*Dear Student,*

*Golden Rice* is an exciting humanitarian project, yet its transgenic nature leads many idealistic young people like you to think twice about its usefulness.

We welcome questions from people who want to understand the motivation and the science behind *Golden Rice*. Our position comes from a profound conviction about the need and potential of *Golden Rice* combined with very good science. Our conviction comes from many years of studying the problems in developing countries and examining in depth all options available, after other alternatives have not managed to provide sustainable solutions to the death of millions of children every year.

The four following answers are introduced by typical questions by students:

1. "*Golden Rice* is not necessary, people could eat fruits and veggies"

Vitamin A Deficiency (VAD) does not occur if people have a balanced diet. But many people in the world cannot afford a balanced diet. More than one-fifth of the world's population goes to bed hungry every day. Poor people in rice-producing countries often can only afford to eat just rice, or rice with a tiny contribution to nutrition from other foods. Only coloured vegetables or fruits contain carotenoids, also called pro-vitamin A. Animals, including humans, can make Vitamin A from carotenoids, especially β-carotene ("beta-carotene", which is the colour in orange carrots). Only animal products contain Vitamin A itself. Many poor people cannot afford animal products, or may not eat them for religious and cultural reasons.

Rice is the main energy source for 50% of the world's human population, which means that every day about 3,000,000,000 (three billion) people eat rice. And in countries like Bangladesh 80% of the calorific value comes from rice. But the part of rice which we eat –called the endosperm– contains no carotenoids, nor (of course, as you now know) Vitamin A.

Capsules containing Vitamin A can be given to VAD sufferers, and the intervention is effective. But the cost of long-term programmes is significant for poor countries, and the logistics of distribution are difficult. In the Philippines, Vitamin A capsules have been distributed since 1993, paid for by USAID. Still up to 55% of children under 5 in the Philippines suffer from VAD, as well as around 20% of mothers.

So what is the effect of VAD. Well, it makes people go blind –about 250,000 people a year. Close your eyes for a few minutes and try to understand the impactthis has on poor people. Without an intervention, be it by pills or improved nourishment, VAD reduces immunity to common diseases and thus becomes a killer. VAD kills 6000 people each and every day. 6000 deaths since this time yesterday. If you or your family member or a friend represented one of those deaths you'd know how devastating one death is, especially if it had been avoidable.

Let's put the 6000-a-day statistic into a context. In terms of deaths its equivalent to one January 2010 Haitian earthquake each and every month; one December 2004 Asian Tsunami, each and every month; its equivalent to two 9/11s (Al Qaeda flying planes into the Twin Towers in New York in February 2001) each and every day. VAD kills more people, mostly children and young mothers, in a year than all the British killed in World War II, and who have been commemorated every November 11th for the 65 years since that war. In the ten years I have been working on Golden Rice VAD has killed more than 9 million people, more people than in the Holocaust , when the German Nazis murdered 6-8 million Jews in concentration camps during World War II.

2. "Golden Rice was created to give vitamin A, and vitamin A is toxic"

Golden Rice was created as a source of β-carotene. Not Vitamin A. β-carotene is ubiquitous in a balanced diet and the environment, and non-toxic when consumed as food. Excess β-carotene, in the unlikely event that an excess was ingested, is stored or excreted. The human body does not make more Vitamin A than it needs from the β-carotene available.

High levels of vitamin A, as opposed to provitamina A, may be toxic. At very high levels. Vitamin A pills given in supplementation programmes contain enough vitamin A to provide for half a year's needs of a child.

The latest results we have suggest that half a tea cup –100g of dried rice– of Golden Rice eaten daily can stop the blindness and the death due to VAD. Go to the kitchen and measure 100g of dried rice. You'll see what a small amount it is.

3. "Why don't you try to find a way for rice to mutate so it naturally produces vitamin A?"

There are more than 20,000 varieties of rice. None of them have any β-carotene in the endosperm, so there is no natural variation that would allow the rice grain to produce and store beta-carotene by breeding. Since the beginning of agriculture more than 10,000 years or so, man has been selecting rice which produces edible seed and can grow well in most conditions, no natural mutation has occurred for β-carotene in the endosperm, even though the leaves in the rice plant are producing it. How long do you think we should wait for natural mutation to occur, when people are dying at the rate of 6000 a day?

It may be possible to induce mutations in breeding materials by using chemicals or irradiation –both common techniques used in seed breeding to induce random gene mutations- but perhaps this doesn't fit the "natural" requirements of many critics green biotechnology. In any event, precise insertion of a few genes is much better understood than random gene

mutation, which can affect 100s or thousands, or tens of thousands of genes randomly. Of course, in both possibilities the best specimens will be selected, but in the induced mutation way, there will be many more changes than the one desired, which will then have to be understood and (literally) weeded out.

Conversely, with a precisely inserted set of one or two genes, a new genetically modified trait can be introduced into an existing variety within 3 or 4 generations, so that the introduced trait is the only difference from the parent variety. This is a significant advantage when the parent variety itself has been carefully bred for specific characteristics of agronomic performance and food quality and quantity.

4. <u>"Why don't you select for natural mutations instead of fiddling with genes?"</u>

I expect you have studied cell division and multiplication. You therefore know that all the cells of an organism contain the same genetic code – the same genome. What makes therefore the rice plans cells form a rice leaf (which do contain β-carotene), or the root of the rice plant, or the aleurone layer of the rice seed (which does contain some minerals and vitamins, as well as oil) or the rice endosperm – the white part which we eat, which is basically just carbohydrate, a small amount of fat and no minerals or vitamins?

Rice is polished to remove the aleurone layer to make it taste and store better. If not polished the fat in the aleurone layer turns stored rice rancid and unpalatable.

Actually, although the genes present in all cells of a plant are the same, in different tissues different genes are activated, under the control of so-called 'transcription factors' and other cellular regulatory mechanisms. So in the endosperm (the white part of rice which we eat) there are genes which in other rice tissues are activated to produce β-carotene, but they are not in the endosperm.

You may also have studied DNA and RNA, and understand that the nucleotide code which codes for amino acids, necessary to produce proteins and all of life, is common to plants, animals and bacteria. Less well known is that genes with very similar functions are found in many different organisms. Genes for beta-carotene production from different organisms, similar to those inactive in the rice endosperm, can be used to force rice grains to produce beta-carotene. To achieve this, those genes are combined with regulatory gene sequences recognised in rice cells, and integrated into the rice genome. The introduced genes will then work to make the enzymes needed in the biosynthetic pathway to β-carotene. Two genes, one from a common soil bacterium, and one from a maize plant, inserted into the rice genome, was all it took to make Golden Rice.

The building blocks of nature, the DNA code and the genes, are absolutely natural. The method used to introduce the genes is to use a common plant bacterium which naturally inserts its genes into plant tissue hosts. Absolutely

natural process. Of course it has taken the ingenuity of man to understand and work out how to do this in a way that is advantageous to man and not the bacterium. If man is natural (and I don't think man is synthetic) this is also a natural process.

What is not natural, is agriculture. Agriculture is the result of an evolutionary process whereby man has been able to stop being, in most places, a 'hunter gatherer' and become a farmer, and where, with modern food production in developed nations, only a small proportion of the population – perhaps 2 or 3% - can produce the food we all need to survive. Modern crops and livestock, are all products of generations of selective breeding.

Genetic modification is one aspect of modern agricultural technology which allows things to be done more efficiently, or allows things to be done which can't be done by other methods. Golden Rice is one of the latter. Genetic modification is not a panacea for improvement in agriculture, but it is one tool in an increasingly hungry world. And technology –in all its forms– is what makes agriculture productive. In countries with little agricultural technology, like many of the 54 countries of Africa, most people have to farm to survive – perhaps 65 -70% of the population. The productivity is so low they have infrequent surpluses to sell, and are poor. They may spend 70% of their meagre incomes on food, while in developed countries people spend only around 12% of their income on food. Additionally, people in Africa may have to depend almost entirely on one crop. In Africa its often sorghum or cassava or cooking banana.  And guess what? Sorghum grains and cassava roots don't have β-carotene and thus millions of children in Africa are facing the same problems as children in Asia.

I hope that by now you will welcome the fact that biofortified versions of these crops are also being created, using genetic modification for the same reason.

Many young students in developed countries, like yourself, have highly idealised ideas of how the would like to deal with the misery in many developing countries of the world. Unfortunately, those ideas cannot be implemented in a practical way. For example, we cannot simply ship our surplus production and distribute it for free where it is needed. Immediately, many locals would lose their jobs, and instead of learning of how to support themselves and become productive members in their societies, they become dependent on foreign help.

Give a man food, and he'll come for more. Give a man knowledge and improved seed, and he'll feed himself, his family and his village.