled to complex protein membrane structures. It was a miracle that it worked. Even my partner Peter Beyer, who was a specialist in the biochemistry of this pathway, did not believe it could work. I was naive enough to continue. And, as I said, it worked to everybody's surprise. And here you see on the left hand side the Golden Rice, which is golden because it produces provitamin A. And the difference between this golden rice and normal rice is that the same natural biochemical pathway that you see in this picture works not only in the leaves but also in the endosperm. And that is the only difference, otherwise these plants are identical (Fig. 2).

It is very difficult to understand why somebody should be afraid of!

"Golden Rice" – an enthusiastic welcome

This scientific breakthrough received a very enthusiastic welcome. Not only by the scientific community, also by the media, by politicians and the society at large. Everybody expected Golden Rice to be in the farmer's field soon. This was in the year 2000. Now we have 2016 and Golden Rice is still not in the field. Hopefully it will reach the fields during my lifetime, which means in a few years because I am close to 83 years old by now. The only reason why it is not in use is because it is a G.M.O. I remind you, that the only difference between white rice and yellow rice is that the same pathway works also in the endosperm (Fig. 3).

Golden rice is the most effective and sustained measure against vitamin A deficiency. You see here, in this dish there are forty grams of golden rice, in the hands of a Filipino coworker in is the Philippine Rice Research Institute. And these forty grams of rice are sufficient to prevent vitamin A malnutrition with all its traumatic consequences.

Golden rice is safe for the consumer and the environment

All these years we have collected huge amount of data to prove that it is so and, if you think about this situation, it is just

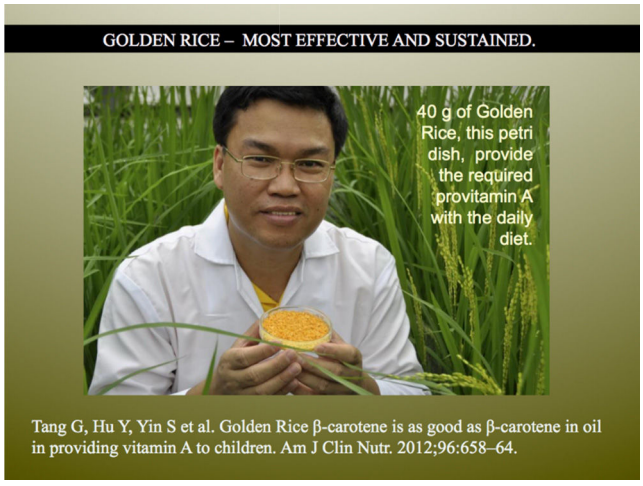

Fig. 3 – Forty grams of Golden Rice per day provide the missing provitamin A in the diet.

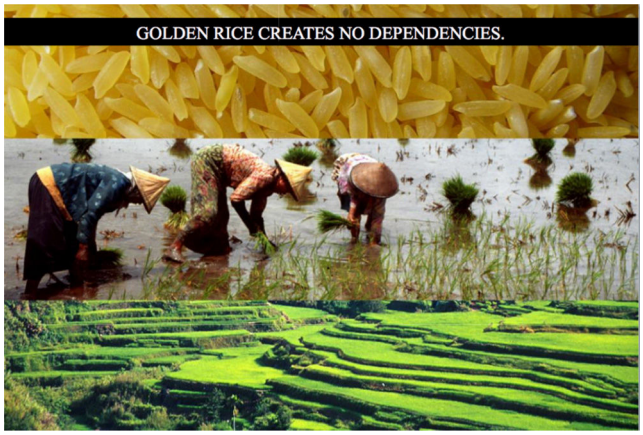

Fig. 4 – The use of Golden Rice does not lead to any new dependencies.

impossible to construct a risk to the environment from a rice plant which contains a few extra micrograms of provitamin A. Maybe the two Greenpeace ecologists who are here can tell us later what the risk for the environment Golden Rice is. The product will be released for consumption and cultivation only if national biosafety authorities are convinced by the data collected that there is not the tiniest risk to the consumer and the environment.

A product from the public sector for public good

Golden rice has been developed in the public domain, with public funding for the science and with financial support for product development and deployment by philanthropic organisations, like the Rockefeller foundation, the Syngenta foundation and Gates foundation. No industry money involved. All intellectual property rights are covered by "**free licences for humanitarian use**". All work is performed on the basis of a contract between the inventors (Ingo Potrykus and Peter Beyer) and all those collaborating institutes who signed this contract. This guarantees that Golden Rice will be used exclusively in the developing countries where the vitamin A deficiency is a health problem, nowhere else, and that there is no Golden Rice export from those countries and that Golden Rice is consumed in those countries where it is produced and that the farmers do not pay any additional cost for the golden rice trade (Fig. 4).

Golden Rice does not create any dependencies. The farmers are the owners of the seed. They use their own traditional production systems. They do not need any additional agrochemicals and they use part of the harvest for the next sowing. So none of those claims from the G.M.O opposition do not apply to Golden Rice.

Agronomically optimised locally preferred varieties are developed through public rice research and breeding institutes in developing countries where vitamin A deficiency is a severe health problem and the rice is a major stable crop. Only after release of national biosafety authorities it will be available to farmers, not one day earlier. The national biosafety y authorities have the autonomous mandate and responsibility of testing and controlling that there is not the slightest risk to the consumer or the environment.

The entire technology is in a seed. If the farmer has one single golden rice seed, it can grow in 3 years, if he wishes, from that seed hundreds tonnes of Golden Rice. When he puts the seed in the soil, it will produce about 2000 seeds in the first generation, 2000 × 2000 (4 million) in the second generation, 4 million × 2000 (8 billion) in the third generation to thousands of tonnes in the next generation of Golden Rice.

A single seed is sufficient to start the project in the hands of the farmer. The only restriction is the conditions for "**humanitarian use**", which I told you already. In addition, we have a clause which states that if a farmer has a profit for more than 10,000 dollars from Golden Rice, it is not considered humanitarian. Why do we have this financial restriction? Because we did not get any support from the public domain for our project. We needed to find help from the private sector. And, in the private sector, Syngenta was interested to develop a commercial product. We reached an agreement where we transferred the rights for commercial product development to Syngenta, if Syngenta in turn supported our humanitarian project. And Syngenta needed, of course, some security that the humanitarian project would not compete with the commercial project. We agreed finally on a 10,000 dollar limit, and this included safely all those hundreds of thousands of subsistence farmers for whom we developed Golden Rice, because there is not a single subsistence rice farmer in the world who expects a profit of more than 1000 to 2000 dollars per year (Fig. 5).

So it is a safe situation. Golden Rice is developed in South Asia so far; in countries like Bangladesh, China, India, Indonesia, the Philippines and Vietnam. I would like to alert Greenpeace that golden rice is not developed for the Philippines. Golden rice development is done in the Philippines because there is an International Rice Research Institute IRRI) and the National Rice Research Institute (PhilRice) working closely together with the potential for speedy development. We wanted Golden Rice primarily for India and for countries like Cambodia, Myanmar and Laos, where vitamin A-deficiency is a far more severe problem. So the Philippines are not there because vitamin A deficiency is a big problem but

Fig. 5 – The entire technology is in the seed and belongs to the farmer, within the frame of the humanitarian project.

because, although there is vitamin A deficiency, there are two powerful institutions doing the development and all institutions are linked in a network, which ensures that progress in development reaches the other countries as well.

Care has been taken to develop those varieties consumed by the poor and not by the middle class. The collaborating rice breeders have done very careful research to see which future rice variety will be consumed by poor populations five years from now. And early on we had a request from basmati rice producers to produce a golden basmati. We did not allow this. We will never allow it because golden rice is an invention to help poor people and not to please middle class people with some fancy golden rice.

Many years have been wasted because of regulations and you see here all that that has to be done to collect all the date required for regulatory procedures, and we are working on it since the beginning of the project and it is not yet completed. But the most prominent hurdle is permission for working the field. I did not say it but, as soon as you have golden rice in the laboratory, it has to go into the breeding programme and you have to transfer the trait into farmers' preferred varieties. This is traditional standard breeding. And this breeding requires the response of the plant to the environment. You cannot do breeding in the laboratory or a biosafety glasshouse; you need the response to the environment to do a breeding programme.

Twelve years have been wasted because of regulation

So if you do not get permission for your golden rice to go into the field, you cannot do breeding. So if somebody wants to prevent effective use of transgenic plants by the public sector, they just have to prevent field release.

Deletion of selectable marker: 2 years
Screening for streamlined integration: 2 years
Screening for regulatory clean events: 2 years
Transboundary movement of seeds: 2 years
Obligatory sequence greenhouse-field: 2 years
Permission for working in the field: more than 10 years !!!
Requirement for one-event selection: 2 years
Experiments for the regulatory dosier: 4 years
Deregulation procedure: 1 year

Golden rice is in India since the year 2000. The first permission for field release took until spring 2016, and was withdrawn again. The first permission in the Philippines came in 2012. We did not know that it was so complicated, but that is our experience.

In the year 2004 we tried one experiment in the United States. We wanted to see how Golden Rice would grow in the fields. It took less than half a year from the application to the plants growing in the fields. That is how different countries handle the same kind of regulation. It is not only the regulation itself, the greater problem is, how these are handled in different countries. Developing countries are heavily influenced by the European attitude, again thanks to the activities of Greenpeace and allies.

The outstanding problem: no permission for field work

All these problems with regulations are the consequence of the infamous "Cartagena Protocol", with its precautionary approach, especially its extreme interpretation. This has blocked plant breeding as effectively as I told you. The Cartagena protocol was the first United Nations conference with participation from N.G.O's. And the N.G.O.s under the leadership of Greenpeace effectively took over the conference and organised the conditions under which every transgenic work is suffering today. The goal of the opposition was probably not so much to disturb the public sector, but to hurt the "big agbiotech industries". In reality big agbiotech industry is using the technology effectively to their advantage. But the public sector is blocked from doing so to work for public good and to compete with industry effectively.

It is mandatory to change regulation

If we want to use the potential of all this in the public domain for the benefit of the poor and disadvantaged it is mandatory to shift regulation from ideology to science, which means that regulations should take care of the product independent of the technology used to produce the product. If there is a possible risk, it does not come from the technology but from the product. By freeing G.M.O plant breeding from its ideological handcuffs the public sector would be able to effectively contribute to food and nutrition security for billions of poor.

Golden Rice – Status

The technology is stable, reproducible, effective in all rice varieties tested so far. It is free of charge for the trait and provides sufficient provitamin A from half a cup of rice to prevent vitamin A-deficiency.

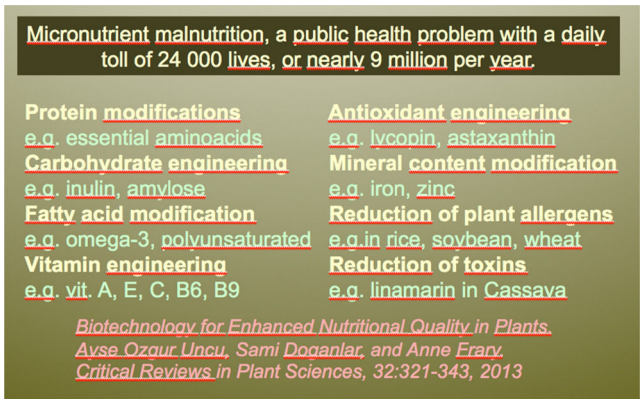

Fig. 6 – Biofortification for enhanced nutritional quality.

Agronomically optimised varieties are under development in The Philippines, Bangladesh, India, Vietnam, Indonesia, and China. This will, hopefully extend into further countries where vitamin A-deficiency is a public health problem. High on the list are Myanmar, Laos, and Cambodia.

Golden Rice – Perspectives

Provitamin A in rice was the beginning. It will be complemented by iron, zinc, high quality protein, further vitamins, healthy fatty acids etc., all combined in one variety.

The concept of provitamin A biofortification has been extended to further crops such as maize, banana, cassava, potato, and sorghum to reach those who depend upon other crops than rice.

The future of GMO-based biofortification for public good will depend on science-based regulation which is, so far, prevented by the influence of the anti-GMO lobby.

The GMO opposition is determined to prevent Golden Rice

A world-wide operating, well financed and politically influential anti GMO-lobby is fighting GMOs "by principle" to cause damage to big ag-biotech industry. This radical position does not allow for an exception with Golden Rice, irrespective of the damage to life and health of poor and rice-depending populations.

Science has opened numerous opportunities for improved micro nutrient nutrition (Fig. 6).

The consequences of GMO regulation will prevent that these proof-of-concept cases will lead to products.

What are the putative risks to the environment which justify a ban on controlled field experiments of Golden Rice?

Golden Rice contains a few microgram of provitamin A in the endosperm, a substance which is present in gram quantities in the leaves. This substance does not provide for any selective advantage in any agronomic or natural environment and, therefore, does not pose any foreseeable risk. What than is the argument to defend a ban and prevent field testing under controlled conditions early on. I would be interested to learn from the Greenpeace ecologists present, with which argument they defend a ban on Golden Rice field testing.

Why is present GMO-regulation unjustified?

(a) There is overwhelming consensus amongst scientists, documented in numerous publications by national and international scientific academies, that existing GMOs are safe fort he consumer and the environment. (b) There is the same consensus that genetic engineering technology does not pose novel or unusual risks. (c) There is the experience from the use of GMOs over 20 years and on hundreds of millions of hectares with not a single documented case of harm. (d) Induced mutagenesis by chemicals, irradiation, or *A. tumefaciens* insertion poses higher risks and goes unregulated. (e) The specific case of Golden Rice, having no other change but a few micrograms of beta-carotene (provitamin A) in the endosperm, a substance we are eating routinely and a substance offering not even a hypothetical selective advantage in any environment, is of no immaginable risk. (f) Risk considerations without weighing the risk against benefits does not make any sense. (g) When doing a risk/benefit analysis - not even a hypothetical risk against the potential of saving life and eyesight of millions of poor – it is correct to state that it is "a crima against humanity" to prevent or to delay the deployment of Golden Rice. And the same is true for precision agriculture (supportprecisionagriculture.org)

In short, I wanted to explain what it may mean to work in a public GMO-project for public good. Under present conditions you not only have to be very persistent, you need a long life. If I do not count the years I spent in technology development, but just straight forward the time I spent on the Golden Rice project than this sums up to 25 years so far, and it is not yet over. What may be even worth – my wife and my entire family suffered from my work because Greenpeace and allies have poisoned the social environment enormously.