

## American Russian Cancer Alliance

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Fox Chase Cancer Center is a founding member of the American Russian Cancer Alliance (ARCA). Other members include the University of Maryland Greenebaum Cancer Center, Baltimore, Maryland, the N.N. Blokhin Russian Cancer Research Center, Moscow, Russia, and the Russian Nuclear Research Center Kurchatov Institute, Moscow, Russia. The mission of ARCA is to pool the intellectual and scientific resources of member institutions to foster clinical innovations and discoveries, to accelerate the evaluation of cancer strategies, and to initiate collaborative clinical and research initiatives among ARCA members. The vision of ARCA is to develop a partnership among American and Russian clinical and research institutions that identifies and capitalizes on the special expertise and experience of the membership for advancement of cancer research and its ultimate translation to clinical application.

Collaboration with Russia is strategically important given the centralization of cancer care and the organization of science and oncologic expertise in Russia. This collaboration complements and extends programs for cancer populations developed in the United States. A unique aspect of this collaboration is the radioisotopes produced at the Russian Nuclear facilities together with the scientific background provided by Russian partners that can lead to development of advanced diagnostic and therapeutic technology in the treatment of cancer. The potential for this radioisotope research has been noticed by members of the United States Congress who have provided a yearly appropriation from the Health and Human Services Committee for research that converts materials produced at Russian nuclear facilities into unique isotopes for treating human cancer. In addition to the radioisotope research, there have been opportunities to expand population science research expertise to Russia, particularly as it relates to tobacco control research.

### **Radioimmunotherapy of cancer.**

**Engstrom, Adams**, in collaboration with **Nikolai Marchenkov, Ph.D.**, Kurchatov Institute, Moscow, Russian Federation

Scientists at Fox Chase Cancer Center are utilizing unique alpha-emitting radioisotopes produced at the Kurchatov Institute for purposes of radioimmunotherapy of solid tumors. A major limitation to treating solid tumors is the inability of radioisotope-conjugated antibodies to localize in sufficient quantities in tumor tissue without excessive exposure to sensitive normal tissues such as the bone marrow. This limitation is particularly true when short-lived isotopes such as Bismuth-213 are employed. G. Adams and L. Weiner<sup>8</sup> have discovered a potential solution to this problem, namely the separation of the delivery of the antibody and the radioisotope into two distinct steps. Using a strategy known as pretargeted radioimmunotherapy (PRIT), an unlabeled form of an anti-tumor antibody containing a ligand-binding domain is administered and allowed to localize

in the tumor and to clear from the circulation and normal tissues. When the majority of the remaining antibody is localized in the tumor, a small rapidly cleared radiolabeled ligand molecule is administered which is capable of being retained by the pre-localized antibody. The objective of the pilot research is to evaluate the efficacy of Bismuth-213 PRIT of solid human tumor-xenografts growing in a mouse model. Bi-213 is an alpha particle emitting radioisotope with a half-life of approximately 45 minutes. The alpha particles it emits are so potent that a few "hits" are sufficient to kill a tumor cell (as compared with thousands of "hits" for the more-commonly employed beta particle emitters such as Iodine-131 and Yttrium-90). During the initial phase of this project, they have developed a bispecific single-chain Fv (bs-scFv) molecule that co-targets a tumor associated antigen and a radiolabeled peptide. The ability of the bs-scFv to target HER2 expressing tumors was then demonstrated in immunodeficient mice bearing

human tumor xenografts. N. Marchenkov's group has successfully extracted sufficient Th-229 (the initial material for a "parent" Th-229/Ra-225 generator) from U-223 and designed, built and maintained a Th229/Ra-225 radionuclide generator suitable for production of Ra/Ac-225. Ra/Ac-225 was then used in the creation of Bi-213 generators. During this period, five generators were shipped to Fox Chase Cancer Center and were used to establish the conditions for using the generator and harvesting Bi-213.

During the coming year, continued improvement will be made in the binding strength of the anti-peptide arm of the bs-scFv to prolong the tumor retention of the Bi-213 conjugated peptide and preclinical therapy studies will be performed in the immunodeficient mouse model.

**Cancer prevention research.** Engstrom, Schnoll,<sup>a</sup> in collaboration with Lev Demidov, M.D., Ph.D., N.N. Blokhin Cancer Center, Moscow, Russian Federation

Because tobacco-related cancers are a major health problem in both the Russian Federated Republic and the United States, Fox Chase Cancer Center investigators initiated tobacco control studies at the N.N. Blokhin Russian Cancer Research Center. A team of investigators assessed the incidence of smoking activity in 399 consecutive cancer patients treated at the Blokhin Cancer Center. Several notable findings emerged from the analysis that can be used to guide the development of interventions in cancer centers throughout Russia. First, the rate of tobacco use (42%) among Russian cancer

patients exceeds that documented among U.S. cancer patients (25–30%). Moreover, the Russian cancer patients appeared to be less ready to quit smoking; 25% of the American patients are in pre-contemplation stage of readiness to quit compared to 6% of the Russian patients. Second, Russian smokers were more likely to be men and more likely to be diagnosed with either lung or colorectal cancer. Surprisingly, 65% of colorectal cancer patients in Russia were smokers. Third, compared to former or never smokers, patients who are current smokers exhibited less knowledge of the harmful effects of tobacco use, reported lower advantages associated with quitting smoking, demonstrated lower perceived health risk from smoking and showed higher fatalistic beliefs. Lastly, patients who were alcohol-dependent exhibited less readiness to change; almost one-third of the Russian patients showed symptoms consistent with a clinical diagnosis of alcohol dependence. Because nicotine and alcohol use are so strongly linked to one another, both behaviors should be addressed within any comprehensive treatment program in Russia. A new study that was initiated this year will evaluate nicotine dependence in Russian smokers. This information will better enable investigators and clinicians to recognize patients that require anti-depressant therapy along with nicotine replacement therapy for their smoking habit. Lessons learned through the ARCA Tobacco Control Program can be applied in other medical sites in Moscow and can be disseminated to practitioners throughout the Russian Federation.

## Publications

Engstrom, P.F., Clapper, M.L., Schnoll, R.A. Prevention of tobacco-related cancers. In *Cancer Medicine*, 7<sup>th</sup> Edition, edited by D.W. Kufe, R.C. Bast Jr., W.N. Hait, W.K. Hong, R.E. Pollock, R.R. Weichselbaum, J.F. Holland, and E. Frei III. B.C. Dekker, Inc., Ontario, Canada, pp. 354-362, 2006.

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