The Lasker Foundation's first ever award to a Chinese scientist working on the mainland has reignited a 30-year controversy over whether one person should be recognized for developing a powerful antimalarial drug that was the product of a massive government project during China's Cultural Revolution. Last Friday in New York City, the foundation presented Tu Youyou, an 80-year-old phytochemist at the China Academy of Traditional Chinese Medicine, with the 2011 Lasker-DeBakey Clinical Medical Research Award for "the discovery of artemisinin, a drug therapy for malaria that has saved millions of lives across the globe, especially in the developing world." But some Chinese scientists disagree with the citation, particularly its exclusive focus on Tu.

Wu Yulin, a retired chemist at the Chinese Academy of Sciences's Institute of Organic Chemistry who helped determine the chemical structure of artemisinin, wrote in response to an inquiry from ScienceInsider that Tu "made contributions to the discovery of the compound" but did not make significant contributions after that. Critics of the Lasker citation emphasize that development of the artemisinin-based combination therapy used today resulted from a scientific relay race that went through many stages. In comments on
Web postings and in an independent newspaper, they argue that more than one person deserves to be cited for the achievement.

Tu’s proponents argue, however, that her discovery stands out. Two supporters—Louis Miller, chief of Malaria Cell Biology at the National Institutes of Health in Bethesda, Maryland, and colleague Xinzhuan Su, also at NIH—described Tu’s contributions in a 16 September Cell article, writing that they have "no doubt that the major credit must go to Youyou." Su says their conclusion was backed by classified documents shown to them by Tu and officials at her institute.

Rao Yi, a neuroscientist at Peking University in Beijing, takes a more nuanced stand in support of Tu. Rao and his colleagues say they have seen a much larger set of classified and internal documents archived at institutions that were involved in artemisinin research and interviewed many of the major players. Rao says, "Although we agree with Miller and Su that Youyou should be recognized as a representative, we find they went too far in reaching conclusions that are not supported by available sources and in attributing credits based on claims that are at least controversial if not wrong." Rao included some of their findings in an article he posted online. He says: "Our article is very specific about clarifying the role of Tu Youyou, and we came to the conclusion that Tu is a representative of the project. We clearly mentioned others such as [contemporary artemisinin researchers] Yu Yagang and Zhong Yurong. We did note that the roles of others need to be further studied and established."

The search that led to artemisinin began in the 1960s when the North Vietnamese government asked China for help in finding a cure for drug-resistant malaria, which was decimating troops in the jungles of Indochina. Under Mao Zedong’s instruction, China launched a secret effort at the height of the Cultural Revolution in 1967. Code-named Project 523, it mobilized more than 500 researchers from some 60 organizations across several military and civilian agencies.

Project 523 planned a three-pronged attack on drug-resistant malaria: research and develop new drugs the Western way, screen traditional medicine and folk remedies to search for a Chinese therapy, and find ways to prevent malaria infection in the first place. Tu’s institute, the Institute of Chinese Materia Medica, was assigned to work on the second approach. According to research by Rao’s group, Yu Yagang, who worked at the same institute as Tu, analyzed a 1965 compilation of traditional remedies for malaria statistically and found qinghao (green-blue wormwood) was one of the ingredients used most often. Yu then worked with another researcher from the Academy of Military Medical Sciences to test a crude extract of qinghao on a rodent model of malaria, finding that the extract killed parasites with 60% to 80% potency. Yu reported the results to Tu, the group leader. Yu soon was reassigned to an even larger effort—searching for a treatment for bronchitis, from which Mao suffered. Tu then asked others in the group to repeat Yu’s experiment, but they couldn’t obtain extracts with consistent potency.

Tu describes her work in some detail in an essay in the October issue of Nature Medicine. She suspected that extraction at high temperature destroyed the active ingredient of qinghao. She went back to the traditional medicine book and, after reading about a preparation that called for soaking qinghao with cold water, proposed using a low boiling point solvent to extract the active chemical. This insight is considered a breakthrough step toward the discovery of artemisinin by her supporters. Tu’s detractors, however, point out that using ether and other low boiling point solvents to extract active ingredients from plants is standard phytochemistry.
Li Ying, a retired chemist at the Chinese Academy of Sciences Institute of Materia Medica in Shanghai, who worked on the synthesis of artemisinin derivatives, wrote in an article in 2008 that Tu's method of extraction and purification yielded crystals containing artemisinin mixed with other chemicals, giving rise to toxicity in clinical trials. At roughly this time, Wei Zhenxing of the Shandong Institute of Pharmacology and Luo Zeyuan of the Yunnan Institute of Pharmacology, after hearing about Tu's breakthrough, each independently derived antimalarial chemicals from local herbs called huang hua hao or yellow-flower wormwood (*Artemisia annua*). Several species were used traditionally as medicinal qinghao, but only *A. annua* eventually proved to contain a sufficient amount of artemisinin. The Yunnan group also found the best cultivated source of *A. annua* in another province. Using this source, they were able to produce pure artemisinin in large quantities, speeding up drug research and development. Tu's group also adopted the Yunnan method.

Meanwhile, researchers working in Shanghai from 1973 to 1975 found that artemisinin has a novel and unusual structure, a so-called peroxide bridge. Artemisinin is the only natural compound known to have this structure. It is key to its antimalarial property and makes artemisinin-based drugs entirely different from those derived from quinine, such as chloroquine, to which malarial parasites have become resistant. Li Ying's group in Shanghai synthesized artemisinin derivatives that were more potent at killing malaria parasites and had more desirable chemical properties (such as solubility in water), making them better drug candidates than natural artemisinin. They are the basis of therapy used today. It was only after secrecy rules were lifted in 1977 that research papers from Project 523 began to come out.

After the Lasker Award ceremony, Tu seemed eager to mollify the critics, telling Xinhua News Agency, "I think the honor not only belongs to me but also to all Chinese scientists."

Because the Lasker Award is often seen as a precursor to the Nobel Prize, the Chinese media are abuzz with anticipation. But some worry that the disagreement over credit might give the Nobel committee pause. Rao says that if he had to choose three scientists—the limit for the Nobel—then he would pick either Yu Yagang, Tu Youyou, and Zhong Yurong for the discovery of artemisinin; or Tu Youyou, Luo Zeyuan, and Li Ying for the early work on artemisinin that led to the drug therapy.

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twangcn
As to Qinghaosu, much more controversial issues still exist, and it is more than a person that can make clear.
Monday, October 03, 2011, 2:41:29 AM – Flag – Like – Reply

twangcn
But I don't think their contribution deserves a Nobel prize, because the drugs can not eraze the parasite drug resistance.
Monday, October 03, 2011, 2:37:12 AM – Flag – Like – Reply

Shi V. Liu
This article came in a very critical time: the final selection of a Nobel Prize for Medicine. It is interesting to read: "Rao says that if he had to choose three scientists—the limit for the Nobel—then he would pick either Yu Yagang, Tu Youyou, and Zhong Yurong for the discovery of artemisinin; or Tu Youyou, Luo Zeyuan, and Li Ying for the early work on artemisinin that led to the drug therapy."

It seems to me that some people have complained against the "wrong" accreditation made by Lasker Award selection committee.

But the official remark of the Lasker award is: "For the discovery of artemisinin, a drug therapy for malaria that has saved millions of lives across the globe, especially in the developing world." This accreditation is very appropriate because it was Dr. Tu who obtained the initial kind of artemisinin by taking a correct extraction approach learned from reading traditional Chinese medicine and found it to be very effective against malaria. All the other works are just helpful for bringing this critical original discovery to its full fruity and may be better utilities.

Thus, I am wondering why someone would rekindle this debate of who should be awarded this Lasker Award and whether Dr. Tu alone should be given a Nobel Prize. This sentiment is echoed with this strange remark in this article that "Tu seemed eager to mollify the critics" after the Lasker Award ceremony and told Xinhua News Agency that she (now) think the honor not only belongs to herself but also to all Chinese scientists.

As a long-time observer of Nobel Prize (http://im1.biz/Nobel.htm) I am truly worrying about the impact of this ScienceInsider article. Nevertheless, I am still confident that Dr. Tu will win this year's Nobel Prize for medicine for the very reason that I have pointed out in my comment: It was Dr. Tu who obtained the initial artemisinin effective against malaria. Nobel Prize has always been given to the original discovery no matter how crude it is and even how simple it looks later.

Friday, September 30, 2011, 6:41:08 AM – Flag – Like – Reply

Shi V. Liu
This article came in a very critical time: the final selection of a Nobel Prize for Medicine. It is interesting to read: "Rao says that if he had to choose three scientists—the limit for the Nobel—then he would pick either Yu Yagang, Tu Youyou, and Zhong Yurong for the discovery of artemisinin; or Tu Youyou, Luo Zeyuan, and Li Ying for the early work on artemisinin that led to the drug therapy."

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The above description essentially portrays Dr. Tu as a person who has robbed credit from others and thus should not be given a Nobel Prize. This sentiment is echoed with this strange remark in this article that “Tu seemed eager to mollify the critics” after the Lasker Award ceremony and told Xinhua News Agency that she (now) think the honor not only belongs to herself but also to all Chinese scientists.

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Friday, September 30, 2011, 6:39:58 AM – Flag – Like – Reply

Unbiased

Controversy is created because award is given to the scientist of a national academy from non-friendly (non-agent) state. Science and other western publications would have glorified if the award had gone to mediocres from agent states or thugs from friendly states. Well done western media for creating controversy where there is non like creating WMD in Iraq when there was non.

Thursday, September 29, 2011, 9:44:46 PM – Flag – Like – Reply