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## The 2015 Nobel Prize Laureates in Physiology or Medicine

Dobitnici Nobelove nagrade za fiziologiju ili medicinu u 2015.

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This year's Nobel Laureates in Medicine, William C. Campbell, Satoshi Õmura and Youyou Tu have developed therapies that have revolutionized the treatment of some of the most devastating parasitic diseases, such as river blindness (onchocerciasis) and lymphatic filariasis, two diseases caused by parasitic roundworms, and malaria caused by parasitic protozoa Plasmodium. These scientists have succeeded to develop novel anti-parasite therapies from bacteria and plants. Campbell and Õmura discovered a new drug, avermectin, the derivative which radically lowered the incidence of river blindness and lymphatic filariasis. Youyou Tu discovered artemisinin, a drug that has significantly reduced the mortality rates of patients suffering from malaria. The discovery of these two drugs has fundamentally changed the treatment of these parasitic diseases and significantly improved the global health of the world's population <sup>1-6</sup>.

William C. Campbell is an American biologist and parasitologist, who got a job in the research laboratory of Merck, Sharp and Dohme, the pharmaceutical firm. He discovered that a component from one of Omura's Streptomyces cultures was very effective in killing off parasites in domestic animals. The bioactive agent was purified and named avermectin. Avermectin was subsequently chemically modified to ivermectin, which turned out to be highly effective in both animals and humans against a variety of parasites. Ivermectin was marketed as a drug for veterinary use in the early 1980s by pharmaceutical giant Merck and was extraordinarily profitable. In 1978 Campbell had suggested to his boss that, in addition to its success in veterinary medicine, the drug might also be effective in treating river blindness in humans. He and his colleagues persuaded Merck to continue research and, when that proved successful, to provide the drug for free, since the potential patients certainly could not afford to pay for it <sup>1,5,7,8</sup>.

Professor Satoshi Ömura is a Japanese microbiologist widely recognized as a world expert in the field of bioorganic chemistry, particularly for the discovery, development, biosynthesis and manipulation of useful chemicals derived

from naturally-occurring microorganisms. He is an expert in isolating natural products, focused on a group of bacteria, Streptomyces which live in the soil known to produce a plethora of agents with antibacterial activities. From many thousand different cultures, he selected about 50 of the most promising, and one of these cultures later turned out to be Streptomyces avermitilis, the source of avermectin. The ivermectin, a dihydro derivative of avermectin was discovered and developed by collaborative research of Õmura and Merck Company as a macrolide anthelmintic antibiotic. It is widely held that the discovery and use of ivermectin represents the greatest public health intervention of the last quarter of the 20th century and can be regarded as on a par with the discovery and use of penicillin <sup>4,7,8</sup>.

The eradication programs for river blindness and lymphatic filariasis, currently being orchestrated by the WHO, are based primarily on the use of ivermectin. Ivermectin has been donated by the Merck Company and the Kitasato Institute since 1987, and the drug is being administered to around 300 million people annually. It is envisaged that river blindness will be eliminated globally by 2025 and lymphatic filariasis by 2020 <sup>8</sup>.

Professor Youyou Tu is a Chinese medical scientist, pharmaceutical chemist, and educator. She is the first Chinese Nobel laureate in physiology or medicine, and the first Chinese citizen to receive the Nobel Prize in natural sciences. She was born, educated and carried out research exclusively in China. 1 Youyou Tu is best known for discovering artemisinin (also known as qinghaosu) and dihydroartemisinin, used to treat malaria, which saved millions of lives. Her discovery of artemisinin and its treatment of malaria are regarded as a significant advance of tropical medicine in the 20th century and health improvement for people from developing countries in South Asia, Africa, and South America <sup>6, 9, 10</sup>.

Malaria was traditionally treated by chloroquine or quinine, but with declining success. By the late 1960s, efforts to eradicate malaria had failed and the disease was on the rise. At that time, Youyou Tu in China revisited the ancient literature and discovered clues that guided her in her quest to successfully extract the active component from *Artemisia annua*. She was the first to show that this component, later called artemisinin, was highly effective against the malaria parasite, both in infected animals and in humans. Furthermore, Youyou Tu volunteered to be the first human subject. "As a head of this research group, I

had the responsibility" she said. Artemisinin represents a new class of antimalarial agents that rapidly kill the malaria parasites at an early stage of their development, which explains its unprecedented potency in the treatment of severe malaria. When used in combination therapy, it is estimated to reduce mortality from malaria by more than 20% overall and by more than 30% in children. For Africa alone, this means that more than 100 000 lives are saved each year <sup>6,9,10</sup>.

## REFERENCES

- Molin A. Nobel Prize in Physiology or Medicine Awarded to William C. Campbell, Satoshi Omura, Youyou Tu. Wall Street Journal; Retrieved 5 October 2015.
- WHO/Department of control of neglected tropical diseases. Sustaining the drive to overcome the global impact of neglected tropical diseases. Second WHO report on neglected tropical diseases. Geneva: World Health Organization; 2013.
- World Health Orgnization. Factsheet on the World Malaria Report 2014. Greneva: World Health Orgnization; 2015.
- Burg RW, Miller BM, Baker EE, Birnbaum J, Currie SA, Hartman R, et al. Avermectins, New Family of Potent Anthelmintic Agents: Producing Organism and Fermentation. Antimicrob Agents Chemother 1979; 15(3): 361-7.
- 5. Egerton JR, Ostlind DA, Blair LS, Eary CH, Suhayda D, Cifelli S, et al. Avermectins, a new family of potent anthelmintic

- agents: efficacy of the B<sub>1</sub>a component. Antimicrob Agents Chemother 1979; 15(3): 372–8.
- Tu YY, Ni MY, Zhong YR, Li LN, Cui SL, Zhang MQ, et al. Studies on the constituents of Artemisia annua L. (author's transl). Yao Xue Xue Bao 1981; 16(5): 366-70. (Chinese)
- Omura S. Microbial metabolites: 45 years of wandering, wondering and discovering. Tetrahedron 2011; 67(35): 6420-59.
- Omura S, Crump A. The life and times of ivermectin a success story. Nat Rev Microbiol 2004; 2(12): 984–9.
- 9. Louis HM, Xinzhuan S. Artemisinin: Discovery from the Chinese Herbal Garden. Cell 2011; 146 (6): 855–8.
- 10. Tu YY. The discovery of artemisinin (qinghaosu) and gifts from Chinese medicine. Nat Med 2011; 17(10): 1217-20.