SAMIR N KHLEIF - NATIONAL CANCER INSTITUTE

PUBLICATIONS AUTHORED BY SAMIR N KHLEIF

2015 Nov **The FDA Guidance on Therapeutic Cancer Vaccines: The Need for Revision to Include Preventive Cancer Vaccines or for a New Guidance Dedicated to Them.**

Cancer Prev Res (Phila)
Cancer Prev Res (Phila) 2015 Nov 9;8(11):1011-6. Epub 2015 Sep 9.
Olivera J Finn, Samir N Khleif, Ronald B Herberman

GRU Cancer Center, Georgia Regent University, Augusta, Georgia.

Cancer vaccines based on antigens derived from self molecules rather than pathogens have been under basic and clinical investigations for many years. Up until very recently, they had been tested primarily in the setting of metastatic disease with the goal to engage the immune system in slowing down disease progression. Many therapeutic vaccine trials, either investigator initiated or led by pharmaceutical companies, have been completed and many are currently ongoing, following the FDA Guidance on therapeutic cancer vaccines published in 2011. Read More

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2015 Sep **Programmed death-1 & its ligands: promising targets for cancer immunotherapy.**

Immunotherapy
Immunotherapy 2015 7;7(7):777-92. Epub 2015 Aug 7.
Rajeev K Shrimali, John E Janik, Rasha Abu-Eid, Mikayel Mkrtichyan, Samir N Khleif

Georgia Regents University Cancer Center, Augusta, GA 30912, USA.

Novel strategies for cancer treatment involving blockade of immune inhibitors have shown significant progress toward understanding the molecular mechanism of tumor immune evasion. The preclinical findings and clinical responses associated with programmed death-1 (PD-1) and PD-ligand pathway blockade seem promising, making these targets highly sought for cancer immunotherapy. In fact, the anti-PD-1 antibodies, pembrolizumab and nivolumab, were recently approved by the US FDA for the treatment of unresectable and metastatic melanoma resistant to anticytotoxic T-lymphocyte antigen-4 antibody (ipilimumab) and BRAF inhibitor. Read More

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2015 May **Akt1 and -2 inhibition diminishes terminal differentiation and enhances central memory CD8(+) T-cell proliferation and survival.**

Oncoimmunology

CONTACT DETAILS

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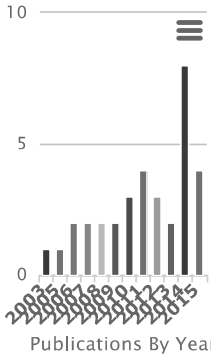

Oncoimmunology 2015 May 3;4(5):e1005448. Epub 2015 Feb 3.
Rasha Abu Eid, Kevin M Friedman, Mikayel Mkrtichyan, Andrea Walens, William King, John Janik, Samir N Khleif

Georgia Regents University, Cancer Center ; Augusta, GA, USA.

The CD8 (+) T-cell response comprises terminally differentiated effector cells and antigen-experienced memory T cells. The latter encompass central (TCM) and effector (TEM) memory cells. TCM cells are superior in their protection against viral and bacterial challenges and mediation of antitumor immunity due to their higher proliferative ability upon antigen re-encounter. Read More

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2015 Mar **Preamble to the 2015 SITC immunotherapy biomarkers taskforce.**

J Immunother Cancer
J Immunother Cancer 2015 24;3. Epub 2015 Mar 24.
Lisa H Butterfield, Mary L Disis, Bernard A Fox, Samir N Khleif, Francesco M Marincola

Sidra Medical and Research Center, Doha, Qatar.

The Society for Immunotherapy of Cancer (SITC) has regularly hosted workshops and working groups focused on immunologic monitoring and immune biomarkers. Due to advances in cancer immunotherapy, including positive results from clinical trials testing new agents and combinations, emerging new technologies for measuring aspects of immunity, and novel candidate biomarkers from early phase trials, the SITC Immune Biomarkers Taskforce has reconvened to review the state of the art, identify current hurdles to further success and to make recommendations to the field. Topics being addressed by individual working groups include: (1) validation of candidate biomarkers, (2) identification of the most promising technologies, (3) testing of high throughput immune signatures and (4) investigation of the pre-treatment tumor microenvironment. Read More

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2014 Dec **The international cancer expert corps: a unique approach for sustainable cancer care in low and lower-middle income countries.**

Front Oncol
Front Oncol 2014 19;4:333. Epub 2014 Nov 19.
C Norman Coleman, Silvia C Formenti, Tim R Williams, Daniel G Petereit, Khee C Soo, John Wong, Nelson Chao, Lawrence N Shulman, Surbhi Grover, Ian Magrath, Stephen Hahn, Fei-Fei Liu, Theodore DeWeese, Samir N Khleif, Michael Steinberg, Lawrence Roth, David A Pistenmaa, Richard R Love, Majid Mohiuddin, Bhadrasain Vikram

Radiation Research Program, National Cancer Institute , Bethesda, MD , USA.

The growing burden of non-communicable diseases including cancer in low- and lower-middle income countries (LMICs) and in geographic-access limited settings within resource-rich countries requires effective and sustainable solutions. The International Cancer Expert Corps (ICEC) is pioneering a novel global mentorship-partnership model to address workforce capability and capacity within cancer disparities regions built on the requirement for local investment in personnel and infrastructure. Radiation oncology will be a key component given its efficacy for cure even for the advanced stages of disease often encountered and for palliation. Read More

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2014 Dec **Pre-immature dendritic cells (PIDC) pulsed with HPV16 E6 or E7 peptide are capable of eliciting specific immune response in patients with advanced cervical cancer.**

J Transl Med
J Transl Med 2014 16;12:353. Epub 2014 Dec 16.

Osama E Rahma, Vincent E Herrin, Rami A Ibrahim, Anton Toubaji, Sarah Bernstein, Omar Dakheel, Seth M Steinberg, Rasha Abu Eid, Mikayel Mkrtichyan, Jay A Berzofsky, Samir N Khleif

Cancer Vaccine Branch, CCR, NCI, 10 Center Drive, Bethesda 20892, MD, USA. skhleif@gru.edu.

The protein products of the early genes E6 and E7 in high-risk HPV types 16 and 18 have been implicated in the oncogenic capability of these viruses. Therefore, these peptides represent attractive vaccine therapy targets.
Thirty-two patients with advanced cervical cancer (HPV16 or 18 positive) were treated with HPV16 E6 (18-26) (Arm A) or HPV16 E7 (12-20) peptide (Arm B) pulsed on PBMCs in order to illicit immune response against the relevant peptide on both arms. Read More

2014 Nov **Selective inhibition of regulatory T cells by targeting the PI3K-Akt pathway.**

Cancer Immunol Res
Cancer Immunol Res 2014 Nov 30;2(11):1080-9. Epub 2014 Jul 30.
Rasha Abu-Eid, Raed N Samara, Laurent Ozbun, Maher Y Abdalla, Jay A Berzofsky, Kevin M Friedman, Mikayel Mkrtichyan, Samir N Khleif

Georgia Regents University Cancer Center, Augusta, Georgia. SKhleif@gru.edu.

Despite the strides that immunotherapy has made in mediating tumor regression, the clinical effects are often transient, and therefore more durable responses are still needed. The temporary nature of the therapy-induced immune response can be attributed to tumor immune evasion mechanisms, mainly the effect of suppressive immune cells and, in particular, regulatory T cells (Treg). Although the depletion of Tregs has been shown to be effective in enhancing immune responses, selective depletion of these suppressive cells without affecting other immune cells has not been very successful, and new agents are sought. Read More

2014 Sep **Episomal expression of truncated listeriolysin O in LmddA-LLO-E7 vaccine enhances antitumor efficacy by preferentially inducing expansions of CD4+FoxP3- and CD8+ T cells.**

Cancer Immunol Res
Cancer Immunol Res 2014 Sep 28;2(9):911-22. Epub 2014 May 28.
Zhisong Chen, Laurent Ozbun, Namju Chong, Anu Wallecha, Jay A Berzofsky, Samir N Khleif

GRU Cancer Center, Georgia Regents University, Augusta, Georgia skhleif@gru.edu berzofsk@helix.nih.gov.

Studies have shown that Listeria monocytogenes (Lm)-based vaccine expressing a fusion protein comprising truncated listeriolysin O (LLO) and human papilloma virus (HPV) E7 protein (Lm-LLO-E7) induces a decrease in regulatory T cells (Treg) and complete regression of established, transplanted HPV-TC-1 tumors in mice. However, how the Lm-based vaccine causes a decrease in Tregs remains unclear. Using a highly attenuated Lm dal dat ΔactA strain (LmddA)-based vaccine, we report here that the vector LmddA was sufficient to induce a decrease in the proportion of Tregs by preferentially expanding CD4(+)FoxP3(-) T cells and CD8(+) T cells by a mechanism dependent on and directly mediated by LLO. Read More

2014 Sep **Is the "3+3" dose-escalation phase I clinical trial design suitable for therapeutic cancer vaccine development? A recommendation for alternative design.**

Clin. Cancer Res.
Clin Cancer Res 2014 Sep 18;20(18):4758-67. Epub 2014 Jul 18.

Osama E Rahma, Emily Gammoh, Richard M Simon, Samir N Khleif

Vaccine Branch, National Cancer Institute, Bethesda, Maryland. Georgia Health Sciences Cancer Center, Augusta, Georgia. skhleif@gru.edu.

Phase I clinical trials are generally conducted to identify the maximum tolerated dose (MTD) or the biologically active dose (BAD) using a traditional dose-escalation design. This design may not be applied to cancer vaccines, given their unique mechanism of action. The FDA recently published "Guidance for Industry: Clinical Considerations for Therapeutic Cancer Vaccines. Read More

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2014 Aug **Ovarian cancer from an immune perspective.**

Radiat. Res.
Radiat Res 2014 Aug 18;182(2):239-51. Epub 2014 Jul 18.
Yousef Zakharia, Osama Rahma, Samir N Khleif

a Georgia Regents University Cancer Center, Augusta, Georgia; and.

Despite major advances in the treatment of ovarian cancer over the past two decades, it is still an incurable disease and requires the development of better treatment strategies. In recent years, we have developed a greater understanding of tumor immunology and the interactions between tumors and the immune system. This has led to the emergence of cancer immunotherapy as the fourth treatment modality in cancer. Read More

Download Full Paper Send a Question to the Author(s) Similar Publications

2014 Mar **The immunological and clinical effects of mutated ras peptide vaccine in combination with IL-2, GM-CSF, or both in patients with solid tumors.**

J Transl Med
J Transl Med 2014 24;12:55. Epub 2014 Feb 24.
Osama E Rahma, J Michael Hamilton, Malgorzata Wojtowicz, Omar Dakheel, Sarah Bernstein, David J Liewehr, Seth M Steinberg, Samir N Khleif

Cancer Vaccine Branch, CCR, NCI, 10 Center Drive, Bethesda, MD 20892, USA. skhleif@gru.edu.

Mutant Ras oncogenes produce proteins that are unique to cancer cells and represent attractive targets for vaccine therapy. We have shown previously that vaccinating cancer patients with mutant ras peptides is feasible and capable of inducing a specific immune response against the relevant mutant proteins. Here, we tested the mutant ras peptide vaccine administered in combination with low dose interleukin-2 (IL-2) or/and granulocyte-macrophage colony-stimulating factor (GM-CSF) in order to enhance the vaccine immune response. Read More

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2014 Jan **Molecular characterization of antigen-peptide pulsed dendritic cells: immature dendritic cells develop a distinct molecular profile when pulsed with antigen peptide.**

PLoS ONE
PLoS One 2014 27;9(1):e86306. Epub 2014 Jan 27.
Amy X Yang, Numju Chong, Yufei Jiang, Jennifer Catalano, Raj K Puri, Samir N Khleif

Vaccine Branch, National Cancer Institute, Bethesda, Maryland, United States of America ; Cancer Center, Georgia Regent University, Augusta, Georgia, United States of America.

As dendritic cells (DCs) are the most potent professional antigen-presenting cells, they are being tested as cancer vaccines for immunotherapy of established cancers. Although numerous studies have

characterized DCs by their phenotype and function, few have identified potential molecular markers of antigen presentation prior to vaccination of host. In this study we generated pre-immature DC (piDC), immature DC (iDC), and mature DC (mDC) from human peripheral blood monocytes (PBMC) obtained from HLA-A2 healthy donors, and pulsed them with human papillomavirus E7 peptide (p11-20), a class I HLA-A2 binding antigen. Read More

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2013 Oct **The regulatory landscape for actively personalized cancer immunotherapies.**

Nat. Biotechnol.
Nat Biotechnol 2013 Oct;31(10):880-2
Cedrik M Britten, Harpreet Singh-Jasuja, Bruno Flamion, Axel Hoos, Christoph Huber, Karl-Josef Kallen, Samir N Khleif, Sebastian Kreiter, Michaela Nielsen, Hans-Georg Rammensee, Ugur Sahin, Thomas Hinz, Ulrich Kalinke

1] TRON - Translationale Onkologie an der Universitätsmedizin der Johannes Gutenberg-Universität Mainz gGmbH, Mainz, Germany. [2] RiboIogical GmbH, Mainz, Germany. [3].

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2013 May **Anti-PD-1 antibody significantly increases therapeutic efficacy of Listeria monocytogenes (Lm)-LLO immunotherapy.**

J Immunother Cancer
J Immunother Cancer 2013 29;1:15. Epub 2013 Aug 29.
Mikayel Mkrtichyan, Namju Chong, Rasha Abu Eid, Anu Wallecha, Reshma Singh, John Rothman, Samir N Khleif

Cancer Center, Georgia Regents University, 1120 15th Street, Augusta GA 30192, USA.

One of the significant tumor immune escape mechanisms and substantial barrier for successful immunotherapy is tumor-mediated inhibition of immune response through cell-to-cell or receptor/ligand interactions. Programmed death receptor-1 (PD-1) interaction with its ligands, PD-L1 and PD-L2, is one of the important strategies that many tumors employ to escape immune surveillance. Upon PD-Ls binding to PD-1, T cell receptor (TCR) signaling is dampened, causing inhibition of proliferation, decreased cytokine production, anergy and/or apoptosis. Read More

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2012 Sep **B7-DC-Ig enhances vaccine effect by a novel mechanism dependent on PD-1 expression level on T cell subsets.**

J. Immunol.
J Immunol 2012 Sep 25;189(5):2338-47. Epub 2012 Jul 25.
Mikayel Mkrtichyan, Yana G Najjar, Estella C Raulfs, Linda Liu, Solomon Langerman, Geoffrey Guittard, Laurent Ozbun, Samir N Khleif

Cancer Vaccine Section, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892, USA.

Programmed death receptor 1 (PD-1) is an important signaling molecule often involved in tumor-mediated suppression of activated immune cells. Binding of this receptor to its ligands, B7-H1 (PD-L1) and B7-DC (PD-L2), attenuates T cell activation, reduces IL-2 and IFN-γ secretion, decreases proliferation and cytotoxicity, and induces apoptosis. B7-DC-Ig is a recombinant protein that binds and targets PD-1. Read More

Download Full Paper Send a Question to the Author(s) Similar Publications

2012 Mar **A gynecologic oncology group phase II trial of two p53 peptide vaccine approaches: subcutaneous injection and intravenous pulsed dendritic cells in high recurrence risk ovarian cancer patients.**

Cancer Immunol. Immunother.

Cancer Immunol Immunother 2012 Mar 17;61(3):373-84. Epub 2011 Sep 17.

Osama E Rahma, Ed Ashtar, Malgorzata Czystowska, Marta E Szajnik, Eva Wieckowski, Sarah Bernstein, Vincent E Herrin, Mortada A Shams, Seth M Steinberg, Maria Merino, William Gooding, Carmen Visus, Albert B DeLeo, Judith K Wolf, Jeffrey G Bell, Jay A Berzofsky, Theresa L Whiteside, Samir N Khleif

Vaccine Branch, CCR, NCI, 41 Medlars Dr., Building 41 Room B900, Bethesda, MD 20892, USA.

Peptide antigens have been administered by different approaches as cancer vaccine therapy, including direct injection or pulsed onto dendritic cells; however, the optimal delivery method is still debatable. In this study, we describe the immune response elicited by two vaccine approaches using the wild-type (wt) p53 vaccine.
Twenty-one HLA-A2. Read More

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2012 Jan **Cancer classification using the Immunoscore: a worldwide task force.**

J Transl Med

J Transl Med 2012 3;10:205. Epub 2012 Oct 3.

Jérôme Galon, Franck Pagès, Francesco M Marincola, Helen K Angell, Magdalena Thurin, Alessandro Lugli, Inti Zlobec, Anne Berger, Carlo Bifulco, Gerardo Botti, Fabiana Tatangelo, Cedrik M Britten, Sebastian Kreiter, Lotfi Chouchane, Paolo Delrio, Hartmann Arndt, Martin Asslaber, Michele Maio, Giuseppe V Masucci, Martin Mihm, Fernando Vidal-Vanaclocha, James P Allison, Sacha Gnjatic, Leif Hakansson, Christoph Huber, Harpreet Singh-Jasuja, Christian Ottensmeier, Heinz Zwierzina, Luigi Laghi, Fabio Grizzi, Pamela S Ohashi, Patricia A Shaw, Blaise A Clarke, Bradly G Wouters, Yutaka Kawakami, Shoichi Hazama, Kiyotaka Okuno, Ena Wang, Jill O'Donnell-Tormey, Christine Lagorce, Graham Pawelec, Michael I Nishimura, Robert Hawkins, Réjean Lapointe, Andreas Lundqvist, Samir N Khleif, Shuji Ogino, Peter Gibbs, Paul Waring, Noriyuki Sato, Toshihiko Torigoe, Kyogo Itoh, Prabhu S Patel, Shilin N Shukla, Richard Palmqvist, Iris D Nagtegaal, Yili Wang, Corrado D'Arrigo, Scott Kopetz, Frank A Sinicrope, Giorgio Trinchieri, Thomas F Gajewski, Paolo A Ascierto, Bernard A Fox

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ally achieved by histopathological evaluation of tissue the primary tumor. Traditional tumor staging (AJCC/UICC- r burden (T), presence of cancer cells in draining and tastases (M). However, it is now recognized that clinical s within the same stage. Read More

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2011 Oct **Anti-PD-1 synergizes with cyclophosphamide to induce potent anti-tumor vaccine effects through novel mechanisms.**

Eur. J. Immunol.

Eur J Immunol 2011 Oct 17;41(10):2977-86. Epub 2011 Aug 17.

Mikayel Mkrtichyan, Yana G Najjar, Estella C Raulfs, Maher Y Abdalla, Raed Samara, Rinat Rotem-Yehudar, Larry Cook, Samir N Khleif

Cancer Vaccine Section, National Cancer Institute, National Institutes of Health, Bethesda, MD 20892, USA.

Programmed death-1 receptor (PD-1) is expressed on T cells following TCR activation. Binding of this receptor to its cognate ligands, programmed death ligand (PDL)-1 and PDL-2, down-regulates signals by the TCR, promoting T-cell anergy and apoptosis, thus leading to immune suppression. Here, we find that using an anti-PD-1 antibody (CT-011) with Treg-cell depletion by low-dose cyclophosphamide (CPM), combined with a tumor vaccine, induces synergistic antigen-specific immune responses and reveals novel activities of each agent in this combination. Read More

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2011 Aug **Therapeutic vaccines for gastrointestinal cancers.**

Gastroenterol Hepatol (N Y)
Gastroenterol Hepatol (N Y) 2011 Aug;7(8):517-64
Osama E Rahma, Samir N Khleif

Despite progress in the management of gastrointestinal malignancies, these diseases remain devastating maladies. Conventional treatment with chemotherapy and radiation is still only partially effective and highly toxic. In the era of increasing knowledge of the molecular biology of tumors and the interaction between the tumor and immune system, the development of targeted agents, including cancer vaccines, has emerged as a promising modality. Read More

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2011 Apr **Defining the critical hurdles in cancer immunotherapy.**

J Transl Med
J Transl Med 2011 14;9:214. Epub 2011 Dec 14.
Bernard A Fox, Dolores J Schendel, Lisa H Butterfield, Steinar Aamdal, James P Allison, Paolo Antonio Ascierto, Michael B Atkins, Jirina Bartunkova, Lothar Bergmann, Neil Berinstein, Cristina C Bonorino, Ernest Borden, Jonathan L Bramson, Cedrik M Britten, Xuetao Cao, William E Carson, Alfred E Chang, Dainius Characiejus, A Raja Choudhury, George Coukos, Tanja de Gruijl, Robert O Dillman, Harry Dolstra, Glenn Dranoff, Lindy G Durrant, James H Finke, Jerome Galon, Jared A Gollob, Cécile Gouttefangeas, Fabio Grizzi, Michele Guida, Leif Håkansson, Kristen Hege, Ronald B Herberman, F Stephen Hodi, Axel Hoos, Christoph Huber, Patrick Hwu, Kohzoh Imai, Elizabeth M Jaffee, Sylvia Janetzki, Carl H June, Pawel Kalinski, Howard L Kaufman, Koji Kawakami, Yutaka Kawakami, Ulrich Keilholtz, Samir N Khleif, Rolf Kiessling, Beatrix Kotlan, Guido Kroemer, Rejean Lapointe, Hyam I Levitsky, Michael T Lotze, Cristina Maccalli, Michele Maio, Jens-Peter Marschner, Michael J Mastrangelo, Giuseppe Masucci, Ignacio Melero, Cornelius Melief, William J Murphy, Brad Nelson, Andrea Nicolini, Michael I Nishimura, Kunle Odunsi, Pamela S Ohashi, Jill O'Donnell-Tormey, Lloyd J Old, Christian Ottensmeier, Michael Papamichail, Giorgio Parmiani, Graham Pawelec, Enrico Proietti, Shukui Qin, Robert Rees, Antoni Ribas, Ruggero Ridolfi, Gerd Ritter, Licia Rivoltini, Pedro J Romero, Mohamed L Salem, Rik J Scheper, Barbara Seliger, Padmanee Sharma, Hiroshi Shiku, Harpreet Singh-Jasuja, Wenru Song, Per Thor Straten, Hideaki Tahara, Zhigang Tian, Sjoerd H van Der Burg, Paul von Hoegen, Ena Wang, Marij Jp Welters, Hauke Winter, Tara Withington, Jedd D Wolchok, Weihua Xiao, Laurence Zitvogel, Heinz Zwierzina, Francesco M Marincola, Thomas F Gajewski, Jon M Wigginton, Mary L Disis

Earle A, Chiles Research Institute, Robert W, Franz Research Center, Providence Cancer Center, Providence Portland Medical Center, Portland, OR, USA. foxb@foxlab.org

Scientific discoveries that provide strong evidence of antitumor effects in preclinical models often encounter significant delays before being tested in patients with cancer. While some of these delays have a scientific basis, others do not. We need to do better. Read More

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2011 Mar **Regulatory approval of cancer risk-reducing (chemopreventive) drugs: moving what we have learned into the clinic.**

Cancer Prev Res (Phila)
Cancer Prev Res (Phila) 2011 Mar;4(3):311-23
Frank L Meyskens, Gregory A Curt, Dean E Brenner, Gary Gordon, Ronald B Herberman, Olivera Finn, Gary J Kelloff, Samir N Khleif, Caroline C Sigman, Eva Szabo,

Chao Family Comprehensive Cancer Center, University of California, Irvine, California, USA. flmeyske@uci.edu

This article endeavors to clarify the current requirements and status of regulatory approval for chemoprevention (risk reduction) drugs and discusses possible improvements to the regulatory pathway for chemoprevention. Covering a wide range of topics in as much depth as space allows, this report is

written in a style to facilitate the understanding of nonscientists and to serve as a framework for informing the directions of experts engaged more deeply with this issue. Key topics we cover here are as follows: a history of definitive cancer chemoprevention trials and their influence on the evolution of regulatory assessments; a brief review of the long-standing success of pharmacologic risk reduction of cardiovascular diseases and its relevance to approval for cancer risk reduction drugs; the use and limitations of biomarkers for developing and the approval of cancer risk reduction drugs; the identification of individuals at a high(er) risk for cancer and who are appropriate candidates for risk reduction drugs; business models that should incentivize pharmaceutical industry investment in cancer risk reduction; a summary of scientific and institutional barriers to development of cancer risk reduction drugs; and a summary of major recommendations that should help facilitate the pathway to regulatory approval for pharmacologic cancer risk reduction drugs. Read More

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2010 Jul **AACR-FDA-NCI Cancer Biomarkers Collaborative consensus report: advancing the use of biomarkers in cancer drug development.**

Clin. Cancer Res.
Clin Cancer Res 2010 Jul 25;16(13):3299-318. Epub 2010 May 25.
Samir N Khleif, James H Doroshow, William N Hait,

National Cancer Institute, Raritan, New Jersey, USA.

Recent discoveries in cancer biology have greatly increased our understanding of cancer at the molecular and cellular level, but translating this knowledge into safe and effective therapies for cancer patients has proved to be challenging. There is a growing imperative to modernize the drug development process by incorporating new techniques that can predict the safety and effectiveness of new drugs faster, with more certainty, and at lower cost. Biomarkers are central to accelerating the identification and adoption of new therapies, but currently, many barriers impede their use in drug development and clinical practice. Read More

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2010 Mar **A pilot clinical trial testing mutant von Hippel-Lindau peptide as a novel immune therapy in metastatic renal cell carcinoma.**

J Transl Med
J Transl Med 2010 28;8. Epub 2010 Jan 28.
Osama E Rahma, Ed Ashtar, Ramy Ibrahim, Antoun Toubaji, Barry Gause, Vincent E Herrin, W Marston Linehan, Seth M Steinberg, Frank Grollman, George Grimes, Sarah A Bernstein, Jay A Berzofsky, Samir N Khleif

Vaccine Branch, NCI, NIH, Bethesda, MD, USA. rahmaoe@mail.nih.gov

Due to the lack of specific tumor antigens, the majority of tested cancer vaccines for renal cell carcinoma (RCC) are based on tumor cell lysate. The identification of the von Hippel-Lindau (VHL) gene mutations in RCC patients provided the potential for developing a novel targeted vaccine for RCC. In this pilot study, we tested the feasibility of vaccinating advanced RCC patients with the corresponding mutant VHL peptides. Read More

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2010 Jan **Immuno-oncology biomarkers 2010 and beyond: perspectives from the iSBTc/SITC biomarker task force.**

J Transl Med
J Transl Med 2010 7;8:130. Epub 2010 Dec 7.
Lisa H Butterfield, Mary L Disis, Samir N Khleif, James M Balwit, Francesco M Marincola

Departments of Medicine, Surgery and Immunology, University of Pittsburgh, Pittsburgh, PA, USA.

The International Society for Biological Therapy of Cancer (iSBTc, recently renamed the Society for Immunotherapy of Cancer, SITC) hosted a one-day symposium at the National Institutes of Health on September 30, 2010 to address development and application of biomarkers in cancer immunotherapy. The symposium, titled Immuno-Oncology Biomarkers 2010 and Beyond: Perspectives from the iSBTc/SITC Biomarker Task Force, gathered approximately 230 investigators equally from academia, industry and governmental/regulatory agencies from around the globe for panel discussions and presentations on the following topics: 1) immunologic monitoring: standardization and validation of assays; 2) correlation of immunity to biologic activity, clinical response and potency assays; 3) novel methodologies for assessing the immune landscape: clinical utility of novel technologies; and 4) recommendations on incorporation of biomarkers into the clinical arena. The presentations are summarized in this report; additional program information and slides are available online at the iSBTc/SITC website. Read More

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2009 Aug **Emerging concepts in biomarker discovery; the US-Japan Workshop on Immunological Molecular Markers in Oncology.**

J Transl Med
J Transl Med 2009 17;7:45. Epub 2009 Jun 17.
Hideaki Tahara, Marimo Sato, Magdalena Thurin, Ena Wang, Lisa H Butterfield, Mary L Disis, Bernard A Fox, Peter P Lee, Samir N Khleif, Jon M Wigginton, Stefan Ambs, Yasunori Akutsu, Damien Chaussabel, Yuichiro Doki, Oleg Eremin, Wolf Hervé Fridman, Yoshihiko Hirohashi, Kohzoh Imai, James Jacobson, Masahisa Jinushi, Akira Kanamoto, Mohammed Kashani-Sabet, Kazunori Kato, Yutaka Kawakami, John M Kirkwood, Thomas O Kleen, Paul V Lehmann, Lance Liotta, Michael T Lotze, Michele Maio, Anatoli Malyguine, Giuseppe Masucci, Hisahiro Matsubara, Shawmarie Mayrand-Chung, Kiminori Nakamura, Hiroyoshi Nishikawa, A Karolina Palucka, Emanuel F Petricoin, Zoltan Pos, Antoni Ribas, Licia Rivoltini, Noriyuki Sato, Hiroshi Shiku, Craig L Slingluff, Howard Streicher, David F Stroncek, Hiroya Takeuchi, Minoru Toyota, Hisashi Wada, Xifeng Wu, Julia Wulfkuhle, Tomonori Yaguchi, Benjamin Zeskind, Yingdong Zhao, Mai-Britt Zocca, Francesco M Marincola

Department of Surgery and Bioengineering, Advanced Clinical Research Center, Institute of Medical Science, The University of Tokyo, Tokyo, Japan. tahara@ims.u-tokyo.ac.jp

Supported by the Office of International Affairs, National Cancer Institute (NCI), the "US-Japan Workshop on Immunological Biomarkers in Oncology" was held in March 2009. The workshop was related to a task force launched by the International Society for the Biological Therapy of Cancer (iSBTc) and the United States Food and Drug Administration (FDA) to identify strategies for biomarker discovery and validation in the field of biotherapy. The effort will culminate on October 28th 2009 in the "iSBTc-FDA-NCI Workshop on Prognostic and Predictive Immunologic Biomarkers in Cancer", which will be held in Washington DC in association with the Annual Meeting. Read More

Download Full Paper Send a Question to the Author(s) Similar Publications

2009 Aug **HPV as a model for the development of prophylactic and therapeutic cancer vaccines.**

Curr. Mol. Med.
Curr Mol Med 2009 Aug;9(6):766-73
Raed N Samara, Samir N Khleif

Cancer Vaccine Section, National Cancer Institute, NCI-NNMC, Bldg 10, Rm. 5101, Bethesda, MD 20889, USA.

HPV has been linked to many human malignancies and, as such, represents a major public health crisis. The understanding of HPV biology, however, has helped tremendously in developing prophylactic vaccines, which should help in decreasing mortality due to HPV infections. Understanding HPV biology has allowed researchers to use the virus as a model for the development of not only prophylactic vaccines, but also therapeutic ones. Read More

Download Full Paper Send a Question to the Author(s) Similar Publications

2008 Sep **Pilot study of mutant ras peptide-based vaccine as an adjuvant treatment in pancreatic and colorectal cancers.**

Cancer Immunol. Immunother.
Cancer Immunol Immunother 2008 Sep 23;57(9):1413-20. Epub 2008 Feb 23.
Antoun Toubaji, Moujahed Achtar, Maurizio Provenzano, Vincent E Herrin, Robert Behrens, Michael Hamilton, Sarah Bernstein, David Venzon, Barry Gause, Francesco Marincola, Samir N Khleif

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There is mounting evidence describing the immunosuppressive role of bulky metastatic disease, thus countering the therapeutic effects of tumor vaccine. Therefore, adjuvant immunotherapy may have a better impact on clinical outcome. In this phase II clinical trial, we aimed to test the feasibility of using a specific mutant ras peptide vaccine as an adjuvant immunotherapy in pancreatic and colorectal cancer patients. Read More

2008 Jan **A systematic approach to biomarker discovery; preamble to "the iSBTc-FDA taskforce on immunotherapy biomarkers".**

J Transl Med
J Transl Med 2008 23;6:81. Epub 2008 Dec 23.
Lisa H Butterfield, Mary L Disis, Bernard A Fox, Peter P Lee, Samir N Khleif, Magdalena Thurin, Giorgio Trinchieri, Ena Wang, Jon Wigginton, Damien Chaussabel, George Coukos, Madhav Dhodapkar, Leif Håkansson, Sylvia Janetzki, Thomas O Kleen, John M Kirkwood, Cristina Maccalli, Holden Maecker, Michele Maio, Anatoli Malyguine, Giuseppe Masucci, A Karolina Palucka, Douglas M Potter, Antoni Ribas, Licia Rivoltini, Dolores Schendel, Barbara Seliger, Senthamil Selvan, Craig L Slingluff, David F Stroncek, Howard Streicher, Xifeng Wu, Benjamin Zeskind, Yingdong Zhao, Mai-Britt Zocca, Heinz Zwierzina, Francesco M Marincola

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The International Society for the Biological Therapy of Cancer (iSBTc) has initiated in collaboration with the United States Food and Drug Administration (FDA) a programmatic look at innovative avenues for the identification of relevant parameters to assist clinical and basic scientists who study the natural course of host/tumor interactions or their response to immune manipulation. The task force has two primary goals: 1) identify best practices of standardized and validated immune monitoring procedures and assays to promote inter-trial comparisons and 2) develop strategies for the identification of novel biomarkers that may enhance our understating of principles governing human cancer immune biology and, consequently, implement their clinical application. Two working groups were created that will report the developed best practices at an NCI/FDA/iSBTc sponsored workshop tied to the annual meeting of the iSBTc to be held in Washington DC in the Fall of 2009. Read More

2007 Aug **The combination of GM-CSF and IL-2 as local adjuvant shows synergy in enhancing peptide vaccines and provides long term tumor protection.**

Vaccine
Vaccine 2007 Aug 12;25(31):5882-91. Epub 2007 Jun 12.
Antoun Toubaji, Sarah Hill, Masaki Terabe, Jiahua Qian, Tamara Floyd, R Mark Simpson, Jay A Berzofsky, Samir N Khleif

Cancer Vaccine Section, Vaccine Branch, NCI, NIH, Bethesda, MD, United States.

Many strategies have been used to enhance the peptide vaccine immune response and to establish therapeutic benefits. This includes the utilization of cytokines to improve antigen presentation or enhance T cell response. Here, we have tested the combination of GM-CSF and IL-2 as locally administered adjuvant to enhance the immune response to the HPV16 E7 peptide. Read More

2007 May **Jordan palliative care initiative: a WHO Demonstration Project.**

J Pain Symptom Manage
J Pain Symptom Manage 2007 May;33(5):628-33
Jan Stjernswärd, Frank D Ferris, Samir N Khleif, Walid Jamous, Imad M Treish, Mohammed Milhem, Mohammed Bushnaq, Ahmad Al Khateib, Mohammad Nayef Al Shtiat, Mary S Wheeler, Ala Alwan

Cancer Control and Palliative Care, World Health Organization, World Health Organization Collaborating Center for Palliative Cancer Care, Oxford, UK. janstjernsward@hotmail.com

A model for pain relief and palliative care for the Middle East has been established in Jordan. King Hussein Cancer Centre (KHCC) in Amman is now a truly comprehensive cancer center as it includes palliative care for inpatients, outpatients, and patients at home. This is especially important in a country and a region where over 75% of the cancer patients are incurable when diagnosed. Read More

2006 Jun **Combined prophylactic and therapeutic cancer vaccine: enhancing CTL responses to HPV16 E2 using a chimeric VLP in HLA-A2 mice.**

Int. J. Cancer
Int J Cancer 2006 Jun;118(12):3022-9
Jiahua Qian, Yujun Dong, Yuk-Ying S Pang, Ramy Ibrahim, Jay A Berzofsky, John T Schiller, Samir N Khleif

Vaccine Branch, NCI, National Naval Medical Center, Bldg 8, Bethesda, MD 20892, USA. qinanj@mailnih.gov

We identified the strategies to induce a CTL response to human papillomavirus (HPV) 16 E2 in HLA-A2 transgenic mice (AAD). A chimeric HPV16 virus-like particle (VLP) that includes full length HPV16 E7 and E2 (VLP-E7E2) was generated. The combination of E2 and E7 has the advantage that E2 is expressed in early dysplasia and neoplasia lesions, where E7 is expressed in more advance lesions. Read More

2006 Mar **Expression of FasL in squamous cell carcinomas of the cervix and cervical intraepithelial neoplasia and its role in tumor escape mechanism.**

Cancer
Cancer 2006 Mar;106(5):1065-77
Ramy Ibrahim, Helen Frederickson, Allyson Parr, Yvona Ward, Joel Moncur, Samir N Khleif

Cancer Vaccine Branch, National Cancer Institute, National Institutes of Health, Bethesda, Maryland 20889, USA.

To date, several mechanisms have been described by which malignant cells escape from the immune system. One of these is through the expression of FasL. The authors hypothesized that the Fas/FasL interaction enables cervical carcinoma cells to induce apoptosis of the cells of the immune system and thereby escape from them. Read More

2005 Dec **Identification of H-2Db-specific CD8+ T-cell epitopes from mouse VEGFR2 that can inhibit angiogenesis and tumor growth.**

J. Immunother.
J Immunother 2006 Jan-Feb;29(1):32-40
Yujun Dong, Jiahua Qian, Ramy Ibrahim, Jay A Berzofsky, Samir N Khleif

The Vaccine Branch, The Center for Cancer Research, National Cancer Institute, NIH, Bethesda, MD 20889, USA.

Vascular endothelial growth factor receptor 2 (VEGFR2/KDR) plays a crucial role in tumor-associated

angiogenesis and vascularization. It has been established that monoclonal antibodies against VEGFR2 can inhibit angiogenesis. In this study, two naturally processed CD8 T-cell epitopes (VILTNPISM and FSNSTNDILI) were identified from murine KDR. Read More

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2003 Apr **Human papillomavirus therapy for the prevention and treatment of cervical cancer.**

Curr Treat Options Oncol
Curr Treat Options Oncol 2003 Apr;4(2):111-9
Samir N Khleif

Center for Cancer Research, National Cancer Institute, National Naval Medical Center, Building 8, Room 4137, Bethesda, MD 20892, USA.
khleif@nih.gov

Cervical carcinoma is associated with human papillomavirus infection. Proliferation of cancer cells depends on the continual expression of the E6 and E7 viral oncogenes. This article includes treatment strategies that can interfere with expression or function of the proteins and immunotherapeutic approaches that can eliminate cells that express E6 and E7 proteins. Read More

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