



Dir. Prof. Leonid Nefyodov

On behalf of the Royal Swedish Academy of Sciences we, as members of the Nobel Committee for Chemistry, have the honour of inviting you to submit proposals for the award of

The Nobel Prize in Chemistry for 2004.

According to the Rules of the Nobel Foundation the discovery or improvement should be indicated for which the award is proposed and reasons given for the suggestion. Work done in the past may be selected for the award only on the supposition that its significance has until recently not been fully appreciated.

A summary of the regulations governing awards is appended as well as a form which may be used for the proposal of candidate(s).

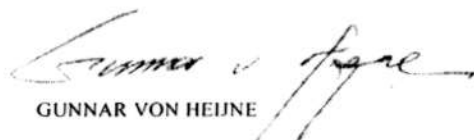
Proposals, which should be addressed to The Nobel Committee for Chemistry, Box 50005, S-104 05 Stockholm, Sweden, cannot be considered unless received by the Committee not later than 31 January 2004. The street address (for express mail delivery) is Lilla Frescativagen 4.

Stockholm, September 2003,


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NOMINATION FOR THE AWARD OF THE 2004 NOBEL PRIZE
IN CHEMISTRY

Nominations on this form should be sent to the Nobel Committee *before* February 1, 2004.
Nominations are not published. The names of nominees are not announced privately or in protocols.

Name of nominee

Dr. Wassil Nowicky

Position or title

President, Ukrainian Anti-Cancer Institute

Address

Margaretenstr. 7, A-1040 Vienna, Austria

Name of nominee

Dr. Anatoliy Potopalsky

Position or title

Chief, Department of the Modification of Structure of Biologically Active Compounds,
Institute of Molecular Biology and Genetics, Academy of Sciences of Ukraine

Address

Zabolotny st. 150, 03143 Kyiv, Ukraine

Name of nominee

Dr. Maria Olievska

Position or title

Institute of Pharmaceutical Chemistry, Lviv Medical University

Address

Pekarska st. 69, 79010 Lviv, Ukraine

The nomination is based on the discovery/improvement of

Thiophosphamide derivatives of isoquinoline alkaloids, method of producing and application thereof. (United States patent 3,865,830)

Description

Reasons for nomination, to be filled in for the benefit of the Committee. (Detailed specification of reasons, bibliography, curriculum vitae and other relevant documents may be appended.)

The chemical synthesis of herbal alkaloids derivatives has resulted in the creation of important new medicinal agents. One of these, Ukrain, is a thiophosphoric acid derivative of alkaloids from *Chelidonium majus* L. It is the first anti-cancer drug to accumulate selectively in malignant cells (in both primary tumor and metastases) without affecting healthy cells. The dose that inhibits the *in vitro* growth of healthy cells is 100 times higher than that shown to be malignocytolytic for all cancer cell lines so far tested.

In the late 1960s Wassil Nowicky, Anatoliy Potopalskiy and Maria Olievska began to study herbal alkaloids in the Department of Pharmacology at Lviv Medical Institute, Ukraine. These studies resulted in the creation of new semisynthetic alkaloid derivatives with various biological effects. In 1969, a patent application was made relating to a new method of synthesizing herbal alkaloid derivatives. United States Patent 3,865,830 'Thiophosphamide derivatives of isoquinoline alkaloids, method of producing and application thereof' was granted on 11 February 1975. However, for clinical using these early compounds had to be dissolved in polyethylene glycol and dimethyl sulphoxide. In 1975, Wassil Nowicky developed a method of producing water soluble herbal alkaloid derivatives. This enabled the drug to be administered not only intramuscularly but also intravenously, resulting in increased effectiveness and safety. In 1979, Wassil Nowicky took out the Austrian patent No. 354644 'Verfahren zur Herstellung von neuen Salzen von Alkaloidderivaten von Thiophosphorsäure' ('Method of producing new salts from alkaloid derivatives of thiophosphoric acid').

In the 1980s, Wassil Nowicky developed further new herbal alkaloids derivatives. For these new compounds he took out United States patent 4,970,212, 'Method of treating human illnesses which compromise the ability to mount an effective immunological response', on 13 November 1990.

One of these new compound (Nowicky called it 'Ukrain') was readily water soluble and became an extraordinarily important medical drug. It is the first anticancer agent that selectively accumulates only in malignant cells (in both primary tumor and metastases) without affecting healthy cells.

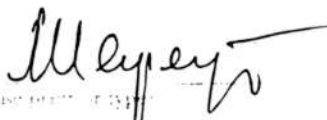
Randomized clinical trials revealed Ukrain to be highly effective in treating even such chemotherapy resistant malignant tumors as pancreatic cancer and colorectal cancer.

In vitro tests of the National Cancer Institute, Bethesda, USA, demonstrated a cytolytic effect of Ukrain (NSC 631570) against all eight colon cancer cell lines tested. In contrast, 5-Fluorouracil (NSC 19893), a cytotoxic agent used as standard therapy in colon cancer, showed barely any growth inhibition of the same cell lines, even in concentrations 100 to 1,000 times higher than those of Ukrain, and did not have a lethal effect even at the highest concentrations. In addition, the dose of Ukrain that inhibits the *in vitro* growth of healthy cells is 100 times higher than the dose has been shown to be malignocytolytic for all cancer cell lines so far tested.

Thus Ukrain is the first malignocytolytic anticancer drug that is both highly effective and non-toxic in therapeutic dosage, with immune modulating, anti-angiogenic and antiviral effects.

Signature

Name of nominator



Please print it type

Prof. Leonid Nefyodov

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Position or title

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13.11.03.

4