International Meeting

OPEN DOORS FOR IMMUNOLOGICAL TREATMENT OF CANCER

October 30-31, 2009
Sofia, Bulgaria

Under the patronage of
Acad. Nikola Sabotinov
President of the Bulgarian Academy of Sciences

On the occasion of the 140 anniversary of the
BULGARIAN ACADEMY OF SCIENCES

HASUMI INTERNATIONAL RESEARCH FOUNDATION-BULGARIA
ACKNOWLEDGMENTS

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Kenichiro Hasumi
Bogdan Petrunov

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Galia Kurteva          Siniša Radulović         Dobrin Svinarov
Mikio Kuraya           Spartak Valev            Ivan Tonev

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Bulgarian Academy of Sciences

THE MEETING IS ORGANIZED WITH THE SPECIAL SUPPORT OF:

AND WITH THE HELP OF:
<table>
<thead>
<tr>
<th>Time</th>
<th>Event</th>
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<tbody>
<tr>
<td>15.15 – 15.45</td>
<td>Registration of participants in the National Center of Infectious and Parasitic Diseases – Aula; 26 Yanko Sakazov Blvd., Sofia, Bulgaria</td>
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<tr>
<td>16.00 – 16.30</td>
<td>Opening session - Greeting addresses from the official guests.</td>
</tr>
<tr>
<td><strong>Session I</strong></td>
<td>Chairman – Academician Evgeny GOLOVINSKY</td>
</tr>
</tbody>
</table>
| 16.30 – 17.10 | **Keynote Lecture** - Clinical appreciation of dendritic cell and radiation therapy on advanced cancer patients  
*Dr. Kenichiro HASUMI*  
Chairman, Shukokai Incorporated; Founder, Hasumi International Research Foundation-Bulgaria |
| 17.10 – 17.50 | **Keynote Lecture** - Ninth International Conference on Progress in Vaccination Against Cancer (PIVAC 9-Sofia 2009) – “Where are we now?”  
*Prof. Elissaveta NAUMOVA*  
Head, Central Laboratory of Clinical Immunology, Medical University-Sofia |
| 17.50 – 18.30 | **Keynote Lecture** - Nano-medicine and cancer – the Bulgarian perspective  
*Prof. Stavri STAVREV*  
Director of Materials’ Research, Space Research Institute - Bulgarian Academy of Sciences |
| 18.30 – 19.00 | Discussion                                                            |
| 19.15 – 21.30 | **GET-TOGETHER PARTY** - National Center of Infectious and Parasitic Diseases – Second floor Lobby |
### SATURDAY, 31 OCTOBER 2009

<table>
<thead>
<tr>
<th>Session II</th>
<th>Chairman – Prof. Dobrin SVINAROV</th>
</tr>
</thead>
</table>
| 09.00 – 09.30 | **Immune surveillance of cancer – 2009**  
*Prof. Iskra ALTANKOVA*  
Head, Clinical Immunology Laboratory,  
Medical University, Sofia |
| 09.30 – 10.00 | **T-regulatory cells in cancer immune therapy**  
*Assoc.-Prof. Milcho MINCHEFF*  
Head, Gene Therapy Laboratory,  
Institute of Hematology and Blood Transfusion, Sofia |
| 10.00 – 10.30 | **New options in chemo-immune therapy of cancer**  
*Assoc.-Prof. Galina KURTEVA*  
Chemotherapy Clinic,  
National Hospital for Cancer Treatment, Sofia |
| 10.30 – 10.45 | **Coffee-brake** |

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<thead>
<tr>
<th>Session III</th>
<th>Chairman – Assoc.-Prof. Milcho MINCHEFF</th>
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| 10.45 – 11.15 | **Introduction of HSP 70 vaccine**  
*Dr. Mikio KURAYA*  
Hasumi International Research Foundation, Tokyo R&D office |
| 11.15 – 11.45 | **Therapeutic vaccines in cervical cancer**  
*Prof. Siniša RADUPOVIĆ Could not attend*  
Institute of Oncology and Radiology of Serbia, Belgrade |
| 11.45 – 12.15 | **Personalized treatment of cancer. Monitoring the efficiency during cancer bio-immuno chemotherapy**  
*Prof. Dobrin SVINAROV*  
Head of TDM&Clinical Pharmacology, Medical University-Sofia |
| 12.15 – 13.15 | **Discussion** |
| 13.15 – 14.15 | **Lunch** |

| Session IV | Chairmen –  
Prof. Ivan CHERNOZEMSKY, Dr. Kenichiro HASUMI |
|------------|-----------------------------------------------|
| 14.15 – 14.35 | **Posters Review – Oral Presentations**  
- The Future of the Combined Approach  
*Dr. Spartak VALEV*, Researcher in Chemotherapy Clinic, National Hospital for Cancer Treatment, Sofia; Member of Club “Young Oncologist”-Bulgaria  
- Intensified chemotherapy with stem cell support for chorioncarcinoma-case report  
*Dr. Ivan TONEV*, Researcher in Gene Therapy Laboratory, Institute of Hematology and Blood Transfusion, Sofia |
| 14.35 – 16.10 | **Final Discussion** - adopting a final Consensus. |
| 16.10 - 16.30 | **Nomination of the best poster. Handing award** from Hasumi International Research Foundation-Bulgaria to a young scientist.  
**Closing ceremony** |
SUMMARIES

(ACCORDING TO THE PROGRAM’S ORDER)
Clinical appreciation of dendritic cell and radiation therapy on advanced cancer patients - Keynote Lecture

Kenichiro HASUMI, M.D., Chairman, Shukokai Incorporated; Founder, Hasumi International Research Foundation-Bulgaria

Clinical appreciation of dendritic cell and radiation. Combination therapy of dendritic cell intra-tumoral injection and IMRT enhances tumor vaccination. This procedure indicated for 53 cancer recurrent patients and 60% response rate observed in the cases of inclusion criteria.

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Elissaveta NAUMOVA, Professor, Head Clinic of Immunology, University Hospital “Alexandrovsk”, Sofia

On 8-10 October 2009 in Hilton Hotel Sofia was held the Ninth International Conference on Progress in Vaccination Against Cancer – PIVAC-9. The ultimate goal of the PIVAC meetings is to update the participants on all aspects of cancer vaccination and contribute to the combat against cancer. The PIVAC ninth consecutive annual meeting was managed to bring together more than 20 leading lecturers and more than 80 scientists from all over the world in this fast moving field of medicine. The invited speakers presented their studies on such interesting topics as the keynote lecture on results of clinical trials of the telomerase vaccine GV1001 in patients with lung cancer and malignant melanoma given by Prof. Gustav Gaurdenack; The importance of the age factor in cancer vaccination by C. Gravekamp and Immunosenescence, cancer and Cytomegalovirus by G. Pawelec in the Cancer immunity and ageing Session; MHC Molecules and the Immune Escape of Cancer by F. Garrido in the Tumor escape Session; with much interest were also accepted by audience the presentations given by D. Gabrilovich on Novel mechanism of combined effects of immunotherapy and chemotherapy of cancer and by B. Rees on Discovery of cancer antigens and biomarkers associated with cancer and patient response to immunotherapy in Immunotherapy in Cancer and Cancer Vaccines Session. The lectures presented in the Clinical trials Session by D. Speiser on Persistent multifunctional human effector CD8 T cells induced by repetitive vaccination with class I antigens, PT Straten on Immunological targeting of the malignant phenotype, K. Thielemans on Next generation DC vaccines and D. Gomez on Racotumomab a monoclonal anti-idiotype tumor vaccine provoked a interesting and constructive discussion. The presentations of A. Madrigal on Immunotherapy in Stem Cell Transplantation and D. Charron on Immune reconstitution and stem cell therapy were ones of the most anticipated by the participants of the meeting. The Standardization and monitoring Session provided opportunity to the speakers C. Gouttefangeas, P.Lehmann, S. Janetzki and S. Walter to share their data on Optimization of immune monitoring assays for multi-center clinical trials. The best abstracts were presented in the Selected oral presentations Session. Three of the young scientists were given awards for their abstracts during the EACR Young Researcher Awards Session. The PIVAC-9 meeting in Sofia had a great success and contributed to the further development of this important field of medicine. Summary of some talks will be presented.

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Nanomedicine and Cancer – the Bulgarian Perspective

Nanodiamond Particles: Properties and Perspectives for Bioapplications- Keynote Lecture

Stavri Stavrev, Professor, Director of Materials’ Research, Space Research Institute - Bulgarian Academy of Sciences

Development of nanotechnologies in the last decade underwent through a real global revolution. It took them only a few years to turn, from objects of purely theoretical researches in the laboratory, into the basis and guarantee for the scientific progress nowadays. There is no area in the life of the society or of economy where the Nanodiamond particles do not open an incredible perspective. The aforesaid is entirely applicable in the area of health care, and especially for cancer and osteoporosis.

This lecture presents a brief analysis of the achievements of Nanomedicine in the two abovementioned illnesses. An overview of the researches for synthesis and production of nanostructures, especially nanodiamonds, in Bulgaria is presented. In the EU-countries, only in Bulgaria Nanodiamonds (ND) are synthesized or produced.

The properties of the ND are explained – these properties that determine the application of Nanodiamonds in the treatment of cancer and osteoporosis. The primary experiments with cell lines and mice are briefly explained.

An overview of the perspectives for the use of nanodiamonds in these fields is presented together with the future tasks of the researchers.

Glossary
Nanometer – one billionth of the meter. We have nano-dimensions when the objects are under 100 nm;
Nanomaterials – their synthesis is not performed by fragmentation of materials but by predictable structuring on an atom level;
Nanotechnologies – technologies for synthesis and application of Nanomaterials. The transition from ‘micro’ to ‘nano’ is qualitative - not quantitative, meaning that this is a jump from manipulation of materials to manipulation of atoms.

Areas derived from the Nanotechnologies
- Nano-electronics, Nano-devices, Nano-sensors;
- Nano-biotechnology; Nano-medicine and health-care;
- Nano-energetic; Chemical Nanotechnologies;
- Nanotechnologies and ecology

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Immune surveillance of cancer – 2009

Iskra Altankova, Professor, Head, Clinical Immunology Laboratory, Medical University, Sofia

The development of cancer is an evolutionary process driven by many genetic and epigenetic phenomena. It turned out that the human tumors are more heterogeneous and complex than it was expected. In the tumor’s genesis exist complex interrelations between the cancer cells and their immediate micro surrounding (stromal cells, blood vessels), which supply them with oxygen and nutritional elements. Under the pressure of the immune system the tumors become less immunogenic and evade the body’s effective immune response. The aim of the contemporary therapy is to ‘translate’ the gathered and accumulated knowledge into therapeutic approaches and to determine new biomarkers which will allow an earlier diagnosis and improved monitoring of the patients’ disease.

* * *
T-regulatory cells in cancer immune therapy
Milcho Mincheff, M.D., Ph.D.; Associate Professor, Head, Gene and Cell Therapy Laboratory, National Hematology Hospital, Sofia

A large number of cancer-associated gene products evoke immune recognition, but host reactions rarely impede disease progression. Recent evidence has resurrected the concept of specialized populations of T lymphocytes that are able to suppress an antigen specific immune response. These T-regulatory cells (T-regs) have been characterized as CD4+ CD25+ FOXP3+ T cells. T-regs are a member of the growing family of regulatory cell populations that serve to limit the activation, trafficking, and/or effector function of both CD4+ and CD8+ T cells. By doing so, pending on what stage of the immune response they act upon, T regs could enhance healing and diminish carcinogenesis by impeding chronic inflammation and creation of tumorigenic milieu at the site of regeneration. Once cancer has been established, though, T regs serve to suppress stimulation to cancer associated antigens thus suppressing immune surveillance and promoting tumor growth. Since ideally immunotherapy against cancer should start by suppressing carcinogenesis, initial efforts should be directed at enhancing T regulatory cell activity and promoting healing. Once disease has established, evoking a cytotoxic immune response against tumor antigens and destruction of cancer cells would require suppression of T regs activity. Immune intervention, therefore, is a “double-edged sword” and involves intimate knowledge of cancer appearance, disease development and progression, while properly selecting and timing of therapeutic agents.

* * *

New options in chemo-immune therapy of cancer
Galina Kurteva, M.D., Ph.D.; Associate Professor, Chemotherapy Clinic, National Hospital for Cancer Treatment, Sofia

The positive results of several phase III trials involving bevacizumab, sunitinib and sorafenib have definitively established antiangiogenic therapy as a novel clinical modality for the treatment of cancer over the last few years. The study of tumor angiogenesis also revealed that some new molecularly targeted agents which were not developed as antiangiogenic drugs, as well as many conventional cytotoxic drugs, can exert ‘accidental’ antiangiogenic effects. In this regard, two preclinical studies published in 2000 suggested that the frequent or continuous administration of conventional cytotoxic drugs in comparatively low doses over extended periods with no prolonged breaks not only seems to optimize the antiangiogenic properties of chemotherapeutic drugs, but also has the added benefit of significantly reduced toxicity, compared to maximum tolerated chemotherapy administration. This form of antiangiogenic or – as now more commonly called – ‘metronomic’ chemotherapy is being intensively studied clinically. In addition to antiangiogenic effects, other mechanisms of action mediated by metronomic chemotherapy might apply, such as the depletion of regulatory T cells. Since the publication of the results of a trial of metronomic cyclophosphamide and methotrexate for the treatment of advanced breast cancer by Colleoni et al. 7 years ago, numerous studies evaluating variations of this approach in breast, prostate and ovarian cancer among other tumor types have been reported. All these studies confirm the excellent safety profile of metronomic chemotherapy regimens. The published metronomic protocols are commonly complemented with agents having antiangiogenic properties such as cyclooxygenase-2 (COX-2) inhibitors, glitazones, thalidomide and bevacizumab. The most striking results so far the mean Ktrans changes after 1 and 3 months of metronomic therapy in patients with stable disease suggest more pronounced antiangiogenic activity after 3 months. This could be an explanation for the often delayed
effects of metronomic regimens which could preclude the use of such therapy as the only treatment modality in the context of rapidly progressive disease. Although reduced Ktrans readings were also obtained in patients with progressive disease at 3 months of therapy, these changes were only minor and seemingly not sufficient to control tumor growth. Alternatively, tumor growth despite demonstration of antiangiogenic activity could be explained by the phenomenon of reduced vascular dependence, i.e., a tumor cell phenotype characterized by increased resistance to conditions created/exacerbated by chronic antiangiogenic therapy such as severe hypoxia, acidosis and lack of nutrients. The results of Steinbild et al. also highlight another potentially important finding for the clinical application of metronomic chemotherapy – the use of oral fluoropyrimidines, such as capecitabine, UFT or S1. Indeed, one preclinical study showed that a ‘doublet’ oral combination of metronomic UFT and metronomic cyclophosphamide had striking therapeutic effects in a new model of advanced visceral human metastatic breast cancer in immunodeficient mice. Given the use of cyclophosphamide in most published metronomic chemotherapy trial reports, as discussed above, the doublet combination of cyclophosphamide with UFT, S1, or capecitabine, especially when combined with an antiangiogenic drug such as bevacizumab, may be particularly promising, and convenient, for metronomic chemotherapy treatment of certain types of cancer, including in the adjuvant setting. The study by Steinbild et al. was not designed to answer some of the questions that will be important for the further development of metronomic capecitabine regimens in particular, and the field of metronomic therapy in general. First, although the DCE-MRI data indicates antiangiogenic effects of capecitabine at the dose of 500 mg bid, this might not be the optimal antiangiogenic dose. Interestingly, Rocca et al. Describe clinical activity and excellent tolerance of a regimen of daily capecitabine 500 mg tid (plus cyclophosphamide (50 mg/day) and bi-weekly bevacizumab) for the treatment of metastatic breast cancer. With respect to dosing, the analysis of circulating endothelial (progenitor) cells or intrapatient dose-escalation up to the ‘individualized maximum repeatable dose’ have been proposed, but further refinement is clearly needed. Second, while COX-2 inhibitors have been previously studied in combination with metronomic chemotherapy the benefit of such a combination remains to be demonstrated in a randomized trial. In fact, not all agents with antiangiogenic activity can be expected to synergize with metronomic regimens, as has been shown for thalidomide and minocycline. The choice of combination partners might also be guided by the safety profile of such agents, the risk of pharmacokinetic/dynamic interference, the ease of administration, and costs. Third, similar to other anticancer therapies, criteria are needed to define which patients are most likely to benefit from metronomic therapies. This might not only include aspects related to the individual patient, but also the clinical context (e.g., adjuvant versus palliative disease setting; bulky disease versus residual disease following induction therapy; integration with other treatment modalities, etc.) and the choice of cytotoxic drug. Finally, better tools are needed to monitor the antiangiogenic effects of metronomic regimens. Hopefully in the near future phase III data will better define the role of this antiangiogenic treatment approach compared to drugs such as bevacizumab, sunitinib and sorafenib, and how it may be best integrated with the latter biologic agents or with other types of biologic agents such as letrozole, trastuzumab, and tumor vaccines/immunotherapy.

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Introduction of HSP 70 vaccine

Mikio Kuraya, Kanako Imai, Elitsa H. Boteva, Risa Asami, Ken-Ichiro Hasumi
Hasumi International Research Foundation, Tokyo R&D office

We have been developing the cancer vaccines. Of the cancer vaccines, we introduce Hsp70 autologous vaccine. Hsp70 is a 70kDa heat shock protein which is categorized as one of the stress proteins. Hsp70 is a universal intracellular protein. By the stress such as heat shock, hsp70 is induced and forms complexes with denatured proteins/peptides. When the stress is lethal, the complexes become antigens on the cell membrane to be removed by immune cells. These proteins/peptides in cancer cells contain cancer antigens. The antigenic complexes are possible to be utilized as a cancer vaccine. When, especially, the complexes are prepared by autologous tumor, the high specificity against tumor would be expected. We have tried to utilize the complexes on the lethally stressed cancer cells as a cancer vaccine.

* * *

Therapeutic vaccines in cervical cancer

Sinisa Radulovic, Professor, Department of Experimental Oncology, Institute for Oncology and Radiology of Serbia, Belgrade, Serbia

Producing effective therapeutic vaccines has proved much more difficult and challenging than developing cancer preventive vaccines. Despite huge research in the area of cancer immunology, FDA/EMEA have not approved any type of cancer treatment vaccine so far. More than 99% of cervical cancers have detectable amounts of human papillomavirus (HPV) DNA. Integration of high-risk HPV into the host cell genome is followed by continual expression of HPV E6 and E7 oncoproteins, making them excellent targets for developing vaccines which could be used in high grade precancerous (CIN) lesions or invasive cancer or in the prevention of cancer recurrence. Therapeutic cervical cancer vaccines have been extensively studied. Strategies used were vaccination with HPV peptides or proteins, alone or in pulsed dendritic cells, DNA vaccines, virus-like particles or viral and bacterial vectors. Lovaxin-C is a recombinant live-attenuated Listeria monocytogenes (Lm) that secretes the antigen HPV-16 E7 fused to a non-hemolytic listeriolysin O protein. In a phase I study Lovaxin-C was administered to advanced cervical cancer patients refractory to existing therapies. The dose-limiting toxicity was hypotension and flu-like syndrome. There were no serious adverse events. Specific T-cell response was detected as well as clinical response to Lovaxin-C. Several other therapeutic HPV vaccines are in clinical development and in most of the studies specific immunological and clinical responses were seen. Efficacious therapeutic vaccine for the treatment of cervical cancer should be expected in the near future.

* * *

Personalized treatment of cancer. Monitoring the efficiency during cancer bio-immuno chemotherapy

Dobrin Svinarov, Professor, Central Laboratory of Therapeutic Drug Monitoring and Clinical Pharmacology, Alexander University Hospital, Faculty of Medicine, Medical University, Sofia, Bulgaria

Individualisation of anticancer therapy is a classic concept renovated by the progress of analytical techniques and the achievements of pharmacogenetics and “omics” sciences. Its major goal is dedicated to provide the best possible patient care and survival, through optimizing the usage of existing drugs, by adjusting the nature and dose of anticancer agents to each patient, based on genetic, physiological and pathological criteria, on tumour nature, on
associated drugs or previous treatment lines. Thus a favourable balance between enhanced efficacy and reduced toxicity utilizing patient's exposure to the active drug form becomes a cornerstone approach to personalized treatment. This article exposes the pre-requisites and clinical trials necessary to demonstrate the usefulness of therapeutic drug management (TDM) for anticancer agents. In particular, the place and role of thiopurine methyltransferase (TPMT) measurement prior to initiation of therapy will be presented, and relationship between pharmacokinetic and pharmacodynamic management for imatinib and 5-fluorouracil will be reinforced as a tool for a better treatment outcome. TDM in oncology is a discipline in progress. Novel approaches that enhance the discovery of predictive and/or prognostic markers in cancer immunotherapy will be reviewed, and an effort to define the state of the science in biomarker discovery and validation as a prerequisite for clinical utilization will be undertaken. Proofs of efficacy are both scarce are difficult to obtain in anticancer therapy. However, taking this limitation into account and using the benefits of technical progress could lead to better cognitive research on the predictive response factors for a larger number of anticancer agents in the future. When the usefulness of TDM has been clinically demonstrated or strongly suggested, it is essential that as many patients as possible benefit from it. This "technological transfer" should be a continuous process that translates research results for TDM specialists and clinicians.

* * *

The Future of the Combined Approach
Spartak Valev, MD, Researcher in Chemotherapy Clinic, National Hospital for Cancer Treatment, Sofia; Member of Club “Young Oncologist”-Bulgaria

Introduction
A number of clinical trials mostly phase II, have clearly demonstrated that cancer vaccines can stimulate effective antitumor cellular immunity which translates into clinical benefit for cancer patients.

Currently, chemotherapy based regimens are the treatment of choice in most advanced cancers. Although their efficacy varies according to histological, immunohistochemical and genetic characteristics of the tumor, alone chemotherapy may induce a fast and significant reduction in tumor burden. For many years chemotherapy and immunotherapy have been regarded as therapeutic approaches that exert antagonistic effects, which is the reason that a very low number of clinical trials have investigated the interactions of these two approaches.

Rationale
Cancer patients often exhibit immunosuppression and thereby decreased immunological recognition of the tumor. This is due to defective proliferation and function of the T-lymphocytes infiltrating the tumor. T-cell anergy is induced by the tumor and appears to be reversible. Therapeutic approaches can facilitate the restoration of T-cell function. Tumor induced immunosuppression increases with tumor burden and patients with bulky disease are typically less responsive to immunization.

An unexpected synergy has been noticed between vaccines and certain chemotherapies. This may be due to the ability of some cytostatic drugs to inhibit specific immune cell populations: T-regulatory cells (cyclophosphamide, lenalidomide) and myeloid suppressive cells (gemcitabine); or the ability to stimulate dendritic cells (alkylating agents).

In which stage and at what setting?
As a novel therapeutic approach, the majority of anti-cancer vaccines have been tested in advanced and metastatic setting, after standard methods have already failed. However, the
mechanisms of action of anti-cancer vaccines suggest that they would be most effective in adjuvant setting after radical surgery.

**Conclusion**

It is a fact that no phase III study has yet delivered a registered product, but there is too much phase II data to be ignored. The correct patient population with regards to histology, stage and other treatment modalities is yet to be determined. The advantage of anti-cancer vaccines is that they are relatively non-toxic and very specific. However, what will probably make anti-cancer vaccine technologies an indispensable treatment method of the future is the ability to enhance response to other treatment modalities such as chemotherapy.

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**Intensified chemotherapy with stem cell support for chorioncarcinoma - case report**

Chavdar Botev, Ivan TONEV, MD, Researcher in Gene Therapy Laboratory, Institute of Hematology and Blood Transfusion, Sofia

A 31- year old male patient, presented with chorioncarcinoma of the left testis with retroperitoneal and lung metastases and beta HCG over 1000 IU. He was treated with orchifuniculoectomy and chemotherapy regimen BEP. Despite the treatment the lung lesions increased in size and pleural effusion. There were signs of progression – increasing of the lung lesions and pleural effusion resulting in severe respiratory failure developed. The pleural effusion was surgically treated, and the patient underwent four cycles of chemotherapy with Ifosfamide + Paclitaxel. Disease activity was followed by by LDH and AP values since the HCGT was extremely high. After the first chemotherapy, 16,49x10^6 CD34+ cells were collected. The next chemotherapies were with higher doses of cytostatic drugs and were supported by stem cell infusions. After the fourth chemotherapy the brain and lung metastases had shrunk significantly and showed signs of central necrosis on CT-scan images. Unfortunately, the patient developed brain oedema and died during the preparation for the fifth cycle of chemotherapy.

**Discussion:** The classical treatment of testicular tumors includes cisplatin-based chemotherapy, followed by surgical resection of the residual tumor. We find that high dose chemotherapy with alternating cytostatics and shorter intervals between treatments with stem cell support prevent from tumor resistance development and may result in better outcome in patients with aggressive, rapidly progressing diseases, such as chorioncarcinoma.

* * *
SPEAKERS & CONTRIBUTORS PROFILES

(Listed according to the order of the program)
Kenichiro HASUMI

Education & Professional Training:
1969-1972: School of Chemistry, Toho University
1972-1978: Saitama Medical School (Obtained Medical Doctor’s License)
1978-1982: Department of Surgery, the Institute of Medical Science
             University of Tokyo
             Department of Anesthesiology, Showa University
             Department of Surgery, Musashino Red Cross Hospital
1982-1988: Department of Immunology, Electro-chemical & Cancer Institute Shukokai Incorporated

Specialties:
Gastroenterological Surgery, Surgery, Immunology, Oncology, Terminal & Palliative Care

Employment:
1988-   : Chairman, Shukokai Incorporated
           1) Hijirigaoka Hospital
           2) Electro-chemical & Cancer Institute
           3) Shukokai Clinic
1994-   : Visiting Professor, Chaoshung Chinese Medical University
           Chaoshung, China
1997-   : Visiting Professor, Thomas Jefferson University, USA
1998-   : Honorable President of Jilin Cancer Center, China
1999-   : Chairman, Hasumi International Research Foundation, USA
1999-   : Director Board of Trustees, Noguchi Medical Research Institute, USA
2005-   : Founder, Advanced Immuno Therapy Center
2005-   : Founder, World Immuno-Society for Health, Switzerland
2006-   : Founder, Hasumi International Research Foundation – Bulgaria
2007-   : Founder & Chairman, ICVS, Tokyo Clinic

Related Activities:
Cancer Preventive Research Project 1996 (Uremia Project) by Hasumi Vaccine with Tehran University, Ministry of Health, Iran.
Clinical Research of Hasumi Vaccine in Brazil 1998
International Cancer Vaccine Symposium 2001, Tokyo, Japan
Clinical Research of Chinese Medicine (Immuno-Hasumi) in China since 2002
International Cancer Vaccine Symposium 2003, Beijing, China
International Cancer Vaccine Symposium 2006, Washington DC, USA
International Cancer Vaccine Symposium 2007, Vienna, Austria
2007 Immune Support of Health through Nature and Science in Hissarya, Bulgaria,
International Cancer Vaccine Symposium 2008, New York, USA

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Chaoshung Chinese Medical University, China
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Teikyo University, Japan
Taipei Medical University
School of Chinese Pharmacology Beijing University of Chinese Medicine

Memberships:
British Royal Society of Medicine
Association for Palliative Medicine of Great Britain and Ireland
European Association for Palliative Care
Japan Cancer Society
Japan Surgical Society
Japan Society for Immunology
Others

Awards:
1996: Granted the Medal of "National Order of the Southern Cross" from Brazilian Government.
1996: Granted Camara Municipal De Sao Paulo
2007 Granted the Spirit of Change Award from The Kimmel Cancer Center, Thomas Jefferson University

Invited Lectures:
1988: “Cancer and Virus, Improvement of Human Functioning”, Wichita, Kansas, USA
1990: “Vaccine Contro Il Cancro? Si, Grazie!”, Roma, Italy
1994: “World Congress on Cancer”, Sydney, Australia
1994: “Cancer & Immunology”, Chaoshung Chinese Medical College, China
1995: “Cancer Immunology Conference”, Tehran University, Iran
1996: “Cancer and Immunology”, Sao Paulo, Brazil
1997: “Cancer Immunotherapy”, Taipei Medical College, Taiwan
“The 5th International Conference, AIDS, Cancer and Related Problems”, St. Petersberg, Russia
1998: “Cancer Vaccine Therapy”, Jilin Cancer Center, China
2000: “The 15th International Conference on Human Functioning”, Wichita, Kansas, USA
“The 18th UICC International Cancer Congress”, Oslo, Norway
“La Historia y Nuevas Direcciones en Vacunas en Cancer”, Sociedad Medica del Instituto Nacional de Cancerologia, Mexico
2004: “The 20th Years’ Anniversary Academic Congress of Traditional Chinese Medicine”, School of Post Baccalaureate Chinese Medicine, China Medical University
2006: “Advanced Cancer Therapy, DC Intratumoral Injection”, Bulgaria Academy of Science
“Advanced Cancer Therapy, DC Intratumoral Injection”, National University of Singapore
“Advanced Cancer Therapy, DC Intratumoral Injection”, Taiwan University
“Advanced Cancer Therapy, DC Intratumoral Injection”, Taipei Medical School Matalem University, Indonesia
2008: “International Symposium of Antitumoral Immunotherapy and aniti-cancer
2009: "Vaccinations", The college of Bouzareah, Algeria
Publications


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Elissaveta Naumova

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Prof. E. Naumova received her M.D., Ph.D. and DSc degrees as well as her specialties in internal medicine and in clinical immunology at the Medical University, Sofia. As a specialist of internal diseases and immunology Prof. Naumova’s clinical interests are focused on diagnostics and treatment of the immuno-mediated diseases: immunodeficits, autoimmune diseases, organ transplantation, stem cells etc. Her research interests are in the field of immunogenetics, stem cells transplantation, transplantation immunology, immunity and cancer, immunity and aging, population genetics etc. She has over 130 publications and serve on the editorial board of Cancer Immunology and Immunotherapy, Clinical Application of Immunological Investigations and URONET. Prof. Naumova is a National Consultant of Clinical Immunology, a President of the Bulgarian Association for Clinical Immunology, a Councilor in the EFI Executive Board as well as a member of the American Society for Histocompatibility and Immunogenetics.
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Date of birth | 11 October 1942 – Vaglarovo village, Haskovo district, Bulgaria

Career/Employment

1982 up today | Head of the Space Materials Department of the Space Research Institute at the Bulgarian Academy of Sciences (SRI-BAS) and Vice-Director of the Space Research Institute

1999 up today | Member of the National Nanotechnology Expert Council

1999 | Elected Professor of nanotechnology, Istanbul Technical University, Turkey

1980-1982 | Head of the Scientific Department of the National Military University

1980 | Elected Assoc. Professor, National Military University

1971-1980 | Lecturer in theoretical mechanics, National Military University

1965-1971 | Ministry of Defense

Education and training

1978 | Ph.D., Thesis in theoretical mechanics, Institute of Hydrodynamics, Academ Garadok - Russia

1972 | Second speciality – applied physics and mathematics

1965 | M.Sc. – technology of machine building

Specialization

Main field: | Space Materials Science

Other fields: | Space physics

Current field of interest: | Development of technologies for synthesis of super hard nanodisperse carbon phases – diamond and fullerenes by detonation synthesis and technologies for their application

Awards

1988 | “Cyril and Methodius” second degree for participation in the scientific program for the space flight of the second Bulgarian astronaut

Membership

Member of the National Nanotechnology Expert Council
Member of the International Coordination Council of High-Power Processing of Materials
Head of the Space Incubator Sofia at the European Business Network

Projects

X-Gear | Coordinator: D’Appolonia, Italy. Contract No 030433; 120 000 €

I-STONE, FP6 | Coordinator: Prof. Paspaliaris, Athens Technical University, Greece. Contract No 515762-2_IP, FP 6; 104 000 €

ESINET, FP6 | Membership in the Space Incubator Network, supported by ESA, EBN, T4TECH, WSL - FP 6; 15 000 €
<table>
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<tr>
<th>Project</th>
<th>Coordinator</th>
<th>Description</th>
<th>Sponsorship</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Coordinator: Prof. V.D. Blank, TISNUM, Troizk, Moscow, Russia. Grant from the Ministry of Technology and Science Policy, Russia</td>
<td>Processing of compacts of ultra-disperse diamond powder for microelectronics</td>
<td></td>
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<tr>
<td>Smart Wire, FP5</td>
<td>Coordinator: Nuova Faudi, Italy; Contract No G1ST-CT-2002-50265; 150 000 €</td>
<td></td>
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<tr>
<td>OSNET, FP 5</td>
<td>Coordinator: Prof. Paspaliaris, Athens Technical University, Greece. Contract No GTC1-2000-28020 -V FP of EC; 20 000 €</td>
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<tr>
<td>Two Nanotechnologies Projects</td>
<td>Ministry of Education and Science, Bulgaria</td>
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<td>Project with the Agency of SME</td>
<td>Project with the Agency of SME, 37 000 BGN</td>
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**Publications**

<table>
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<th>Category</th>
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<tr>
<td>Number of papers in journals</td>
<td>132</td>
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<tr>
<td>Number of communications to scientific meetings</td>
<td>5</td>
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<td>Books</td>
<td>4</td>
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<td>Patents of invention</td>
<td>7</td>
</tr>
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**List of patents**

- **BG Pat. No.104645, 31.07.2000**: New Carbon allotropic modification
- **BG Pat. No.100054, 09.10.1995**: Method for improving the working parameters of lubricating oils
- **BG Pat. No.99083, 30.09.1994**: Method for synthesis of diamond monocrystals
- **BG Pat. No.99082, 30.09.1994**: Method for synthesis of diamond monocrystals
- **BG Pat. No.50504, 28.01.1992**: Method for production of Aluminium-base composites

**PUBLICATIONS:**

4. Dimitrios Bikiaris; Costas Chrissafis; Costas Paraskevopoulos; S. Stavrev; Aris Docoslis; Alexandros Vassiliou “Characterization and thermal degradation mechanism of isotactic polypropylene/carbon black nanocomposites”, Elsevier Editorial System(tm) for Thermochimica Acta, Nonisothermal kinetics, 2007


* * *

Iskra ALTANKOVA

Prof. Iskra Altankova, MD, DSc, was born in 1949 in Sofia in a family of physicians – surgeons. She finished high school in 1968 in Varna and her higher education cum laude in 1974 in the Medical Academy – The Higher Medical Institute-Varna. In the same year, upon winning a competition, she was appointed as an assistant-professor in the Laboratory of Clinical Immunology and Transplantation at the Department of Nephrology to the National Institute of Nephrology, Urology and Transplantation, Medical Academy in Sofia. In 1977 she was appointed as a research fellow in the Immunologic Laboratory at the Department of Internal Medicine to the National Institute of Internal Medicine and Physiotherapy, and in 1992 becomes Associate Professor in the same laboratory situated in the University hospital “St. Ivan Rilski”. Since 1994 till present she is Head of the Laboratory of Clinical Immunology. Since 1999 she is Professor in Immunology. After restructuring of the hospital and turning it into University Multi-profile Hospital for Active Treatment “St. Ivan Rilski” she acted as a Head of Medical Diagnostic Laboratory in the hospital. At present, she is Professor, Head of the Laboratory of Clinical Immunology and Head of the Diagnostic-consultative Complex at the hospital. Her basic activities have always been connected with the immunologic diagnostics of various diseases, teaching to graduate and post-graduate students, management and teaching to PhD students and research. She has been systematically qualified in Bulgaria and abroad. She has specialized for 15 months (1981-1982) in the Royal Postgraduate Medical School - Hammersmith Hospital, London, under the management of Prof. D. C. Peters, in 1986 for 40 days in the Medical Faculty-Vienna on the problem of acquiring and characterization of monoclonal antibodies, in Germany, Belgium and Sheffield, England – 1-week courses in fluocytometry (in 1995, 1996, 2000), twice in Belgium – in Environmental Health (1992 and 1993, TEMPUS Program) and in France - Franche-Comté University
of Besanson within TEMPUS program for teaching immunology. She acquired basic medical specialty “Immunology” in 1995.
Since 1991 she is part of the Department of Clinical Laboratory and Clinical Immunology at the Medical Faculty – Sofia, where she teaches clinical immunology to 5th year students. She participates in postgraduate education of physicians and biologists in clinical immunology, internal diseases, nephrology etc. In 1999 she acquired the scientific degree Professor in immunology. She was director of studies of 2 successful PhD theses in immunology and scientific consultant of another PhD thesis. She was tutor of 3 postgraduate students - physicians specializing in immunology.
Her scientific interests are connected with development and implementation in clinical practice of new diagnostic immunologic methods, studies on pathogenetic mechanisms of chronic glomerulonephritis and renal inflammatory diseases, role of fibronectins in the immune response, therapeutic modulation of the immune response to treatment of various diseases, new therapeutic approaches to carcinoma treatment etc. In 1984 she completed her PhD thesis and in 1997 obtained Doctor of Science degree. Research activities: 116 scientific publications in Bulgarian and foreign medical journals (28 articles in impact factor foreign journals, 20 participations in monographs and textbooks, 68 articles in peer reviewed Bulgarian scientific journals); 90 participations in national and international congresses and symposia; 8 approved and implemented innovations. She is manager and participant of 10 scientific grant projects, 5 of which being international. She is a member of the Bulgarian Scientific Union, Bulgarian Society of Immunology, European Nephrology, Dialysis and Transplantation Association, International Society of Nephrology. She has been a National Consultant in immunology to the Ministry of Health and at present is a member of the Expert Committee in Immunology to the MoH.
Language knowledge: excellent command of English and Russian.

**Milcho MINCHEFF**

**Education**

1964 -1969 English Language School
1969 -1975 Sofia Medical University, Medical Academy, Sofia - M.D.
1978 -1981 Sofia Medical University, Medical Academy, Sofia - Ph.D.
1981 Sofia Medical University, Institute of Hematology and Blood Transfusion, Sofia
Specialty in Hematology Oncology

**Professional Career**

- **General Practitioner**, Internal Diseases Ward, County Hospital, Rousse, Bulgaria, 1975-1978
- **Ph.D. Student in blood cell cryobiology**, Institute of Hematology and Blood Transfusion, Medical Academy, Sofia, Bulgaria, 1978-1981
- **Assistant Professor**, Institute of Hematology and Blood Transfusion, Medical Academy, Sofia, Bulgaria, 1981-1990
- **Visiting Scientist**, American Red Cross, Rockville, Maryland, 1987-1990
- **Senior Scientist**, Head, Transfusion Immunology Lab, Transfusion and Cryopreservation Research Program, NMRI, National Naval Medical Center, Bethesda, Maryland, 1994 – 2000
- **Research Associate Professor**, Head, Tumor Immunology Laboratory, Department of Medicine, The George Washington University Medical Center, 2000 – present
- **Associate Professor**, Head, Gene Therapy Laboratory, Institute of Hematology and Blood Transfusion, Sofia, Bulgaria, 1990-present
### Honors and awards

<table>
<thead>
<tr>
<th>Year</th>
<th>Description</th>
<th>Institution/Location</th>
</tr>
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<tr>
<td>1969</td>
<td>Gold Achievement Medal</td>
<td>English Language School, Rousse, Bulgaria</td>
</tr>
<tr>
<td>1970-1975</td>
<td>Special Fellowship</td>
<td>Sofia Medical University, Medical Academy, Sofia, Bulgaria</td>
</tr>
<tr>
<td>1978-1981</td>
<td>Special Postgraduate Fellowship Award</td>
<td>Sofia Medical University, Medical Academy, Sofia, Bulgaria</td>
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<tr>
<td>1986-1987</td>
<td>International Fellowship Award</td>
<td>Fred Hutchinson Cancer Research Center, Seattle, WA, USA</td>
</tr>
<tr>
<td>1990</td>
<td>Public Health Service Meritorious Award</td>
<td>Ministry of Health, Sofia, Bulgaria</td>
</tr>
<tr>
<td>1996</td>
<td>Invited Lecturer, 24th Congress of the International Society of Blood Transfusion, Makuhari, Japan</td>
<td>March/April 1996: Plenary and Educational Lectures</td>
</tr>
<tr>
<td>1996</td>
<td>Invited Lecturer, Meeting of the Danish Society of Blood Transfusion, Copenhagen, Denmark</td>
<td>November 26, 1996: Plenary and Educational Lectures</td>
</tr>
<tr>
<td>1999</td>
<td>Invited Lecturer, Keystone Symposium on “Gene based vaccines: mechanism, delivery system and efficacy”, Breckenridge, CO, USA</td>
<td>April 10-14, 2002: Plenary and Educational Lectures</td>
</tr>
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<td>1999</td>
<td>Invited Lecturer, 25th International Symposium of Blood Transfusion, Groningen, The Netherlands</td>
<td>1999: Plenary and Educational Lectures</td>
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<td>2000</td>
<td>Invited Lecturer, Second Macedonian Congress of Immunology, June 13-17, 2000, Ohrid, Macedonia</td>
<td>Plenary and Educational Lectures</td>
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<td>2000</td>
<td>Invited Lecturer, First Macedonian Congress of Macedonian Society of Blood Transfusion, October 10-13, 2000, Ohrid, Macedonia</td>
<td>Plenary and Educational Lectures</td>
</tr>
<tr>
<td>2000</td>
<td>Invited Lecturer, Keystone Symposium on “Advances in Breast and Prostate Cancer” Lake Tahoe, NV, USA</td>
<td>March 2000: Plenary and Educational Lectures</td>
</tr>
<tr>
<td>2002</td>
<td>Invited Lecturer, Keystone Symposium on “Gene based vaccines: mechanism, delivery system and efficacy”, Breckenridge, CO, USA</td>
<td>April 10-14, 2002: Plenary and Educational Lectures</td>
</tr>
<tr>
<td>2003</td>
<td>Invited Lecturer, VIIth National Congress of Hematology, October 10-11, 2003, Sofia, Bulgaria</td>
<td>Plenary lecture</td>
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### Professional Societies
- Transplantation Society
- International Society of Blood Transfusion
- International Society for Cryobiology
- American Association of Tissue Banks
- International Society for Artificial Organs

### Publications
- 50 papers, 5 patents, 34 abstracts from meetings.

### Papers:
Galina KURTEVA

Assoc-Prof. Galina Kurteva, MD Ph.D;
Address: National Specialized Hospital for Cancer Treatment,
Clinic of Medical Oncology,
6 “Plovdivsko Pole” Str.
Sofia 1756, Bulgaria;

Education: Medical Academy, Sofia, 1980;

Speciality: Internal Diseases – 1989; Oncology - 1994;

Degrees: MD in Clinic of Medical Oncology

Fields of Research

Chemotherapy of Colorectal Cancer
Chronochemotherapy
Intraarterial Chemotherapy
Investigation of new anticancer drugs in clinical trials

Memberships in Professional Organisations

American Society of Clinical Oncology
Balkan Union of Oncology
Mediterranean Association of Chemotherapy
Scientific association of Oncology
Association Of Chemotherapy in Bulgaria
Bulgarian Association of Clinical Research /BACR/

Languages

English, Russian

International experience

Moscow, Oncologic Centre, Oncologic School 1989
Budapest, Oncologic School 1996

References

Professor V. Dimitrov  D.Sc. Department of Surgical Oncology in National Centre of Oncology

Principal Publications

1. Krasteva  E., G. Kurteva  ; CNF in advanced breast cancer; First Boolean Congress of Oncology, July 3-7, Athens, 1996
2. Pipercova E., G. Kurteva, P. Kurtev; Role of 99 m Tc Albumin Microspheres for assessment of vascularisation of liver metastases in patients with colorectal cancer; Radiologica diagnostica, Vol. 35-5, 323-327, 1994
3. G. Kurteva; Intraarterial Chemotherapy with Farmorubicine in patients with liver metastases of colorectal cancer; Vol. 30, 2, 93.1992, Oncology
5. Marek Pawlicki, Jacek Jassem, Peter Bosze, Chana Lotan, Galina Kurteva et al., ; A multicenter study of recombinant human erythropoietin (epoetin alpha) in the management of anaemia in cancer patients receiving chemotherapy, Anti-Cancer Drugs, Vol.8, 1997, p. 949-956
6. M. Mincheff, I.Altankova, S. Zoubak, St. Tchakarov, Ch. Botev, St. Petrov, E. Krasteva, G. Kurteva, P. Kurtev; Inn vivo transfection and/or cross priming of dendritic cells following DNA and adenoviral
immunization s for immunotherapy of cancer- changes in peripheral mononuclear subsets and intracellular IL-4 and IFN-Y lymphokine profile, Critical Reviews in Oncology/ Hematology 2001, 39, 125-132

Participation in clinical trials:
1. Randomised double blind trial in postmenopausal women with primary breast cancer who have received Adjuvant Tamoxifen for 2-3 years, comparing subsequent Adjuvant Exemestane treatment with further Tamoxifen - 960EXE031-C/13/96
2. A trial to investigate the safety and efficacy of Durgesic in strong opioid naïve and strong opioid pre- treated subject with cancer pain. FEN-INT-20
3. A starifered phase II trial of Docetaxel 100 or 75 mg/m2 as second line chemotherapy in patients with metastatic breast cancer who have failed a prior treatment with antracycline. SIO13
4. A randomized phase II trial evaluating different shedules of CPT-11 combined with infusional or bolus 5-Fu/ FA as front line therapy for advanced colorectal cancer- CPT-CMA-202.

** **

Mikio KURAYA

M.D., Ph.D. in Medical Science
Biochemistry and Immunology

Education:
- Graduated from the Department of Chemistry, Faculty of Science, Fukuoka University in 1981.
- Finished the Ph.D. course at the major in Chemistry, Division of Science, Fukuoka University in 1986.
- Ph. D degree in Medical Science was obtained from Nagoya City University Graduate School of Medicine (1993).

Research Carrier/Work history
- Department of Microbiology, Fukuoka University School of Medicine from 1986 to1988.
- Department of Tumor Biology, Karolinska Institute, Sweden - from 1988 to 1991 (Profs. Eva and George Klein)
- Department of Biochemistry, Fukushima Medical University School of Medicine - from 1991 to 2004.
- Department of Molecular Biology, Nagoya City University School of Medicine from 2004 to 2006.
- Hasumi International Research Foundation from 2006 to the present.

** **

Sinisa RADULOVIC

Qualifications: M.D., Ph.D., CPI, Spec Clin Pharm, Professor of Research
Address in Yugoslavia: Institute for Oncology and Radiology of Serbia
Pasterova 14, 11000 Beograd, Serbia
Languages: Serbian (mother tongue), English (fluent), fair knowledge of German and Russian
EDUCATION

1960-1968  Primary education, Kovin, Yugoslavia
1968-1972  Secondary education, Grammar school (natural sciences), Yugoslavia
1972-1978  Faculty of Medicine, University of Belgrade, Yugoslavia

Postgraduate Studies & Specialisations

1978-1979  Clinical Internship, University Medical Centers in Belgrade and Kragujevac
1979      State License for Medical Doctors (# 105141)
1982      Basic and Advance Diploma Courses in Sport Medicine
1980-1984  Master of Medical Science degree.
           Department of Pharmacology, Faculty of Medicine, University of Belgrade.
           Scope of study: Mechanism of action of different drugs affecting calcium ion metabolism.
           Title of MSc thesis: Calcium antagonists and intestinal smooth muscle.
1984-1987  Specialization in clinical pharmacology  Departments of Internal Medicine and Pharmacology, Faculty of Medicine, University of Belgrade.
           The specialization covered full time work in the following departments and medical wards: Pharmacology, Internal medicine, Psychiatry, Pediatrics, Ineffective Diseases, Anesthesia & Reanimation.
1989-1991  Fellowship in Experimental Medicine
           Department of Medicine, Tulane University Medical School, New Orleans and Endocrine, Polypeptide and Cancer Institute, Veterans Affairs Medical Center, New Orleans, Louisiana, USA
1992      Ph.D. degree. Institute for Oncology and Radiology, University Clinical Center, Belgrade and Tulane Medical School, New Orleans, U.S.A.
           Title of thesis: Preclinical pharmacology of bombesin antagonists.
1998      Oncology-Clinical Exchange Program, M.D. Anderson Cancer Center, December

EMPLOYMENT

2006-     Scientific Director. Institute for Oncology and Radiology of Serbia, National Cancer Research Center, Belgrade
2001-2006 Chief, Department for Drug Development, Institute for Oncology and Radiology of Serbia, National Cancer Research Center, Belgrade
1999-2001 Scientific Director. Institute for Oncology and Radiology of Serbia, National Cancer Research Center, Belgrade
1994-1999 Chief, Department for Experimental and Clinical Oncology.
           Principal responsibilities: Phase II, III and IV clinical trials, creating therapeutic protocols, rational pharmacotherapy, consultations, drug surveillance and rationalization of drug treatment. Chief of Institute Drug Committee.
1985-1988 Head of Section of Medicine in R&D Department, "Hemofarm", Pharmaceutical Company, Vrsac
1980-1985 Lecturer, Department of Pharmacology, Faculty of Medicine, University of Belgrade.
           Lectures and lab demonstrations to medical students.
1978-1979 Internship. University Medical Centers Belgrade and Kragujevac.

TEACHING EXPERIENCE

1980-1985 Lectures and lab demonstrations on pharmacology and toxicology to II year medical students at Medical Schools in Belgrade (6 hr/wk) and Kragujevac (2 hr/wk)
1992-present Lectures to postgraduate students of medicine on Oncology and students of pharmacy during Drug Information Specialization
1998-present Lecture on Cancer pharmacology to Ph. D. students in oncology, hematology, family practice physicians and clinical pharmacology
1999-present ACRP-Lecturer, Course on Good Clinical Practice and Course on Publishing in Biomedicine
2004-present Lecturer, Specialization on Pharmaceutical Care, Faculty of Pharmacy, University of Belgrade-long-distance learning
2005-present Lecturer, Course on Pharmaceutical Medicine, School of Medicine, University of Belgrade
2005-present Lecturer, Postgraduate studies, Research Methodology, Clinical Research in Medicine, School of Medicine, University of Belgrade
2007-present Lecturer, PhD studies, Research Methodology, Clinical Research in Medicine, School of Stomatology, University of Belgrade and Medical School, University of Nis

MEMBERSHIPS

National:
• Serbian Medical Society, 1978
• Section on Pharmacotherapy of SLD (1995, Board member)
• Yugoslav Physiological Society (1979)
• Yugoslav Pharmacological Society (1979, secretary and treasurer 1980-1984)
• Pharmacotherapy Section of Medical Society of Serbia (1989)
• Yugoslav Society for Sport Medicine (1980)
• Yugoslav Society Against Smoking (1978)
• Section of Pharmaceutical Medicine (2002, founding member)
• European Association of Palliative Care

International:
• American Association for Cancer Research-AACR (1991)
• American Society for Clinical Oncology-ASCO (1998)
• European Society of Medical Oncology-ESMO (1992, ESMO board exam in 1995)
• European Association for Cancer Research-EACR (1994)
• Medical Association of Supportive Care in Oncology-MASCC (1992)
• International Society for Pharmacoepidemiology (ISPE)(1994)
• Hellenic Society for Lung Cancer (1994)
• Balkan Union of Oncology-B.U.ON, 1993, founding member, Sec .General (from 2002)
• World Association of Medical Editors- WAME (2002)
• Association of Clinical Research Professionals- ACRP (2004), Board member of Serbian chapter of ACRP, Certified Clinical Trial Investigator-2006
• Drug Information Association – DIA (2005)
• Société Internationale de Senologie -S.I.S.(2009)

Member of Editorial Board of Yugoslav Journal “Opsta Praksa” (General Practice) (1995)
Member of Advisory Board of Yugoslav Journal “Iugoslav Physiology et Pharmacology Acta” (2002)
Member of Editorial Board of Yugoslav Journal “Archive of Oncology” (1995-1998, 2003-)
Associate Editor in ”Journal of Balkan Union of Oncology” (1996)
Member of Editorial Board of “The Open Lung Cancer Journal (2008)

Member of Yugoslav Drug Committee (1992-1994; 1997-1999)
President of the State Committee for Clinical Trial Approval (MoH and Drug Agency)-2002-
Member of the Board of Medicine in Serbian Ministry of Science and Technology-2002-
Member of the National BioEthics Committee, Unesco Serbia

Current professional activities
- Preclinical pharmacology
- Clinical trials
- Supportive care

Research Projects
1. Experimental oncology (1996-2000), part of Project by Ministry of science and technology of Serbia: Medical research in Oncology
2. BRCA1 and BRCA2 mutations in familiar breast and ovarian cancer (2001-2003)-collaboration with Institute for Scientific Research Demokritos in Athens
3. Clinical implication of the molecular heterogeneity of solid tumors (2002-2005), Ministry of science and technology of Serbia #1691
5. Molecular and genetic aspects of cancer (MNTS 145035B, 2006-ongoing)

Participation in clinical trials
- Cardio protection with Cardioxane® in patients with breast cancer treated by FAC regimen (EUROCETUS).
- Eprex® in cancer anemia induced by cisplatin containing chemotherapy (CILAG-JANSEN).
- Taxotere plus mitoxantrone in metastatic Breast Cancer (RPR) - PI.
- Ethyl cytoprotection in NHL (Schering).
- DPPE (BMS 217380-01) combined with Doxorubicin vs. Doxorubicin alone in metastatic/recurrent breast cancer (BMS) - PI
- DRL-301, A comparative trial of Droloxiﬁne and Tamoxiﬁne as first-line hormonal therapy in women with advanced breast cancer (Pfizer) - PI
- OEXE 031—Randomized double-blind trial in postmenopausal women with primary breast cancer who received adjuvant tamoxifen for 2-3 years comparing subsequent adjuvant Exemestane treatment with further Tamoxifen (PHARMACIA),
- Trial of Tiazofurin in combination with Allopurinol in patients with platinum refractory ovarian cancer (ICN) - PI
- Paclitaxel/CDDP for neoadjuvant treatment of UCNT (BMS), SI
- Herceptin/Taxol in breast cancer - extended access program (BMS) - PI
- Methadone vs. Morphine as first line treatment for cancer pain - a randomized study. ID00-021. MD Anderson Cancer Center, The University of Texas - projects in palliative care and symptom control.
- Dexamethasone in the management of chronic nausea in cancer patients. ID00-31. MD Anderson Cancer Center study, The University of Texas projects in palliative care and symptom control
- Prospective, randomized phase III trial of I.V. vinflunine plus best supportive care as second line therapy versus best supportive care after a platinum-containing regimen, in patients with advanced transitional cell carcinoma of urothelial tract (Pierre Fabre), SI
- A PHASE 3, THREE-ARM, RANDOMIZED, OPEN-LABEL STUDY OF INTERFERON ALFA ALONE, CCI-779 ALONE, AND THE COMBINATION OF INTERFERON ALFA AND CCI-779 IN FIRST-LINE POOR-PROGNOSIS SUBJECTS WITH ADVANCED RENAL CELL CARCINOMA (Wyeth) – PI
- YMB1002-201A: “PHASE I STUDY OF THE SAFETY AND PHARMACOKINETICS OF DPPE ALONE AND IN COMBINATION WITH DOXORUBICIN IN PATIENTS WITH ADVANCED BREAST CANCER” YM Biosciences-PI
- A PHARMACOKINETIC INTERACTION PHASE I, OPEN LABEL, MULTI-CENTRE STUDY EVALUATING THE PLASMA PHARMACOKINETICS OF TAXOTEREAalone and in combination with YMB1002 in Patients with Advanced Metastatic Breast Cancer or Other Advanced Cancer suitable for treatment with Taxotere- YM Biosciences-PI
- A Single Center, Open Label, Parallel Group, Pharmacokinetic Study in Healthy Subjects to Determine the Systemic Concentration of CoFactor after Infusional Administration (Adventrix)-PI
- Protocol Number: Lm-LLO-E7-01, A Phase 1 Open Dose Escalation Study to Determine the Safety and
Immunogenicity of Vaccination with *Listeria monocytogenes* expressing Human Papilloma Virus type 16 E7 (Lovaxin C) for the Treatment of Progressive, Recurrent and Advanced Squamous Cell Cancer of the Cervix (Advaxis), PI

- A SU011248 treatment protocol for patients with cytokine refractory metastatic RCC who are ineligible for participation in other SU011248 protocols and may derive benefit from treatment with SU011248 (Pfizer), SI
- A Phase I Trial of a Fixed Dose of MVA-BN®-HER2 With 1st- or 2nd-Line Treatment of HER-2-Positive Metastatic Breast Cancer – PI
- A Phase 3b, Randomized, Open-Label Study of bevacizumab (Avastin™) + temsirolimus vs. bevacizumab (Avastin™) + interferon-alfa as First-Line Treatment in Subjects with Advanced Renal Cell Carcinoma-PI
- Study IMA-910-101: *An open label, multicenter Phase II/III study to investigate the effectiveness, safety and immunogenicity of a monotherapy with intradermal IMA910 plus GM-CSF following pre-treatment with low-dose cyclophosphamide in advanced and metastatic colorectal carcinoma patients who have successfully completed a 12 week first line treatment with oxaliplatin-based chemotherapy-PI*

Publications in extenso:
- 158 in peer review international journals
- 43 in Yugoslav journals
- 21 monographs and book chapters

**Dobrin Svinarov**

**PRESENT POSITION**

- Head, Central Laboratory of TDM & Clinical Pharmacology, Alexander Hospital, Faculty of Medicine, Medical University.
  St. G. Sofiiski 1 Street,
  1431 Sofia, Bulgaria

- Professor, Department of Clinical Laboratory and Clinical Immunology Alexander Hospital, Faculty of Medicine, Medical University.

**COLLEGES/UNIVERSITIES**

**DEGREES**

- Medical Academy, Sofia, Bulgaria, 1974-1980, MD
- PhD in Medical Sciences, Sofia, Bulgaria, 1987
- Associated Professor of Clinical laboratory Medicine, 1991
- Doctor of Medical Sciences, 1992
- Full Professor of Clinical Laboratory Medicine, 1994

**CERTIFICATES/FELLOWSHIPS**

- Certification in Clinical Laboratory Medicine, 1984
- Fellow, National Institutes of Health, Bethesda, MD, USA, 1987
- Certification in Pharmacology, Medical University, Sofia, 1996
- Visiting Medical Faculty Certificate to practice medicine at the teaching hospitals of Ohio. State Medical Board of Ohio, Issued on July 8 1999, Columbus, Ohio, USA.
- Training Certificate in Clinical Research, Clinical Research Foundation at Children’s Hospital, November 24, 1999, Columbus, Ohio, USA.
- Certificate for Visiting Professor of Pediatric Clinical Pharmacology during the period April 27 1999 – May 12, 2000, at Children’s Hospital, Columbus, Ohio, USA.
- Certification in Clinical Pharmacology, Medical University, Sofia, Bulgaria, 2000.
SOME SCHOLARSHIPS & AWARDS/HONOURS
- "Gold Hypocrites" Medal for Highest Scientific Achievement in Graduating Medicine, Medical Academy, Sofia, Bulgaria, 1980.
- Councilor, International Association of Therapeutic Drug Monitoring and Clinical Toxicology, 1997-99.
- Frederick and Virginia Smith Stecker Scholar “Improving the health of children around the world through continuing education”, May 1, 1999 – May 1 2000, Children’s Hospital, Columbus, Ohio, USA.
- Honor sign “Bulgarian Physician” for outstanding professional achievements and ethics, May 19, 2004

PROFESSIONAL EXPERIENCE

University Appointments
1980 – 1984 - Assistant Professor, Department of Clinical Laboratory, Medical Academy, Sofia.
1985 – 1990 - Chief-Assistant Professor, Department of Clinical Laboratory, Medical Academy, Sofia.
1991 – 1993 - Associate Professor, Department of Clinical Laboratory, Medical Academy, Sofia.
1994 - Present Professor, Department of Clinical Laboratory and Clinical Immunology, Medical University, Sofia.
1999 – 2000 - Visiting Professor and Faculty Member, Department of Pediatrics, Div. of Pharmacology & Toxicology, Children’s Hospital, The Ohio State University, Columbus, OH, U.S.A.

Hospital Appointments
1980 – 1984 - Physician-ordinator, Local Hospital, Shumen.
1980 - 1984 - Clinical Laboratory Assistant, Department of Laboratory Medicine, Alexander University Hospital, Medical Academy, Sofia.
1984 - 1988 - Clinical Laboratory Specialist, Department of Laboratory Medicine, Alexander University Hospital, Medical Academy, Sofia.
1988 - 1992 - Head, TDM Laboratory, Department of Laboratory Medicine, Alexander University Hospital, Medical Academy, Sofia.
1992 - 2004 - Head, TDM/CT Section, Department of Clinical Laboratory and Clinical Immunology, Alexander University Hospital, Medical University, Sofia.
2004 - Present - Head, Central Laboratory of TDM & Clinical Pharmacology, Alexander University Hospital, Faculty of Medicine, Medical University, Sofia.
1999-2000 - Stecker Scholar, Visiting Professor, Faculty Member, Department of Pediatrics, Div. of Pharmacology & Toxicology, Children’s Hospital, The Ohio State University, Col., OH, U.S.A.

Other
1992 - 1993 - Member, National Committee for Grants in Aid of Research, Ministry of Education.
1994 - 1997 - Member, Clinical Laboratory Subcommittee, Medical Section, Higher State Attestation Commission.
1994 - 1997 - Secretary, Commission for Clinical Laboratory Medicine, Higher Expert Counsel, Ministry of Health.
1997- 2000 - Member, Medical Section, Higher State Attestation Commission.
1997- Present - National Referee and Consultant for Clinical Laboratory Medicine, Ministry of Health.
2000 - Present - Member, Clinical Laboratory Subcommittee, Medical Section, Higher State Attestation Commission.
2001 - Present - Member, Standard of Laboratory Practice Committee, International Association of Therapeutic Drug Monitoring and Clinical Toxicology.
2003 –Present - Member, National Positive Drug List Committee, Council of Ministers
2005 - Present - Member, Scientific Advice Working Party, European Medicines agency (EMEA)
OTHER PROFESSIONAL ACTIVITIES

Advisory Committees
Co-Founder, International Association of Therapeutic Drug Monitoring and Clinical Toxicology, 1990.
Co-Founder, Balkan Clinical Laboratory Federation, 1993.
Member, Award Committee, Bulgarian National Academy of Medicine, 1995 - 2005.

Journals
Reviewer, Therapeutic Drug Monitoring, Lippincott - Raven
Reviewer, Clinical Drug Investigation, Adis International
Secretary, Balkan Journal of Clinical Laboratory, 1994 - 1996
Co-Editor-in-Chief, Balkan Journal of Clinical Laboratory, 1996 – 1999
Editorial Board Member, Therapeutic Drug Monitoring, 2005

Professional Associations
Bulgarian Society of Clinical Laboratory
Bulgarian Society of Clinical Pharmacology
Bulgarian National Academy of Medicine
Balkan Clinical Laboratory Federation
International Association of Therapeutic Drug Monitoring and Clinical Toxicology
Drug Information Association
American Association of Clinical Chemistry

SELECTED PUBLICATIONS (Original papers, reduced to 5)

* * *

Spartak VALEV

Adress: "Pencho Slaveykov" blv 5, ent. B, app. 13; Sofia, Bulgaria
Mobile:  
E – mail:  

Education
1998, July
Graduation at the English class of the Foreign Language School “Boyan Penev”, Sofia
1998, September
Student at the Medical Faculty of the Medical University of Sofia
2004, November
Graduation at the Medical Faculty of the Medical University of Sofia
Diploma: 11800
2005, December - present
PhD student at the Chemotherapy Clinic, National Cancer Center; Project: “Individualization of Chemotherapy of Metastatic Breast Cancer”

Curriculum
2000, October
Course of “Molecular Biology and Modern Aspects of Biochemistry” at the Department of Biochemistry, Medical University of Sofia
2001 - 2003

Member of the circle of Pharmacology at the Department of Pharmacology, Medical University of Sofia

2003, August

Participation in the project of “Identifying Novel Tumor Suppressor Genes on Chromosome 5q Involved in Colorectal Cancer”, Hospital Clinic, Barcelona.

Working Experience

2005, January – 2005, December

Assistant at the “Laboratory of Cytogenetics and Molecular Biology”, National Center of Hematology and Transfusiology, Sofia

Certificates

2006, October

“Introduction to Good Clinical Practice”

Language Skills

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<tr>
<td>English</td>
<td>Fluent</td>
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<td>German</td>
<td>Good</td>
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<td>Russian</td>
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Computer Skills

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<tr>
<td>MS Windows</td>
<td>Excellent</td>
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<td>MS Office</td>
<td>Excellent</td>
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<td>SPSS</td>
<td>Good</td>
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Presentations and Awards:


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Ivan TONEV

Work Address: 6 Plovdivsko pole str.
NCHT, Laboratory for cellular and gene therapy
1756 Sofia, Bulgaria

Education:

- 2001 – College and Graduate School: Sofia Medical University, M.D.
- 2002 – Post graduate: specialty in internal medicine – completed individual courses on cardiology, gastroenterology, clinical laboratory, clinical immunology, endocrinology, roentgenology, clinical hematology and rheumatology

Languages:

- English, fluent – spoken and written
- Russian, average – spoken and written
- German, beginner – spoken and written (Dialog beruf starter)

Computer skills:

High school with programmer’s profile, fluent work with the most often used programs, fast adaptation to work with unfamiliar programs

Professional Experience:

2001 – 2004 – Medical Representative; Schering - Plough - Bulgaria
2004 – 2008 – Laboratory for cellular and gene therapy, National Center for Hematology and Transfusion Medicine in Sofia, Bulgaria
2008 - present – Laboratory for cellular and gene therapy, National Specialized Haematology Hospital in Sofia, Bulgaria

List of Publications:


* * *
Hasumi International Research Foundation-Bulgaria
is established by Dr. Kenichiro Hasumi on January 25, 2006 in Sofia, Bulgaria.

- The Foundation was incorporated upon the initiative and in combining the efforts and activities of Japanese, Bulgarian and other experts in the areas of Medicine and Social assistance, opinion leaders and citizens.
- The Foundation is registered with the Sofia Town Court on February 10, 2006.
- The Foundation designates itself as an organization carrying out activities in public benefit.
- Hasumi International Research Foundation-Bulgaria is registered with the Central Register of the Ministry of Justice of Republic of Bulgaria on March 31, 2006

**OBJECTIVES**

1. The main objective of the Foundation is to support the fight against oncological and immunological diseases and their related conditions by searching of new, improvement and better implementation of existing scientific and practical methods, systems and means for prophylaxis, diagnostics, treatment, rehabilitation and pain-release as well as to assist clinical research.
2. Additional objective of the Foundation is to ensure better living conditions in homes, hospices and specialized institutions for aged and disabled people.

**SCOPE OF MAIN ACTIVITIES**

In order to achieve its objectives, the Foundation shall pursue the following main activities:
1. Organization and facilitation of scientific and applied research, through clinical studies of new products, methods and approaches for prophylactics, diagnostics, treatment, rehabilitation, improving the quality of life, etc.
2. Dissemination of modern knowledge by means of organizing seminars, conferences, courses, issuing and distribution of scientific and popular literature;
3. Establishment of and support to homes and hospices for people with advanced disease and aged people;
4. Support for young specialists, including applying for stipends, specializations, courses, scientific events, etc.
5. Building contacts and implementing of partner activities with patients' organizations;
6. Collaboration, providing actual and precise information and raising the expert knowledge of media representatives;
7. Conducting other lawful activity related to the objectives of the Foundation.

**OUR PROGRAMMES**

Finding out, popularizing and development of Bulgarian and international natural and synthesized products and methods in the field of Immunology.

Convening of **Regular October National Meetings** with international participation:

- **2007** – “Immune Support of Health through Nature and Science in Bulgaria”, Jointly with the Bulgarian Academy of Sciences; Hisarya, October 19-20;
- **2008** – “The Elderly People - Life with a Future”, Jointly with the Ministry of Labour and Social Policy of the Republic of Bulgaria; Plovdiv, October 10-12;

**CONTACT INFORMATION**

HASUMI INTERNATIONAL RESEARCH FOUNDATION-BULGARIA
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Bulgarian Academy of Sciences
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