The Scientific Legacy of the 20th Century
Pontifical Academy of Sciences, Acta 21, Vatican City 2011
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Genetic engineering of plants: my experience with the development of a key technology for food security

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I have chosen a rather personal title for my presentation. Because of my age, I happen to be one of the pioneers of the development of this infamous GMO-technology and I considered it interesting to present you with a personal account of the development of this highly controversial technology (Genetically Modified Organisms) you all are familiar with to date. I am also responding to the prologue by Werner Arber and Jürgen Mittelstrass. I would like to show you my *personal testimony of the acquired new scientific knowledge including its application and the expected future impact especially for the welfare of human societies*, and I will include some personal recollections.

Since my youth I have been a zoologist by interest and it is surprising that I did my PhD at a Max Planck Institute for 'Plant Breeding Research'. The reason was, that I was impressed by the director of this institute, and that he encouraged the college teacher of sports and biology to work on a PhD thesis in his institute. At that time, it was in the early 60s, a hypothesis from the 1930s, that plant cells are potentially 'totipotent', by the Austrian botanist, Gottlieb Haberlandt, could be experimentally verified for the first time. This first evidence came from work with embryogenic carrot cell suspension cultures just during the time of my PhD thesis. Although working myself on chloroplast inheritance, I was very deeply impressed by this phenomenon of totipotency. Subsequently it could be shown that even highly differentiated plant tissues contain cells that have the capacity to develop into a complete fertile plant. During the course of my own first years in science I was able to add a few experimental examples, and in the course of a few years – in the early seventies – it was possible to take living cells from virtually every organ of a plant, including the germ cells (leading to haploid organisms), and allow them, under totally defined conditions, to regenerate to complete plants. I should stress that we had learned which experimental conditions we had to provide for the cells to embark onto the pathway to a complete plant. But we do not really understand – up to date – how the cells fulfil this miracle. So I was, and still am, fascinated by this capacity, but if I tell you why I was fascinated you will be disappointed. I was not fascinated by the scientific problem to be studied. I was fascinated

by the potential this phenomenon was offering for plant breeding. This indicates that I am not a 'scientist' in its true sense, but that I am rather an 'engineer'. My mind is primed towards solutions of concrete problems. If plant cells are totipotent, this would offer the possibility for plant breeding to work with millions of genetically identical single cells in the Petri dish (instead of thousands of plants in the field), to modify their genome and regenerate 'genetically modified' plants. In the early experiments with the model plant Petunia we explored all that would be technically possible. As the cell wall was to be considered an absolute barrier to virtually all genetic modifications we had in mind, we started to develop the first cases of cell wall-free 'naked' plant cells (protoplasts). We were interested in combining total genomes, in combining parts of genomes, in introducing complete nuclei, other organelles, such as chloroplasts or mitochondria, and we were interested in introducing pure DNA. As soon as it was possible to regenerate fertile plants from such cell wall-free cells, we tested all these novel genome combinations indicated above, and easily ended up with a few *Nature* publications out of this work. However, my motivation was to use this potential to contribute to plant breeding research, but to food security and model plants such as Petunia were not too promising in this respect. This was also in the early days of the Green Revolution. With the rapidly growing world population, we would need to continue on the path initiated by the work of Norman Borlaug, who became one of my heroes. I felt that I had to leave the easy work with model plants and shift to more important plants for food security, and this was the beginning of my work with cereals in 1972. In the subsequent decades I worked with wheat, barley, oats, maize and later with rice, cassava and sorghum. The concept for all our work was based on the well-documented fact that somatic plant cells are 'totipotent'. Well, I got a very tough lesson. I spent more than ten solid years of enormous experimental efforts in trying to convince cereal cells to behave as one could expect from them, but differentiated cereal cells refused to be 'totipotent' – and they still do so to date. After ten years of intensive experimentation and more than a hundred and twenty thousand variations in experimental culture conditions, using every possible growth factor and every possible media factor combination including up to seven factor gradients in a single Petri dish, I finally accepted that graminaceous plant species are obviously basically different from herbaceous plants with respect to 'totipotency'. The cause may have something to do with the strategy of how cereals defend themselves differently from mechanical attacks, compared to herbaceous dicots. If a herbaceous dicot is wounded, the cells adjacent to the wound dedifferentiate, re-embryonalise and replicate to close

the wound with newly formed wound tissue. If a cereal tissue is wounded, the response is totally different: the wound-adjacent cells in a cereal produce phenols and undergo a programmed cell death, and there is no wound healing. This wound healing reaction which is the biological basis for tissue culture – and totipotency – does not exist in graminaceous species. This was a big surprise and we were in trouble, because all our plans on the genetic engineering of cereals were based on the concept of totipotency. It took some time to forget about this concept. An alternative finally opened up through a development using meristematic (embryogenic) cells, preventing their differentiation, establishing embryogenic cell cultures (comparable to stem cell line research with animals) and using protoplasts from those embryogenic cells. On this rather 'unusual' basis for plants it was finally possible to also approach genetic engineering with cereals. There was, however another important consequence from this experience with cereals and it was that, most probably, *Agrobacterium* was no longer to be considered a useful vector for transformation. At that time, virtually all laboratories interested in the genetic engineering of plants were developing *Agrobacterium* as the gene transfer vector. From our experience with cereals it was obvious that the dicot-type wound response dependent transfer of a plasmid by *Agrobacterium* into plant cells would not function in cereals. As this meant that *Agrobacterium* was not an appropriate vector for gene transfer to cereals, we had to develop an alternative gene transfer technique on the basis of naked plant cells, allowing us to introduce naked DNA into naked plant cells independent from any biological vector. We had tried this already in the early 70s, a time when many laboratories worked on rather desperate experiments to demonstrate gene transfer into plants. To improve the situation we approached genetic evidence for putative integration of foreign DNA in contrast to those who looked for phenotypic data. Let me briefly describe an experiment – which failed – to give you a flavour of the situation around 1972: we hoped that naked plant cells would take up foreign DNA. To test whether DNA can be taken up and can be integrated we used a genetic system which was state-of-the art for this purpose at that time: we had a homozygote, recessive white flowering Petunia, the white flower colour representing a recessive, monogenic trait, and we had a dominant, monogenic and red flowering Petunia. We isolated total DNA from the red flowering petunia and treated protoplasts from the white flowering petunia with that DNA, hoping that, among thousands of offspring, we might find one with pink flowers (the sexual cross yielded pink flowers). This looks like a very rough experiment nowadays: at that time it was state-of-the-art and better than anything else. Well, the big surprise came when we finally had

a greenhouse full of Petunia plants regenerating from these DNA-treated protoplast: the first plant had pink flowers – fantastic! – the second plant flowered pink as well, the third plant flowered pink, the fourth plant flowered pink etc. At the end, the entire greenhouse was filled with pink flowering plants. This was, of course, no evidence for 100% transformation, but an artefact. In 1984 we did it better: we isolated a single defined microbial gene for antibiotic resistance and treated tobacco protoplasts using cell membrane modifying agents; we applied selection pressure for successful integration and selected among hundreds of millions of cells for developing cell colonies; we recovered fertile plants from those and we demonstrated the Mendelian pattern of inheritance for this single dominant trait, and we demonstrated the integration of this DNA into the host cell genome. This was the first clear-cut demonstration that genes can be introduced into naked plant cells without the contribution of any biological vector, thus finally opening the route for gene transfer to cereals. But this experiment was done with tobacco and not cereals. However, we had a technique at hand to introduce genes into naked cells and we applied this technique to cereals and our first transgenic cereal – it was rice – was published in 1988. Well, this was eighteen years from the time I was starting to work with these ideas. From then on we applied this technology to introduce agronomically important traits into cereals and other crop plants. We were determined to contribute to food security and tried in a first round of experiments to use this technology to rescue harvests which otherwise would have been lost to insects or destroyed by fungi, bacteria or viruses. We were introducing resistance genes into rice, and in 1991 we sent our first insect-resistant rice to our collaborating International Rice Research Institute in the Philippines. This GMO-rice did not reach IRRI. It was kidnapped by Greenpeace with the help of a sociology student from my university. This may indicate that by that time we already had a very radical opposition against this technology in Switzerland.

By then, from 1989 to 1990, I realized that food security does not only mean enough calories to avoid hunger. It also means having the right quality of food to avoid 'hidden hunger'. From then on I focused on this problem. Hidden hunger describes the fact that people who don't have a diversified diet are suffering from deficiencies in minerals, vitamins and essential amino acids – with most severe health consequences. Since by that time many laboratories, including powerful laboratories of large agbiotech multies, were working on resistance to any kind of biological or physical stress, and no laboratory was interested in the problem of hidden hunger – there was not much financial return to be expected – this became the field

of my lab. I started to focus on the problem of vitamin A deficiency. Vitamin A deficiency is a major public health problem and it affects 190 million preschool-age children and 19 million pregnant women around the world. Details from the WHO global database are given in Figure 1 (p. 368).

To reduce vitamin A-deficiency the World Health Organization (WHO) invests between 90 to 100 million dollars per year in the distribution of vitamin A capsules. We felt that a complementing intervention was a valuable task to test our technological possibilities. The distribution of vitamin A-deficiency around the world is given in Figure 2 (p. 368): exceptions are only Western Europe, North America and Australia, all the other countries are affected. The medical consequences from vitamin A deficiency are quite severe: irreversible blindness – every year we have about 250,000 children becoming blind due to vitamin A malnutrition; an impaired immune system – leading to the death of 2 million children from normal infectious diseases like measles; anaemia – because vitamin A plays an essential role in iron mobilisation and transport; impaired hematopoieses and maternal mortality during pregnancy – 19 million pregnant women at risk each year.

What was the scientific challenge we faced at the beginning of the 1990s? The status quo is the following. The rice plant produces large amounts of provitamin A in all green tissues (plants never produce vitamin A; plants produce provitamin A and our bodies convert provitamin A into vitamin A). Rice plants contain large amounts of provitamin A, but this is not accessible for our nutrition, because we can't eat the green parts; we eat the white starch-storing tissue in the seed, the 'endosperm' which doesn't contain any provitamin A. Therefore, poor people who can't afford to buy a diversified diet and depend upon rice as their major food source, are vitamin A-deficient. What alternatives were visible? One option was to try to find, within the entire gene pool of rice and its relatives around the world, a plant with 'yellow endosperm', indicating the presence of provitamin A. Such a plant, after the confirmation of the provitamin A nature of the yellow colour, could then be used as starting point for a breeding programme to transfer this trait into modern rice varieties. Well, the rice breeders had already been doing everything to find such a plant. They had studied more than 80,000 different genotypes but had not found any yellow endosperm and therefore had no possibility of initiating a breeding programme. Actually, the rice breeders were asking 'genetic engineering' for help and that's how I became aware of the situation. So what could we do on the basis of the knowledge about molecular biology and genetic engineering at that time? There were two alternatives and these were discussed in a brainstorming meeting at The Rockefeller Foundation in New York in 1991, organised in response to my request

for financial support. The foundation assembled 30 world experts of the biochemical pathway leading to provitamin A in any organism. The straightforward solution, as seen at this meeting, was trying to disclose the 'switch' that turns off the pathway in the white endosperm tissue. It was obvious that all necessary genes were present in rice, but they were selectively switched off in the endosperm. And there was good hope that this would be a relatively simple approach because there was a maize mutant known with a yellow endosperm, where such a switch had been identified. We – my partner Peter Beyer and I – proposed the alternative: to engineer the pathway. The assembled authority of these world experts felt (rightly) that this would be rather unfeasible, and they had very good arguments for their notion. Fortunately The Rockefeller Foundation decided to support both approaches. The group which had received funding to find the switch is still trying to find the switch and our 'totally unfeasible' approach – trying to engineer the entire biochemical pathway into rice endosperm – was successful. But this was, of course, not foreseeable in 1991. And we were fortunate that it worked. But it worked (Figure 3, p. 369).

Proof-of-concept was ready in February 1999. It came at the same date as my retirement as full professor from the Institute of Plant Sciences at ETH Zurich, and it came just one month before I had to leave. The rule says that you have to leave at the end of the semester in which you pass 65 years of age. But I was still able to present the results – including results on rice which had more iron to counteract iron deficiency – at my farewell symposium. Figure 4 (p. 369) shows what Golden Rice looks like. The left rice is yellow because it contains provitamin A and the right is white because it doesn't contain provitamin A. The colour is an indicator of the presence of provitamin A and, of course, we have all the necessary molecular evidence that this is the case.

Well, this was at the time of my retirement and, as a 'normal' scientist, I would have stopped there. The consequence would have been, however, that what I have been presenting to you about the vitamin A-rice would have remained an academic anecdote, but it would not have helped any vitamin A-deficient child. It has been stressed repeatedly during the few days of our Plenary that 'it is sufficient to do good science'; everything necessary will follow automatically. What we had done was definitely 'good science'. It became the most frequently cited plant paper for the three-year period from 2000-2003. If we had stopped there, it wouldn't have had any impact on vitamin A-malnutrition. The situation may be different in cases where there is an interest from the medical community or from industry to pick up a scientific novelty and to convert it into an economically viable product.

In our case however, there was no interest from industry because there was no foreseeable 'market' and consequently no chance for a return of the necessary investment. And there was no public institution ready to invest in the development of a 'humanitarian' product. Consequently, we decided to leave the convenient 'ivory tower' and we went into what turned out to be a very harsh environment. And we ran into many, many unforeseen non-academic problems that were not at all pleasant. For more information please see my paper on 'Lessons from the humanitarian Golden Rice project …' in the PAS Proceedings 2010, citation given at the end of this article. I won't refer here to the well-known problems with the professional GMO opposition. The first surprise came from the area of intellectual property rights. As long as one does basic science, patents don't play a negative role; they are a valuable source of technical information which can be used freely. But when one sets out to develop a 'product', patents suddenly play a key role. As typical scientists we didn't know how many patents we had been using with our technology. To find out, The Rockefeller Foundation commissioned two patent lawyers and the result was shocking: we had used 72 patents and a number of material transfer agreements. Since the concept of our 'humanitarian' project was to provide our 'Golden Rice' free of charge to subsistence farmers, this was a catastrophe, because it meant that we would have to bargain for free licenses for 72 patents. This appeared like an impossible task and the GMO opposition was certain that this was the end of our plans. However, thanks to our establishment of a 'public-private partnership' with agbiotech industry (Syngenta) we got help from experienced patent lawyers, who found out that we had to take care of only 12 patents, as the rest of the 72 patents were not recognized in those developing countries which were our target. So we had to get free licenses for 12 patents and, because of the popularity of our project, which was picked up by the press very readily – you may recall that it was even a cover story in *Time* magazine in 2000 – thanks to our colleague Peter Raven, who organised a press conference after inviting me to the 16th Botanical Congress in St Louis – the patent holders were very willing to provide us with free licences. The surprising outcome was, that whereas everybody had expected that the first insurmountable hurdle for our humanitarian project would be constituted by the problem of intellectual property rights, this didn't delay our project for a single day.

We then had to learn what it means to develop a product and that is basically very different from doing basic research. In summary, it requires solving many 'unacademic' tasks for which there is no funding and personnel in academia, including e.g. repetition of the same experiment hundreds of

times to find one transgenic event which is hopefully suitable for the development of a successful commercial product. That's very difficult in an academic environment, because there is no scientific novelty to be expected. Nobody in academia can invest the necessary time and nobody is willing to finance that. Another severe problem is the consequence of the GMO status. GMO plants are, as you all know, considered extremely dangerous plants. Nobody can tell why, but that's an established paradigm. The consequence is that work with GMO plants is restricted by numerous complicated and extremely restrictive hurdles. For a project aimed at using a GMO plant for improvement of a crop variety, e.g. to develop a vitamin A-rice variety, the fact that work in the field is prohibited inhibits possible progress to the extreme. Plant breeding is a numbers game; plant breeders need large numbers of plants to find an optimal variety: this is not possible in a growth chamber – as requested by law – where you can work with 50 instead of 500,000 plants. Also, plant breeding depends upon evaluation of agronomic traits in addition to the target trait, and it simply isn't possible to evaluate such traits in a growth chamber. Another very big hurdle was finding financial support for this work. It turned out that there's no public institution or funding agency in academia set up to support work beyond proof-of-concept. It was even very difficult to get modest bridging funds for the continuation of the project. Working on GMO product development requires (because of the regulation-caused costs) not the 'normal' EUR 100,000 to 500,000 like a 'normal' scientific project, or the exceptional one million euro. The costs for the development of a GMO-product accumulate to ca. USD 24 million. We had to spend much of our time during the last 11 years trying to acquire funding from year to year, from half year to half year, because, of course, nobody could provide 24 million USD for the completion of this project. We acknowledge gratefully all support received from altruistic sources such as The Rockefeller Foundation, USAid, Syngenta Foundation, Gates Foundation, and other foundations and this helped us to go on step by step. We established a public-private partnership because we learned very quickly that, as naïve academics, we had no idea what all this would involve to arrive at a GE product. We have built a board of experienced experts in many areas that are important to advance such a project to success. We had support from the private sector for our development. In order to develop local rice varieties we had to identify GMO-competent institutions in the developing countries that had the capacity to work with transgenic plants, not an easy and widespread capacity. We established collaboration on the basis of sub-license agreements (defining the 'humanitarian purpose' and the conditions for collaboration) with public rice research

institutes in our target countries India, Vietnam, China, Indonesia, the Philippines and Bangladesh. All this did not delay the progress of the project for long and it has been working fine since the early 2000s. These institutions are developing national varieties, they have the capacity, and part of them get sufficient funding.

A serious problem in this context is that, because of the expenses involved, regulation forces the entire breeding programme for all countries to be built on one selected lead event. This is very undesirable from the biological point of view. It would be far better to build on biological diversity also when breeding for different varieties. However, as the deregulation of one single transgenic event costs ca. 24 million USD, nobody can afford to build new varieties on several selected events. Prerequisite for the selection of such a 'lead event' amongst numerous transgenic events are reliable data on agronomic and target trait quality, which can't be collected in the growth chamber and absolutely require growth in the field. However, it took eight years to get the first permission for the first field release in the Philippines, our major partner country for testing Golden Rice in the field. Imagine what it means to select a lead event on the basis of agronomic traits which can't be studied because you are not allowed to work in the field! All these and hundreds of further hurdles are the consequence of GMO-regulation.

Despite of the numerous GMO-specific hurdles Golden Rice will reach farmers soon, however and unfortunately, with more than 10 years' delay compared to a novel non-GMO variety. The timeline for release is 2012 in the Philippines, 2013 in Bangladesh, 2014 in India and Vietnam, 2015 in China and Indonesia and further countries will follow. The figure below indicates our choice of collaborating partners in different countries: the countries highlighted in yellow are representing the actual programme and the grey ones are those into which I would very much like to extend the programme, but for which we have no financial support so far (Figure 5, p. 370).

In the following figure you see the expected impact for one representative country. According to a state-of-the-art socio-economic ex ante study for India, the annual burden of vitamin A-deficiency amounts to 71,600 lives lost per year: Golden Rice could save 39,700 of those lives. For those who may wonder why not more, the answer is very simple: only half of the Indian population depends upon rice, the other half depends upon wheat and, of course, Golden Rice cannot solve the problems of those who are vitamin A-malnourished but have wheat as their major staple. With regard to the rice-dependent poor, the success rate could reach an overwhelming 95%. Golden Rice interventions are extremely economic, because it could save one life year for 3 USD and, without the costs of regulation, Golden Rice could save one life year for 30 cents.

Golden Rice would substantially contribute to the UN Development Goal: eradication of extreme poverty and hunger (Figure 6, p. 370).

A World Bank study shows that the gain from the technology could be 15.6 billion dollars per year because of increased productivity of unskilled workers. It could lead to reduced child mortality (Golden Rice has the capacity to save India alone 40,000 lives), improved maternal health (vitamin A malnutrition is the prime important case for motherhood mortality, and Golden Rice could be of substantial help there). Golden Rice is followed by high iron, high zinc, high quality protein rice because there are these deficiencies as well and it is followed by the same traits – high vitamin A, zinc, iron, quality protein – in cassava, banana, sorghum, potato, to support those poor populations who are not dependent on rice but on other crops and Figure 7 (p. 371) indicates those countries that would benefit from transgenic cassava, banana and sorghum.

The examples given above demonstrate what potential genetic engineering with plants has to offer in the area of micro nutrient malnutrition or 'hidden hunger'. Golden Rice is the only case where scientific proof-of-concept has been carried through product development and deregulation and where the practical application will soon demonstrate the effectiveness of the concept of 'biofortification'. For all the other examples scientific proof-of-concept has been established, but product development and deregulation will delay use for at least ten years, as was the case with the vitamin A-rice – if the necessary funding (ca. USD 25 million per case) can be secured at all. GMO-regulation prevents use of the technology for public good and effective use of the potential of the technology will require a substantial change in public attitude and regulation.

This problem leads to the last theme of my presentation and to a few remarks about an important Study Week organized by the Pontifical Academy of Sciences on the topic of *Transgenic Plants for Food Security in the Context of Development*, to which about 40 renowned scientists from very diverse scientific backgrounds where invited to discuss, on the basis of peer reviewed literature, the recent advances in the scientific understanding of GMO plants and the social conditions under which GMO technology should be made available for the improvement of agriculture, especially for food security in developing countries. A short account has already been given by our colleague Peter Raven. The key message from this study week is the following: there is no scientifically valid argument justifying any specific concern about transgenic plants, and both practical experience of their use over more than twelve years on large acreages world-wide and by millions of small scale farmers, as well as all regulatory oversight and specific

biosafety research over 25 years, confirm this view. On the contrary, GMO-technology has been proven to be the safest and most predictable technique for producing new plant varieties. There is not a single documented incidence of harm, so far, to either consumer or the environment. Despite this overwhelming scientific evidence and practical experience, unjustified 'extreme precautionary' regulation, exclusively for GMOs, is maintained and enforced worldwide, with the consequence that GMO-technology is so expensive that it has led to a *de facto* monopoly in favour of a few financially powerful industries and to the exclusion of any possible altruistic application in the interest of public good. Golden Rice is the only exception and may be for a long time. There is, therefore, a moral imperative to change regulation from present ideology-based regulation to science-based regulation which would be based on novel traits instead of on the regulation of the technology used. The Proceedings of the Study Week have been published in parallel by Elsevier and the Pontifical Academy of Sciences. They are a rich source of science-based information on all aspects of this controversial but life-saving technology and should be studied by all who are interested in an unbiased view on the subject. They contain the full papers of all presentations, but more importantly also a 'Statement' endorsed by all participants, providing an authoritative and comprehensive summary. I would like to thank Peter Raven, who was instrumental in managing a draft and the formulation of the final Statement to which all forty participants agreed without exception, including the late President of this Academy. This Statement is available in 16 important world languages and it has been distributed to 200 countries. We hope that other academies will join and help distribute this information and that this statement and the publications will serve as a catalyst for a more rational attitude towards GMO-technology.

References

Transgenic Plants for Food Security in the Context of Development. Proceedings of a study week of the Pontifical Academy of Sciences. Editors: Ingo Potrykus & Klaus Ammann. *New*Biotechnology, vol. 27 (5), 30 November 2010, pp. 443-717.

This 'open-source' publication is accessible via internet under www.ask-force.org/web/PAS-Studyweek-Leaflet-2010.pdf and under the Vatican homepage www.vatican.va/roman_curia/pontifical_academies/acdscien/2010/newbiotechnology nov2010.pdf.

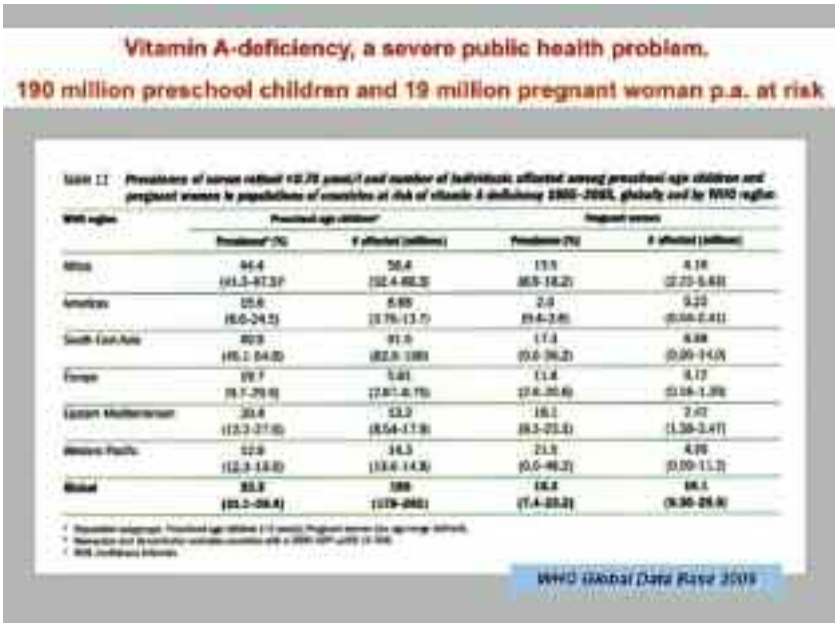


Figure 1.

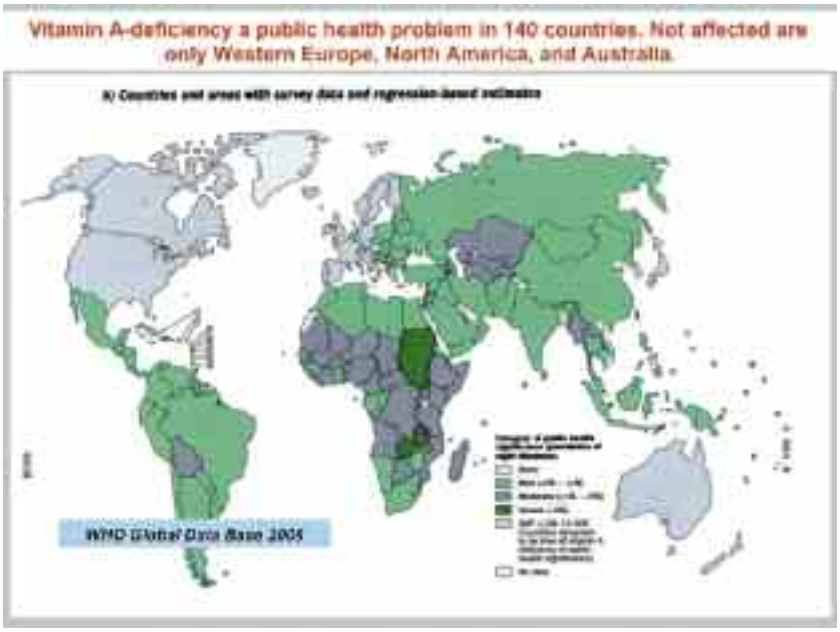
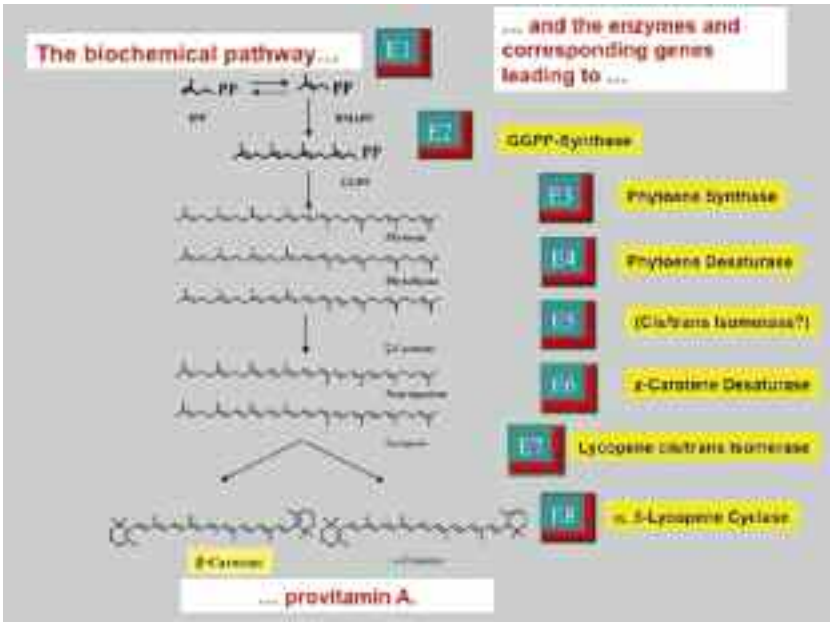


Figure 2.



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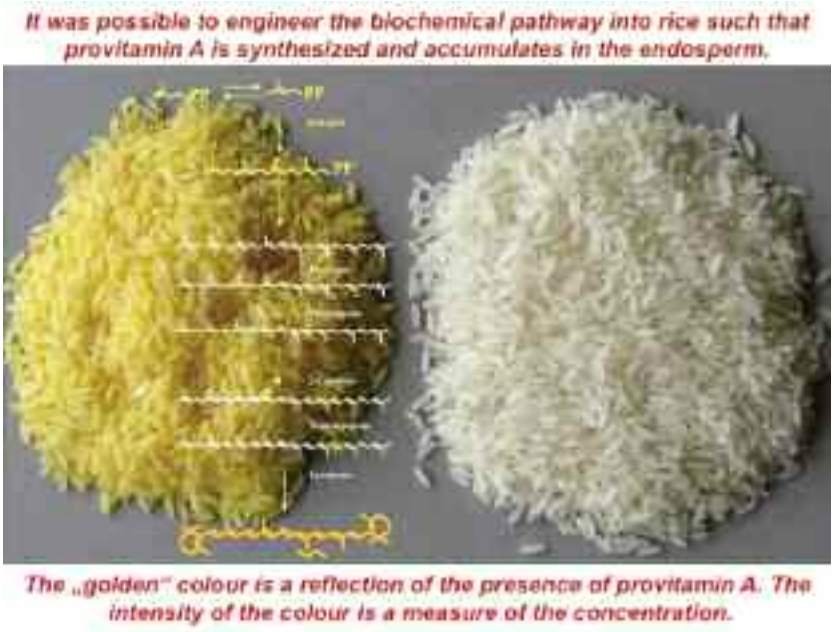
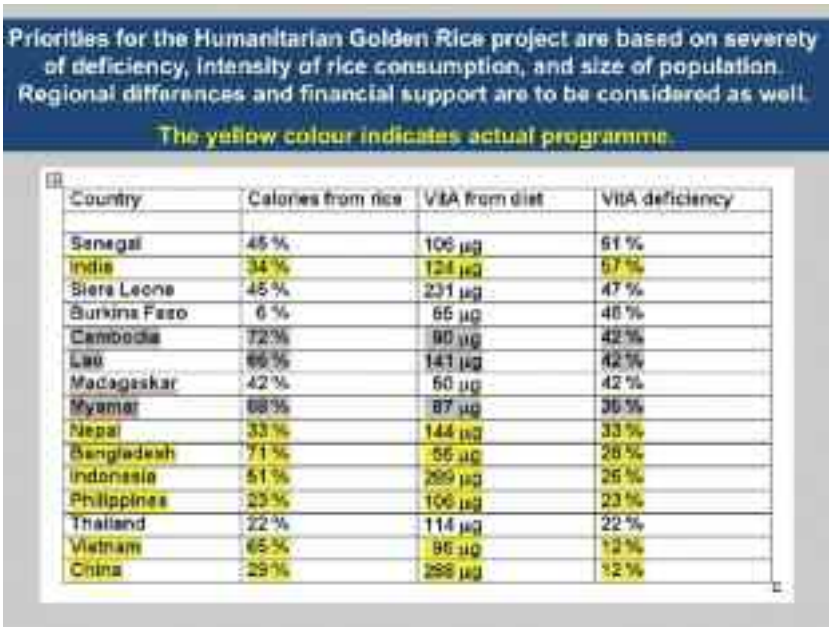


Figure 4.



Country	Calories from rice	VitA from diet	VitA deficiency
Senegal	45 %	106 µg	61 %
India	34 %	124 µg	57 %
Siera Leone	45 %	231 µg	47 %
Burkina Faso	6 %	66 µg	46 %
Cambodia	72%	80 µg	42 %
Lao	69 %	141 µg	42 %
Madagaskar	42 %	60 µg	42 %
Myamar	68 %	87 µg	36 %
Nepal	33 %	144 µg	33 %
Bangladesh	71 %	56 µg	26 %
Indonesia	51 %	289 µg	26 %
Philippines	23 %	106 µg	23 %
Thailand	22 %	114 µg	22 %
Vietnam	45 %	96 µg	12 %
China	29 %	288 µg	12 %

Figure 5.

Figure 6.


Countries where vitamin A-deficiency is a severe public health problem
Afganistan Angola Azerbaijan Bangladesh Benin Bhutan
Bolivia Cameroon Burundi Burkina F. Cambodia Cameroon
Chad Congo Cote Ivoir Korea DR Eritrea Ethiopia
Gambia Georgia Ghana Guinea Haiti Jamaica
Iraq Kazakhstan Kenya Kyrgystan Lao Lesotho
Liberia Madagascar Malawi Mexico Morocco Mozambique
Myanmar Nepal Niger Nigeria Philippines Senegal
Sierra Leone Somalia Sudan Swaziland Sri Lanka Tajikistan
Togo Tuvalu Uganda Ukraine Uzbekistan Yemen
Zambia Zimbabwe
Countries where vitamin A-deficiency is a moderate public health problem
Albania Algeria Argentina Belarus Brazil China
Ecuador Egypt Eq. Guinea Gabon Guatemala Honduras
India Indonesia Jordan Libya Lebanon Lithuania
Mongolia Namibia Pakistan Papua NG Paraguay Peru
Romania Russia Serbia South Africa Suriname Syria
Thailand Tonga Tunisia Turkey Uruguay Viet Nam
Countries with high rice consumption (200-400 g per day)
Countries with high consumption of Cassava, Sorghum, Banana, Potato
All countries would benefit from high iron, zinc, quality protein
Extreme precautionary regulation will prevent all possible solutions
Data from WHO Global Data Base 2009
Biofortification offers the potential to reduce micro-nutrient malnutrition worldwide, substantially, and in a sustained manner.
To be effective, will require a change in public attitude and GE-regulation.

Figure 7.