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Federal Science Center of Coal and Coal Chemistry
Institute of Human Ecology

CANCER

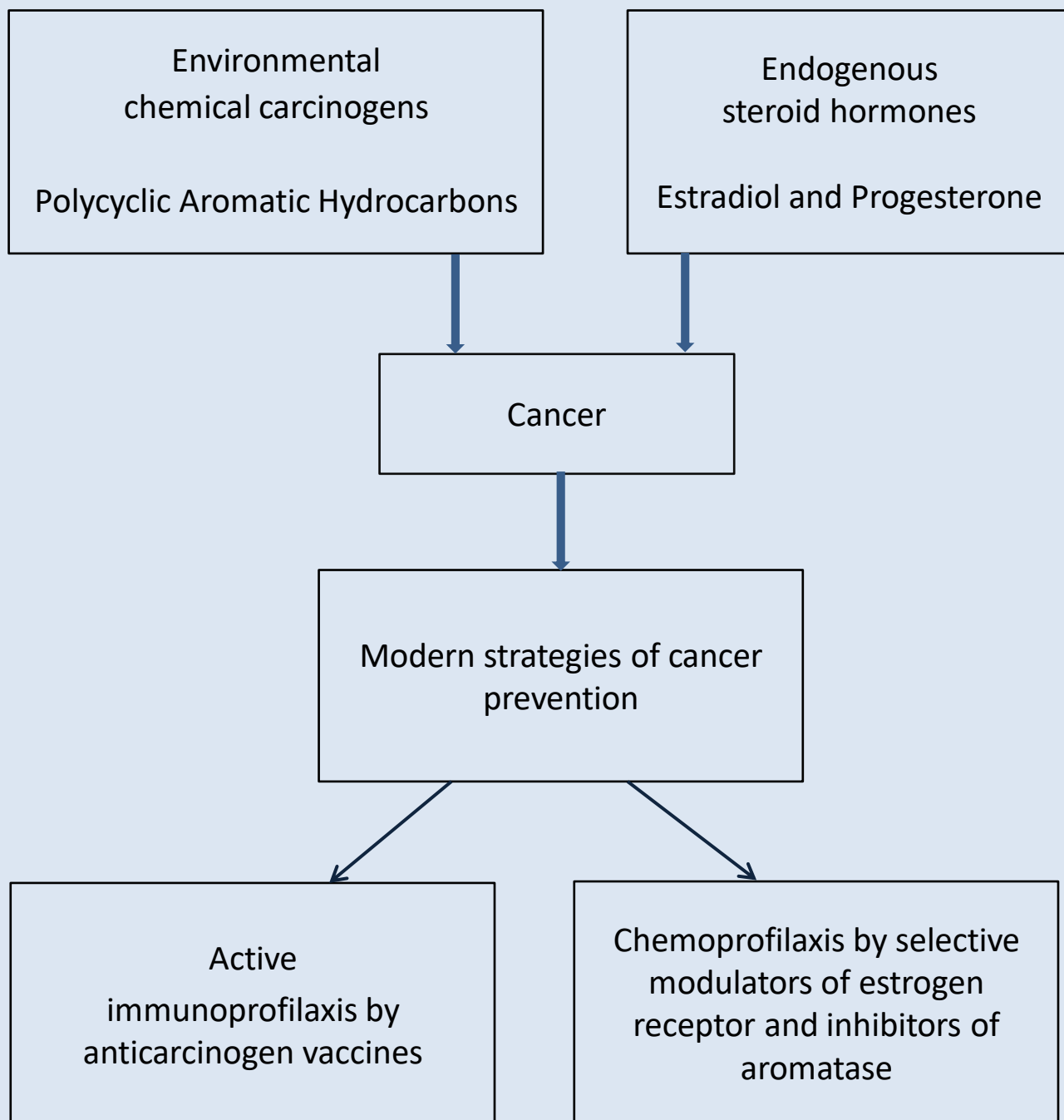
IMMUNOPREDICTION and IMMUNOPREVENTION:
theory, clinical research,
and biotechnological approaches

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Development of the active cancer immunoprophylaxis with anticarcinogen vaccines:

- Franks W., Greech H, University of Toronto, Canada;
- Moolten F. et al. Boston University, USA;
- Peck M. et al. Institute for cancer research, Philadelphia, USA;
- Curtis G. et al. University of Nebraska Medical center, USA;
- Silbart L. et al. University of Connecticut, USA;
- Černohorská H. et al. University of Pardubice, Czech Republic;
- Verdina A. et al. Institute Nazionale Tumori, Italy;
- Schellenberger M, et al. Institute of Immunology, Luxemburg

The main results:

- Immunization of animals by conjugates of carcinogens adjuvants induced the production of carcinogen specific antibodies;
- Secretory IgA class antibodies against carcinogenes inhibited transport of environmental carcinogens through epithelium into blood and target cells;
- Blood serum antibodies against carcinogenes stimulated transport of environmental carcinogens through epithelium into blood and target cells.

It was proposed to use the adjuvants inducing of the preliminary secretory antibodies for anti-carcinogenic vaccines production.



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Development of the cancer chemoprevention by selective modulators of estrogen receptor and inhibitors of aromatase:

- LaCroix A. et al. Fred Hutchinson Cancer Research Center, Seattle, USA;
- Ropka M. et al. University of Virginia School of Medicine, USA;
- Bouchardy C. et al. University of Geneva, Switzerland;
- Visvanathan K., Lippmans S. et. 16 members of Breast Cancer Risk Reduction Committee of the American Society of Chemical oncology (ASCO);
- Goss P., Massachusetts General Hospital Cancer Center, Boston, USA and 142 collaborators from Spain, France, Canada, UK;
- Cuzick J., Queen Mary University of London, UK and 409 collaborators from Australia, Germany, Italy, Finland.

The main results:

Published articles showed that the selective modulators of estrogen receptor (tamoxifen, raloxifene, toremifene) and the inhibitors of aromatase (exemestane, anastrozole) reduced 30-70% of the breast cancer risk;

Lung cancer mortality reduced in breast cancer women treated with anti-estrogens.

So, carcinogens induced steroids depending tumors may be prevented by the pharmaceutical agents.



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The main problems

All people are exposed to the environmental chemical carcinogens, but only a few of them may have cancers



Only persons with high cancer risk need the profilactic treatment



It is necessary to use the informative biological markers for the accurate cancers predictions for the high effective cancers preventions



The unknown mechanisms of the chemical carcinogenesis in human would be revealed taking into account the joint action of the environment carcinogens and endogenous steroids



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Out studies based on the published data:

- Environmental benzo[α]pyrene and endogenous estradiol act jointly stronger than separately as mutagens;
- Estradiol stimulates proliferation of target cells as promoter of carcinogenesis;
- Progesterone inhibits proliferation of target cells as anti-promoter of carcinogenesis;
- The specific antibodies against steroids increase hormones concentration in blood serum after immunization of animals by steroids hormones conjugated with proteins;
- Anti-idiotypic antibodies modulate biological effects of corresponding idiotypic antibodies.

It was proposed the complex immunoassay of idiotypic and anti-idiotypic antibodies against benzo[α]pyrene, estradiol, and progesterone which will be accurate markers for risks of cancers induced by carcinogens and depended on steroids.



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We have considered:

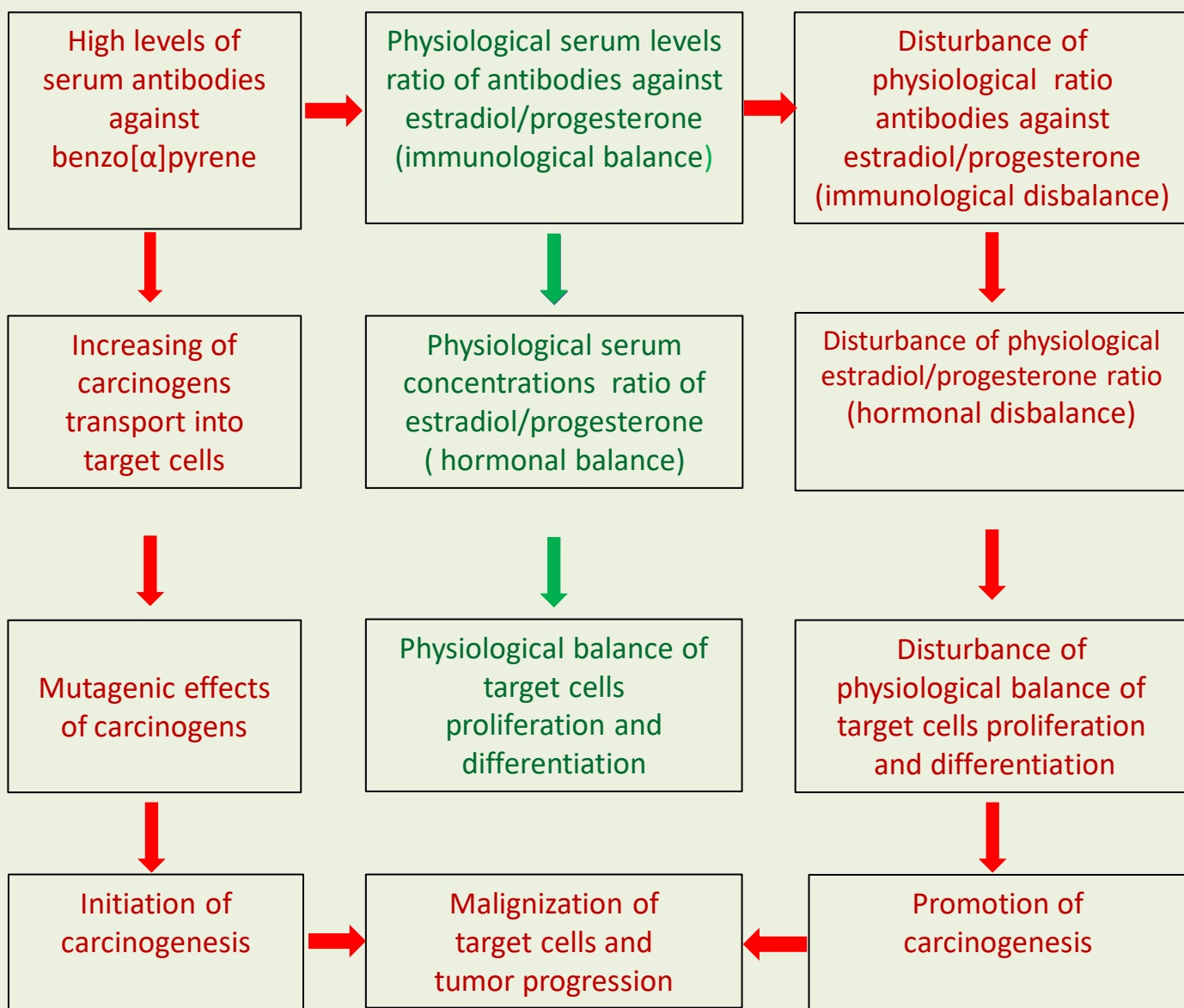
- Levels of the serum antibodies against estradiol and progesterone correlated with the levels of antibodies against benzo[α]pyrene in human blood serum;
- Low levels of antibodies against benzo[α]pyrene together with low levels of antibodies against estradiol and high levels of antibodies against progesterone in blood serum associated with low risk of lung cancer in men and breast cancer in women;
- High levels of antibodies against benzo[α]pyrene together with high levels of antibodies against estradiol and low levels of antibodies against progesterone in blood serum associated with high risk of lung cancer in men and breast cancer in women;
- High levels of antibodies against estradiol together with low levels of antibodies against progesterone in blood serum associated with high concentrations ratio estradiol/progesterone in healthy women;
- Anti-idiotypic antibodies against estradiol and progesterone modified the influence of corresponding idiotypic antibodies on hormones concentrations in blood serum;
- Anti-idiotypic antibodies against benzo[α]pyrene changed associations of corresponding idiotypic antibodies with lung cancer in men and women;
- Disbalance between antibodies against benzo[α]pyrene, estradiol, and progesterone associated with the lost of estrogen and progesterone receptors in tumor cell during breast cancer progression;
- The quantity of chromosome aberration in blood cells was increased in workers of coal and coal-chemistry industry in Kemerovo region (Kuzbass).

The theory of immuno-hormonal disbalance in chemical carcinogenesis has been proposed.



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Theory of immuno-hormonal disbalance at chemical carcinogenesis





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High cancer risk takes place in persons with immunohormonal disbalance depending on high levels of IgA class antibodies against environmental carcinogens in blood serum.

Only these persons need defence from environmental carcinogens for cancer prevention. However active immunoprophylaxis by anticarcinogenic vaccines will be dangerous because of immunohormonal disbalance increasing.

Passive immunoprophylaxis by probiotics expressing of human antibodies against environmental carcinogens may be alternative strategy for cancer prevention.



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Perspectives for cancer prediction:

- Preparing of new materials for immunoassay of idiotypic and anti-idiotypic antibodies against benzo[α]pyrene, estradiol and progesterone in human blood serum;
- Creating new complex immunoassay for detection of idiotypic and anti-idiotypic antibodies against benzo[α]pyrene, estradiol, and progesterone in human blood serum;
- Studying of idiotypic and anti-idiotypic antibodies against benzo[α]pyrene, estradiol, and progesterone in human blood serum of cancer patients and workers of carcinogen dangerous industries;
- Cytogenetic study (chromosomal aberration) in cancer patients and workers of carcinogen dangerous industries;

Determination of the most accurate immunological markers of individual risks of cancer and mutagenesis.



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Our results in molecular immuno-biotechnology:

- Peptide-immunomimetic of chemical carcinogens which binds antibodies against benzo[α]pyrene and benz[α]anthracene (Rus. Patent №2357975);
- Mouse hybridoma cells for production of monoclonal antibodies against benzo[α]pyrene and benz[α]anthracene (Rus. Patent №2423519);
- Quantitative ELISA for detections of antibodies against benzo[α]pyrene in human biological liquids (Rus. Patent №2702900);
- ELISA of idiotypic and anti-idiotypic antibodies against benzo[α]pyrene in human biological liquids (Rus. Patent application);
- Method of affine chromatography preparation of single-chain recombinant antibodies;
- Mouse single-chain anti-idiotypic antibodies against polycyclic aromatic hydrocarbons and its encoding DNA;
- Human single-chain antibodies against polycyclic aromatic hydrocarbons and its encoding DNA;
- DNA of single-chain antibodies against polycyclic aromatic hydrocarbons for protein expression in *Rorippa palustris*.

The effective biotechnological developments were constructed for the new immunochemical materials and methods for cancers predictions and preventions.



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Perspectives for cancer prevention:

-Cancer prevention by selective modulators of estrogen receptor and inhibitors of aromatase will be enhanced by using of new immunological methods of cancer prediction;

-DNA incoding of human singe-chain antibodies against polycyclic aromatic hydrocarbons will be used for production of gene-modified probiotics defending of human from environmental carcinogenes;

-DNA incoding of mouse singe-chain antibodies against polycyclic aromatic hydrocarbons will be used for production of gene-modified plants which will be filter water and purify the air polluted by chemical carcinogenes



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New model of complex cancer predictions and preventions will be suggested for using in coal mining and coal processing industry regions polluted by polycyclic aromatic hydrocarbons in collaboration with:

- Kemerovo regional oncological hospital;
- Kemerovo diagnostic advisory center;
- Kemerovo state medical university



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The main publications:

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- Glushkov A.N., Polenok E.G., Ustinov V.A. Immunomodulation of human carcinogenesis by the serum antibodies to environmental carcinogens and endogenous steroids. **Open Journal Immunol.** 2016. V. 6(3). P. 67-72.
- Minina V.I., Sinitsky M.Yu., Druzhinin V.G., Fucic A., Bakanova M.L., Ryzhkova A.V., Savchenko Y.A., Timofeeva A.A., Titov R.A., Voronina E.N., Volobaev V.P., Titov V.A. Chromosome aberrations in peripheral blood lymphocytes of lung cancer patients exposed to radon and air pollution. **Eur. J. Cancer Prevention**. 2016. V. 25(4). P.70-77.
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- Arnst K.V., Studennikov A.E., Ustinov V.A., Glushkov A.N. Isolation, production and characterization of a new single chain anti-idiotypic antibody against benzo[a]pyrene. **Journal of Immunoassay and Immunochemistry**. 2017. P. 1-11.
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- Andrew N. Glushkov, Elena G. Polenok, Stella A. Mun, Lyudmila A. Gordeeva. Immunization against environmental chemical carcinogens: pro and contra. **Medical Hypotheses**. 2019. V. 131. P. 109303.
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