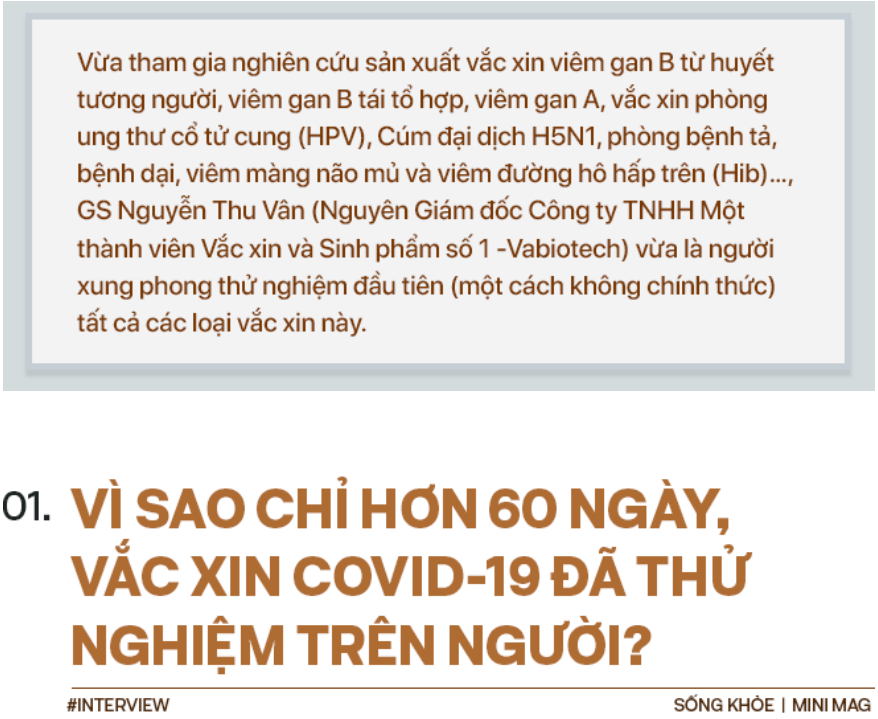
The 'Gamvid-19 vaccine gamble' and the memory of Vietnam's major breakthrough made WHO unbelievable

Production of Covid-19 vaccine will be risky. But we still have to do it so that if tomorrow, the Covid-19 epidemic will regress or disappear, or the Corona virus will return to the new strain, we still have a new technology to produce vaccines.



Truong Thu Huong: *A person who has directly studied many influenza viruses, according to her, if compared to H5N1, the SARS-CoV-2 virus has a stronger or weaker toxicity?*

Prof. Thu Van : Influenza viruses A / H5N1 and SARS-CoV-2 are highly toxic. Although WHO estimates the H5N1 death rate to be 60%, Covid-19 is currently at 4.34% but I think the two viruses are similar in severity.

H5N1 is a flu virus capable of causing severe lung damage but is rarely transmitted directly from person to person, while SARS-CoV-2 is highly contagious. Looking back on the history of medicine in our country, there

has never been a disease that spread as fast, as quickly and strongly as Covid-19.

H5N1 (2004-2005) or SARS-2003 . only infect some patients. We can focus on zoning and curing for many cases, soon prevent outbreaks. H1N1 (2009), although spread much but is a mild disease, can use Tamiflu effectively treat.

But now, Covid-19 is spreading across the country, leaving tens of thousands of suspected people in isolation and more than 100 cases. The disease also tends to be increasingly difficult to control as it surrounds Vietnam as a series of countries heavily affected by the disease.

Having witnessed many outbreaks of disease, I was worried about the community and always wondered how to produce vaccines so quickly, timely responding to the prevention needs of everyone. Unfortunately, the vaccine production process has to go through so many steps, it cannot be immediately available.

Truong Thu Huong: *But now, when confronting the Covid-19 epidemic, aren't the US and China very fast (after just over 60 days) have vaccines tested on humans?*

Prof. Thu Van : The time was so short because they quickly created antigen based on mRNA gene technology. The vaccine is very safe because it only contains a genetic fragment of the virus synthesized in the laboratory, which is completely incapable of causing illness to the person who is injected.

The vaccine testing process still takes place in full steps. Prior to clinical trials in humans, the United States and China all tested in animals to test safety, toxicity, evaluate all animal reactions to vaccines and determine their ability to respond. Immunological effects on laboratory animals. When all the requirements in a laboratory are what we call preclinical trials, the vaccine can be given to human clinical trials only after obtaining the Association's approval. ethical co-research in biomedical research.

Human clinical trials will take place in 3 phases. Stage 1, the vaccine is given to about 20-30 healthy adults to check the safety of the vaccine on the person being vaccinated; Phase 2 about 200-300 people; and phase 3 will have about 2000-3000 target subjects participating in the test (sensitive subjects).

The US vaccine is a type of 2 shots, each 28 days apart. Thus, after the test day of 16/3, to mid-April to come, will be able to evaluate the preliminary results. If they respond well, they can proceed to phase 2, and then phase 3.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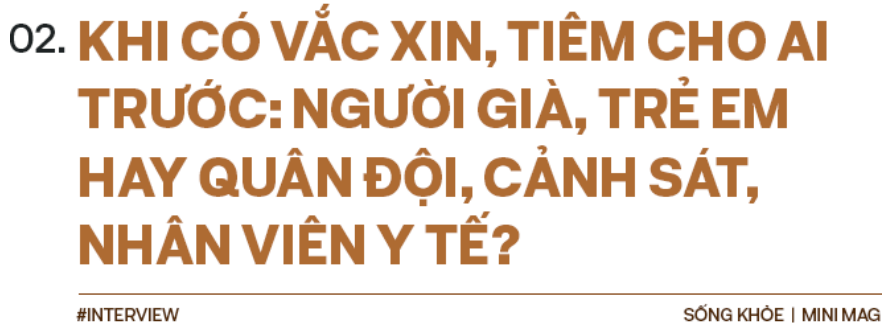
However, what scientists produce, before preparation, can only be called an active ingredient. To be correctly called a vaccine, it also takes a long time of clinical trials, at least within 18 months (according to US notice). After clinical results, it takes more time to wait for a license from the FDA (the US Food and Drug Administration). The review and approval process is also not easy.

In our country, after completing the stages and submitting to the Ministry of Health for review, approval, production permits and commercialization, the fastest takes up to 1 year. Assuming the US works faster, it will take about 6 months. So, in about two years, the world will have something called the Covid-19 vaccine.

The risk in producing this vaccine is huge because maybe, after about 2 years when the vaccine is completed, the disease has ended and the market has no demand. The Corona virus, when reappearing, may have switched to another strain. In fact, in medical history, this virus has had 7 strains (HCoV-229E; HCoV-OC43; SARS-CoV; HCoV-NL63; HKU; MERS-CoV and SARS-Co-V2).

If the virus only mutates slightly, does not change to the antigen, the vaccine can still be used. But if there is a new strain, the whole process of vaccine research, production and testing will have to be repeated from the beginning. And the rotation will be like that, when the vaccine is done the disease may be gone.

Gambling is so risky so that's why, many big pharmaceutical companies, though very rich, will never spend money on vaccines for diseases like Covid-19 or SARS, MERS. . unless the US government or other organizations financed the money.



Truong Thu Huong: *The big risk is the main reason, making the US many years ago to decide to sponsor many countries, including Vietnam to research and produce H5N1 vaccine instead of assigning them to their companies. direct implementation?*

Prof. Thu Van: In the past, when we were researching to make an H5N1 vaccine, the US provided Vabiotech $ 1 million. They also made it clear: in order to protect the people of their country, the US Government must finance other countries to research and produce vaccines, to prevent the spread of disease from outside to the United States.

At the time of the H5N1 epidemic, the WHO meeting in Geneva, countries also stated the views, which countries must take care of the vaccine for that country. Because when an epidemic occurs on a global scale, every country has to worry about fighting epidemics.

If Vietnam cannot produce the vaccine on its own, it cannot rely on outside help. Information about the US or Chinese vaccine testing is very encouraging, but probably not enough for Vietnamese people to fully enjoy.

That is the main reason why, in the face of a risky gamble - large investment in manpower and material to produce Covid-19 vaccine with high technology - Vabiotech still decided to research the production itself. I think this is for a national health security strategy.

Whether tomorrow, the Covid-19 epidemic regress, or disappear, we still have a technology to produce vaccines. When it came back, with a changing nature or somehow, it was not foreseen, Vietnam had a weapon to fight. Vaccines will be made faster because they already have technological processes.

Truong Thu Huong: *Taking the highest responsibility in the H5N1 vaccine research and production project, could you talk a little bit about the stress situation at that time in our country?*

Prof. Thu Van: The influenza A / H5N1 epidemic lasted quite a long time, from 2003 to 2005, it could not be put out immediately. Between 2003 and the end of 2005, our country had 42/92 deaths, many families with 2-3 people were sick at the same time.

At that time, I was in the advisory group of the World Health Organization and had to go abroad for many meetings. The scripts are given. Even the hypothesis that, if a vaccine is produced but the quantity is limited, who should be given priority, is discussed.

Back then, I thought that simply if vaccines were available, priority would be given to the elderly, children - vulnerable subjects. But WHO experts say that, first of all, people must be vaccinated for the defenders of the country: the military, the country's managers, the police, the medical staff, the fire department, the rescue team. Without these forces, the country could not stabilize, the disease could not be put out.

Such discussions continue to be very exciting. Experts have thought about countless situations, but then the scenario, there is a disease that will break out globally as Covid-19 today, over 15-16 years, unfortunately has come true.

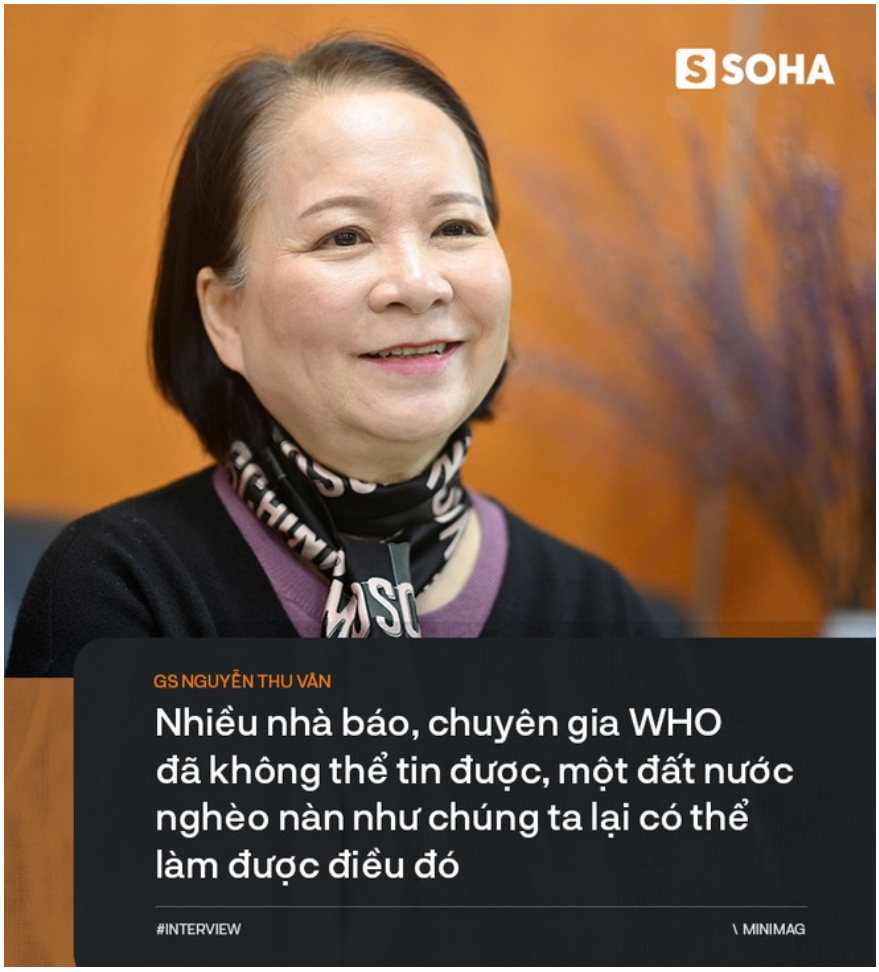
03. "ĐÂY LÀ BƯỚC ĐỘT PHÁ LỚN TRONG Y HỌC THẾ GIỚI NHƯNG LẠI ĐƯỢC VIỆT NAM THỰC HIỆN"

Tr??ng Thu H??ng: *In addition to the pressure of epidemics, what other pressures do people like you suffer from when researching vaccines?*

Prof. Thu Van: The research process of producing influenza A / H5N1 vaccine is very memorable because it is the first time in the world to have a flu vaccine manufactured using cell culture technology. This is a major breakthrough in world medicine but it has been implemented by Vietnam. Many journalists and WHO experts could not believe it, a poor country like us can do it.

Many journalists, reporters from RT, CNN, BBC, and WHO have come to Vabiotech to find me for interviews. I have to reject many people because many reporters always aim to emphasize Vietnam's weak position. Others are skeptical: is a country with poor infrastructure such as Vietnam that produces vaccines with such completely new technology, dangerous? Because in the past, despite making many vaccines, most other Vietnamese vaccines have materials and technology transferred from foreign companies.

The H5N1 vaccine is a completely self-made Vietnamese strain, in cooperation with the US and Japan.



Truong Thu Huong: *It is surprising that WHO has so many doubts about Vietnam's vaccine production capacity because it is clear that we are among the top 40 countries capable of researching and producing vaccines. world?*

Prof. Thu Van: In order to gain our position today, we have gone through so many challenges, many efforts, many times at the risk of being asked by WHO to eliminate the production of vaccines produced by Vietnam. counter research. Meanwhile, with poor facilities, our country has produced a lot of vaccines.

I remember from 1959 to 1960, polio broke out in the northern provinces of Vietnam with about 17,000 children, of which more than 500 died. Every year, tens of thousands of children suffer from permanent paralysis. The incidence is up to 126.44 / 100,000 people. Professor Hoang Thuy Nguyen at that time invested a lot of effort to produce oral polio vaccine and research and development on monkey kidney cells.

In the early years, the institute's production facilities were still quite rudimentary and did not meet GMP (Good Manufacturing Practices) standards. The WHO experts, when reviewing here, have insisted that Vietnam stop producing polio vaccine. Prof. Hoang Thuy Nguyen and Prof. Dang Duc Trach must use their prestige to stand up to the Ministry of Health and the WHO. But the main problem is still to prove, our country's vaccines produce quality assurance and usability.

At that time, Prof. Hoang Thuy Nguyen, supported by WHO Regional Office Western Pacific in Manila, assigned me to bring the polio vaccine manufactured by the Institute to Japan for examination. The Japanese are

very enthusiastic but they are also very disciplined. If a strange sample was brought into a laboratory there, they would never have done it, even without prior notice and hand-carried it, they would have requested immediate cancellation.

When I took the vaccine to my appointment appointment, they gave me a self-test and Japanese experts supervised it. Following their instructions, the Vietnamese vaccine results were very good and Japanese experts agreed and concluded that this polio vaccine met all regulatory requirements for human use. We use that result and report it back to the Ministry of Health and WHO. Finally, they also have to recognize the polio vaccine of Vietnam.

Thanks to polio vaccine produced by Vietnam in 2000, our country has eradicated polio after many years of this epidemic.

04. NHỮNG CUỘC ĐẤU TRÍ CĂNG THẲNG VỚI WHO

#INTERVIEW SỐNG KHỎE | MINI MAG

Truong Thu Huong: *In your opinion, what is the key that makes WHO not believe that Vietnam can produce vaccines?*

Prof. Thu Van: Many years ago, the very intense intellectual battles with WHO made me think that, with great prestige, Prof. Hoang Thuy Nguyen could protect such polio vaccine but in return, I, What will the latter have to do to do the same? And I also wonder, why does a global health organization like WHO seem to not believe that Vietnam is self-sufficient in vaccines?

Looking back, I realized that, with experts from countries with very modern facilities, used to see advanced vaccine production facilities, when I came to Vietnam and saw such poor and backward facilities, they are not

easy to trust right away.

But not only does WHO lack trust in us. The teacher in Japan that I respect very much (the first one who taught me how to get the vaccine - the hepatitis B vaccine from human plasma) also once disagreed with my technical approach, because It is contrary to the technique he taught when he developed the experimental production of this vaccine in Vietnam, in the condition that his country did not allow to apply his technique, and if we do not change or improve, we will not When will you get the hepatitis B vaccine?

He came back from the US and was the one who made hepatitis B vaccine from human plasma for Japan to use for many years before the replacement of the recombinant hepatitis B vaccine. He told me very enthusiastically, where wrong is always criticizing it. From washing bottles to clean, how to prepare laboratory equipment, teachers are both hands-on, direct teaching.

But once, he was angry with me for being so opposed to a view, that an expert at WHO had to stand for peace. The reason for that anger is that in Japan, when producing hepatitis B vaccines, they often choose plasma donors with very high surface antigen titre. But in Vietnam, the collection of plasma is quite difficult and the titre of Vietnamese people is not high. If you apply the principle of the teacher, only select plasma with a concentrated titre of 4+ (using gel diffusion techniques) or more to use, there is no sample in Vietnam.

So I had to choose another technology, ELISA (enzyme-binding immunoassay), which could capture more antigen particles. Because of this, my teacher and I argued so badly that he didn't talk to me. Later, seeing our good results, he gradually calmed down.

Thinking back many years ago, we studied vaccines in very primitive conditions, nothing called modern. When awarded by the Vietnam Technical Innovation Support Fund (VIFOTEC) for research work on the production of hepatitis B vaccine from human plasma, many of the research team joked that perhaps we had to collect Collecting all the laboratory equipment used at the time, very simple . for exhibition display. Because many years ago, from such rudimentary tools, Vietnam could also produce quality vaccines, which made the world recognized that way.

I see now, modern medicine is so, but the quality of the vaccine is just like that: always up to the standards that make the world respect.

05. "NẾU VẮC XIN CÓ VẤN ĐỀ GÌ, CHÚNG TÔI LÀ NGƯỜI ĐẦU TIÊN ĐI TÙ"

#INTERVIEW SỐNG KHỎE | MINI MAG

Truong Thu Huong: *When researching on producing any vaccine, she was always the first person to get the test. Is this a personal rule?*

Prof. Thu Van : I have studied viruses and vaccines for many years, so I am not afraid of becoming an unofficial tester of 0 (because as a rule, production researchers are not allowed to participate in testing). Not only me but everyone in the group also tried it out.

Virus toxicity only exists when the virus is alive. The vaccine manufacturing technology has eliminated the virulence of the virus. Currently, mRNA technology will help prevent a virus-free vaccine, but only contain a gene segment of the virus synthesized in the laboratory. Previous vaccines, such as H5N1, were produced using reverse genetic engineering: they retain antigen and eliminate the virulence of the virus. Currently, this is still considered modern technology.

Why do I always try first? Probably because I'm always worried, what kind of vaccine will I and my colleagues make, when tested on humans? Even when tested and had very good results in animals, the reaction mechanism of the human body is still very different and is not certain. At that time, I usually did not worry about safety and health, but only worried whether the vaccine would respond or not. Because only when the immune response is present, does the vaccine protect people from being vaccinated.

Truong Thu Huong: *If the vaccine is always so safe, in the research and production process, what is the thing that makes you most worried?*

Prof. Thu Van: As people in the profession, we understand very well that vaccines cannot be life-threatening. But unfortunately, what happens to the patients after the vaccination, we are very vulnerable to injustice and this injustice is not easily explained.

In the past, when I was a Vabiotech Director, I used to tell people, " *We study vaccines for the good of the community, but if something happens to us and you, must be the first prisoners, "* So strict compliance with the

steps in the production process is especially important, without mistakes.

We always determined such thoughts. At any time, risks can occur because vaccines are given to the public and the body's response varies. If the authorities did not find the cause of the problems during the vaccination deployment, the public always said that the fault was the vaccine manufacturer.

06. SỐ PHẬN TRONG XÓ TỦ CỦA VẮC XIN H5N1

#INTERVIEW SỐNG KHỎE | MINI MAG

Truong Thu Huong: *As a person who directly researched and produced H5N1 vaccine but then could not commercialize this product, how do you feel?*

Prof. Thu Van: The team started to research H5N1 vaccine from 2004-2005 and until 2008-2009 finished clinical trials but then, H5N1 only happened to poultry. The company decided, temporarily reorganizing the project, not thinking about commercial production anymore.

However, the H5N1 vaccine dossier is prepared, ready for pandemic, will be registered and produced as well. Not only in Vietnam, but also in other countries in the world: there is always a vaccine to be used when the market is in need.

If talking about business, we can consider the H5N1 vaccine was not effective because we put a lot of effort but no revenue.

But scientifically it is still a success. Vietnam has had vaccines, built a production process so that if there is an epidemic later, it is ready to release according to the needs of the community. Or the same process, if there is an outbreak with another strain, it can be applied and follow very quickly.

For me, producing vaccines is about protecting the community, not commercial. So scientific success has been considered a great success. Moreover, the disease did not occur, is it still better?

Truong Thu Huong: *She said that it takes 9-10 years to evaluate the effectiveness of vaccines. Why is that? With Covid-19 vaccine, what do you predict about the effectiveness of this vaccine?*

Prof. Thu Van : The vaccine production process (not based on genetic engineering) will have to go through many steps: cell culture, virus culture, virus harvest, purification, purity, inactivation, preparation . From the beginning to the last stage, it usually takes about 2 months to produce, then the inspection takes 2-3 months. If there are good pre-clinical results in animals, clinical trials will be conducted on humans.

After phase 3 of clinical trials, the vaccine may be licensed for use. However, many manufacturers continue to research and evaluate the real effectiveness of vaccines for further research and improvement. The evaluation process is very effective for a variety of reasons.

As for the Covid-19 vaccine, no vaccine has been produced using genetic technology in the world so far. Therefore, the immune response of Covid-19 vaccine to date is still a question mark. Also wanting to know the effectiveness of a vaccine, as I said, will take quite a long time.

Truong Thu Huong: *The last question, please address the hottest issue: Does Vietnam have a door in the race to make the Covid-19 vaccine?*

Prof. Thu Van: As I said, high-tech vaccine (mRNA) like Covid-19 will consume a lot of resources, but Vietnam will cooperate with the UK with a different technological approach and still have to proactive research for national health security. In current epidemics, the best, most effective and effective way to protect the community is vaccines.

When an epidemic happens on a global scale, if Vietnam cannot produce its own vaccine, no country will give it, because every country has to worry about fighting the epidemic. For example, if Covid-19 vaccine is available now, there are 7 billion people in the world, would those 7 billion people get the vaccination vaccine? The US vaccine has 2 doses, calculated to produce 14 billion doses to be enough for all humanity. A terrible number like that no one can produce enough!

Therefore, we cannot rely on foreign vaccines but still need to find ways to research, produce, and control the source of the vaccine: autonomy in quality, quantity and price of the vaccine.

As I said, producing Covid-19 vaccine will be risky. But we still have to do it so that if tomorrow, the Covid-19 epidemic regresses, or disappears or the Corona virus returns to the new strain, we still have a new technology to produce vaccines.

Truong Thu Huong: *Thank you GS for this conversation!*

Chúng tôi có thể sản xuất được vắc xin viêm gan B cũng nhờ người đầu tiên đặt vấn đề này là GS Hoàng Thủy Nguyên – Nguyên Viện trưởng Viện Vệ sinh dịch tễ Trung Ương – một trong hai người thầy mà tôi rất cảm phục.

Thông qua tổ chức WHO, GS Nguyên đã đặt vấn đề với họ, đề nghị WHO hỗ trợ chuyển giao công nghệ sản xuất vắc xin cho NIHE. GS tổ chức cán bộ viện thành 2 nhóm, một nhóm đi học sản xuất vắc xin viêm gan B ở Tokyo, nhóm khác đi học cách sản xuất vắc xin viêm não Nhật Bản ở Osaka (Nhật Bản).

Đối với GS Thủy Nguyên, khi tôi về đây, GS Nguyên đã là Viện trưởng Viện vệ sinh dịch tễ trung ương. Tôi chưa thấy có người Viện trưởng nào lại gương mẫu và vì nhân viên, học trò như vậy. Tuy là người đứng đầu Viện nhưng GS không ngại đi lau hành lang, rửa xe nếu thấy chúng bụi bẩn. Mọi việc, GS thường không nói nhiều mà luôn tự mình làm trước để làm gương cho mọi người. Vì sự tận tâm, trách nhiệm như thế nên trong viện, mọi người đều rất kính trọng thầy. Thế hệ đi trước như thế, chẳng có lý gì chúng tôi lại không nỗ lực, khát khao để đưa nền vắc xin Việt Nam phát triển lên một tầm cao mới.

GIÁO SƯ NGUYỄN THU VÂN