SITC/iSBTc Cancer Immunotherapy Biomarkers Resource Document
Online Resources and Useful Tools - A Compass in the Land of Biomarker Discovery

Bedognetti et al.

Journal of Translational Medicine
2011, 9:155
http://www.translational-medicine.com/content/9/1/155 (19 September 2011)
SITC/iSBTc Cancer Immunotherapy Biomarkers Resource Document: Online resources and useful tools - a compass in the land of biomarker discovery

Davide Bedognetti1,2,3*, James M Balwit1, Ena Wang1,2, Mary L Disis1,4, Cedrik M Britten5, Lucia G Delogu1,6, Sara Tomei1,2,7, Bernard A Fox1,8, Thomas F Gajewski1,9, Francesco M Marincola1,2 and Lisa H Butterfield1,10

Abstract
Recent positive clinical results in cancer immunotherapy point to the potential of immune-based strategies to provide effective treatment of a variety of cancers. In some patients, the responses to cancer immunotherapy are durable, dramatically extending survival. Extensive research efforts are being made to identify and validate biomarkers that can help identify subsets of cancer patients that will benefit most from these novel immunotherapies. In addition to the clear advantage of such predictive biomarkers, immune biomarkers are playing an important role in the development, clinical evaluation and monitoring of cancer immunotherapies. This Cancer Immunotherapy Resource Document, prepared by the Society for Immunotherapy of Cancer (SITC, formerly the International Society for Biological Therapy of Cancer, iSBTc), provides key references and online resources relevant to the discovery, evaluation and clinical application of immune biomarkers. These key resources were identified by experts in the field who are actively pursuing research in biomarker identification and validation. This organized collection of the most useful references, online resources and tools serves as a compass to guide discovery of biomarkers essential to advancing novel cancer immunotherapies.

Introduction
Immunotherapy has emerged as an important treatment strategy for patients with cancer. With several recent approvals by the U.S. Food and Drug Administration (FDA), cancer immunotherapy has become the latest addition to the toolbox of effective cancer treatments that includes chemotherapy, signal transduction inhibitors, anti-angiogenic agents, radiotherapy, and surgery.

Successful development and testing, regulatory approval and clinical application of cancer immunotherapies require the identification and validation of biomarkers of efficacy. The importance of reliable biomarkers to guide immune-based and personalized cancer therapies is clear. Biomarkers can aid in early disease diagnosis, help clinicians identify patients most likely to benefit from these expensive treatments, and facilitate drug discovery, development and biological/clinical evaluation of cancer immunotherapies.

For over twenty-five years the Society for Immunotherapy of Cancer (SITC; formerly the International Society for Biological Therapy of Cancer, iSBTc) has advanced the science, development and application of biological therapy/immunotherapy of cancer. The society has long recognized the importance of biomarkers for cancer immunotherapy, which has been the focus of a number of SITC/iSBTc symposia and workshops [1-5], and has published recommendations [6] and summaries [7-10].

To support the efforts of investigators involved in research to identify and validate biomarkers for cancer immunotherapy, the authors and members of the SITC Biomarkers Taskforce have identified key biomarker references and online resources and organized these into this SITC/iSBTc Cancer Immunotherapy Biomarkers Resource Document. This document provides an overview of suggested publications and resources for studies on
biomarkers for cancer immunotherapy. This resource document is divided into two sections: Part I: Immunotherapy Biomarker References; and Part II: High Throughput and New Technologies for Biomarker Discovery: Arrays, Platforms, Tools for The Bench and Online Resources. While many important references and resources in the field are included in this document, it does not intend to represent an exhaustive list of all relevant publications, products or resources in the growing, and important field of immune biomarkers. A comprehensive list of online tools for bioinformatics and molecular biology research is available from the Bioinformatics Links Directory [11,12].

A draft of the present document was originally provided to attendees of the SITC/iSBTc Symposium on Immuno-Oncology Biomarkers, 2010 and Beyond: Perspectives from the iSBTc Biomarker Task Force [1], which was held September 30, 2010 at the National Institutes of Health in conjunction with the society’s 25th Annual Meeting. Following the symposium, the draft document was posted on the society’s website for open comment. The comments were reviewed by the authors and incorporated into this manuscript. The references and online resources are organized as outlined in Table 1.

**Part I. Immunotherapy Biomarker References**

1. Guideline and Meeting Reports

*Recommendations from the iSBTc/FDA/NCI Workshop on Immunotherapy Biomarkers*

Butterfield LH, Disis ML, Fox BA, et al.: A systematic approach to biomarker discovery; Preamble to “The iSBTc-FDA Taskforce on Immunotherapy Biomarkers”. J Transl Med 6:81, 2008

Butterfield LH, Palucka AK, Britten CM et al.: Recommendations from the iSBTc-SITC/FDA/NCI Workshop on Immunotherapy Biomarkers, Clin Cancer Res 17:3064-3076, 2010

**2009 Report of the US - Japan Workshop on Immunological Biomarkers in Oncology**

Tahara H, Sato M, Thurin M, et al.: Emerging concepts in biomarker discovery; The US-Japan Symposium on immunological molecular markers in oncology. J Transl Med 7:45, 2009

**2010 Guidelines of the NCI-Investigational Drug Steering Committee (IDSC) Biomarker Task Force**

Dancey JE, Dobbin KK, Groshen S, et al.: Guidelines for the development and incorporation of biomarker studies in early clinical trials of novel agents. Clin Cancer Res 16:1745-1755, 2010

**2010 Report of the Translational Research Cancer Centers Consortium (TrC3) Immunotherapy Network Annual Meeting**

Lesinski GB, Carson WE, Repasky EA, et al.: Meeting Report: The 13th Annual Meeting of the Translational Research Cancer Centers Consortium (TrC3); Immune Suppression and the Tumor Microenvironment, Columbus, Ohio; March 1-2, 2010. J Immunother, 2010

**2008 Report on EU-USA Workshop on System Biology in Cancer Research**

Aebi L, Auffray C, Baney E, et al.: Report on EU-USA workshop: how systems biology can advance cancer research (27 October 2008). Mol Oncol 3:9-17, 2009

**2007 AACR-FDA-NCI Cancer Biomarkers Collaborative Consensus Report**

Khleif SN, Doroshow JH, Hait WN: AACR-FDA-NCI Cancer Biomarkers Collaborative Consensus Report: Advancing the Use of Biomarkers in Cancer Drug Development. Clin Cancer Res 16:3299-3318, 2010

**2005 Report on Workshop on Cancer Biometrics Held at NIH Masur Auditorium**

Lotze MT, Wang E, Marincola FM, et al.: Workshop on cancer biometrics: identifying biomarkers and surrogates of cancer in patients: a meeting held at the Masur Auditorium, National Institutes of Health. J Immunother 28:79-119, 2005

**2002 Report on Workshop on Immunologic Monitoring of Cancer Vaccine Trials**

Keilholz U, Weber J, Finke JH, et al.: Immunologic monitoring of cancer vaccine therapy: results of a workshop sponsored by the Society for Biological Therapy. J Immunother 25:97-138, 2002

2. Clinical Trials

A. Recent Immunotherapy Trials in Cancer Patients - Positive Randomized Phase III Studies

**Examples**

*gp100:209-217 (210M) Peptide Followed by High-Dose IL-2 - Metastatic Melanoma* Schwartzentruber DJ, Lawson D, Richards J, et al: gp100 peptide vaccine and interleukin-2 in patients with advanced melanoma. N Engl J Med 364:2119-27, 2011

*Anti-GD2 Antibody with GM-CSF, Interleukin-2, and Isotretinoin - High-Risk Neuroblastoma* Yu AL, Gilman AL, Ozkaynak MF, et al.: Anti-GD2 antibody with GM-CSF, interleukin-2, and isotretinoin for neuroblastoma. N Engl J Med. 363: 711-23, 2010

*Ipilimumab and Dacarbazine in Metastatic Melanoma Patients - Untreated Metastatic Melanoma* Robert C, Thomas L, Bondarenko I, et al.: Ipilimumab plus dacarbazine for previously untreated metastatic melanoma. N Engl J Med 364:2517-26, 2011

*Ipilimumab in Metastatic Melanoma Patients - Previously Treated Metastatic Melanoma* Hodi FS, O’Day SJ, McDermott DF, et al.: Improved survival with ipilimumab in patients with metastatic melanoma. N Engl J Med 363: 711-23, 2010
Table 1 Structure of the Biomarker References and Online Resources Provided

| Part I. Immunotherapy Biomarker References                                                                 |
|----------------------------------------------------------------------------------------------------------|
| 1. Guideline and Meeting Reports                                                                           |
| 2. Clinical Trials                                                                                          |
| A. Recent Immunotherapy Trials in Cancer Patients - Positive Randomized Phase III Studies                  |
| B. Emerging Biomarkers for Immunotherapy of Cancer - Clinical Trials                                       |
| C. Correlation between Immune Response and Clinical Outcome in Cancer Patients, Positive Studies          |

| 3. Gene Expression Profiling in Cancer Immunotherapy                                                       |
| 4. Useful Reviews                                                                                           |
| 5. Bioinformatics for Biomarkers Discovery                                                                 |
| 6. New Technologies for Biomarkers Discovery                                                               |

| Part II. High Throughput and New Technologies for Biomarker Discovery: Arrays, Platforms, Tools for The Bench and Online Resources |
|-----------------------------------------------------------------------------------------------------------------------------|
| 1. Genomic Biomarkers Discovery                                                                                             |
| A. Single Nucleotide Polymorphisms (SNP) Arrays                                                                            |
| B. Comparative Genomic Hybridization (CGH) Arrays                                                                            |
| C. Mitochondrial Genome Arrays                                                                                             |

| 2. Epigenomic Biomarkers Discovery                                                                                  |
| A. Methylation Arrays                                                                                                 |
| B. microRNA (miRNA) Arrays                                                                                             |
| C. Chromatin Immunoprecipitation (ChIP) Arrays (ChIP on chip)                                                          |

| 3. Transcriptomic Biomarkers Discovery                                                                             |
| A. Expression Arrays                                                                                                  |
| B. Quantitative Assays                                                                                               |

| 4. Proteomic Biomarkers Discovery                                                                                  |
| A. Protein and Phosphoprotein Assays                                                                                |
| B. Multicolor Cytometric Systems                                                                                     |

| 5. Next Generation Sequencing: Whole Genomic and Transcriptomic Sequencing Systems                                |
| 6. Software and Tools for Data Analysis                                                                             |
| A. Microarrays/Sequencing Data Analysis                                                                            |
| B. Next Generation Sequencing Data Analysis                                                                        |
| C. Multicolor Cytometric Data Analysis                                                                             |

| 7. Software and Tools for Function and Pathway Analysis                                                            |
| 8. siRNA Libraries                                                                                                    |
| 9. Public Databases                                                                                                   |
| 10. Tools for the Bench and Other Useful Websites                                                                    |
| A. Primer Design Software                                                                                             |
| B. Transcription Factors Binding Sites Prediction Software                                                           |
| C. Design of Antisense Oligonucleotides, Nucleic Acid Probes, siRNA Software                                         |
| D. miRNA Prediction                                                                                                   |
| E. Alternative Splicing Analysis                                                                                      |
| F. Linkage Disequilibrium Analysis                                                                                   |
| G. Analysis Support, Laboratory Optimization and Other Useful Websites                                              |
| H. Nanotechnology                                                                                                     |
| I. Clinical Trials Registries                                                                                         |

---

*Sipuleucel-T Immunotherapy - Metastatic Prostate Cancer* Kantoff PW, Higano CS, Shore ND, et al.: Sipuleucel-T immunotherapy for castration-resistant prostate cancer. N Engl J Med 363:411-422, 2010

*Interferon & Adjuvant Treatment - High Risk Melanoma* Eggermont AMM, Suciu S, Santinami M, et al.: Adjuvant therapy with pegylated interferon alfa-2b versus observation alone in resected stage III melanoma:
final results of EORTC 18991, a randomised phase III trial. Lancet 372:117-126, 2008

**Idiotype Vaccine Therapy - Complete Remission Follicular Lymphoma** Schuster SJ, Neelapau SS, Gause BL, et al: Vaccination with patient-specific tumor-derived antigen in first remission improves disease-free survival in follicular lymphoma. J Clin Oncol 20: 2787-2794, 2011

**B. Emerging Biomarkers for Immunotherapy of Cancer - Clinical Trials Examples**

**Parameter: HLA Cw*06 Allele**  
**Setting: Interferon α Adjuvant Treatment - High-Risk Melanoma** Gogas H, Kirkwood JM, Falk CS, et al.: Correlation of molecular human leukocyte antigen typing and outcome in high-risk melanoma patients receiving adjuvant interferon. Cancer 116:4326-33, 2010

**Parameter: CCR5 and CXCR3 Polymorphisms and Gene Expression**

**Setting: Adoptive Therapy - Metastatic Melanoma**  
Bedognetti D, Uccellini L, Wang, et al.: Evaluation of CXCR3 and CCR5 polymorphisms and gene-expression as predictive biomarkers of clinical response to adoptive therapy in melanoma patients. J Immunother 33:860, 2010 (Meeting Abstract)

**Parameter: Differentiated Effector Phenotype, “B and T Lymphocyte Attenuator” (BTLA) Expression in CD8 + TIL**

**Setting: Adoptive Therapy - Metastatic Melanoma**  
Laszlo G. Radvanyi, Chantale Bernatchez, Minying Zhang, et al. Adoptive T cell therapy for metastatic melanoma: The MD Anderson experience. J Immunother 33:860, 2010 (Meeting Abstract)

**Parameter: VEGF Serum Level**

**Setting: IL-2 Therapy - Metastatic Melanoma** Sabinino M, Kim-Schulze S, Panelli MC, et al.: Serum vascular endothelial growth factor and fibronectin predict clinical response to high-dose interleukin-2 therapy. J Clin Oncol 27:2645-2652, 2009

**Parameter: Telomere Length**

**Setting: Adoptive Therapy - Metastatic Melanoma** Dudley ME, Yang JC, Sherry R, et al.: Adoptive cell therapy for patients with metastatic melanoma: evaluation of intensive myeloablative chemoradiation preparative regimens. J Clin Oncol 26:5233-5239, 2008

**Parameter: IFN-α Polymorphisms**

**Setting: Anti-CTLA-4 Therapy - Metastatic Melanoma** Bedognetti D, Uccellini L, Wang, et al.: Evaluation of CXCR3 and CCR5 polymorphisms and gene-expression as predictive biomarkers of clinical response to adoptive therapy in melanoma patients. J Immunother 33:860, 2010 (Meeting Abstract)

**Parameter: IFN-γ Polymorphisms**

**Setting: Immuno (Trastuzumab) Chemotherapy - Metastatic Breast Cancer** Musolino A, Naldi N, Bortesi B, et al.: Immunoglobulin G fragment C receptor polymorphisms and clinical efficacy of trastuzumab-based therapy in patients with HER-2/neu-positive metastatic breast cancer. J Clin Oncol 26:1789-1796, 2008

**Parameter: Phosphorylated - STAT-1/STAT-3 Ratio**

**Setting: Neoadjuvant IFN-α Therapy - Stage IIIIB Melanoma** Wang WJ, Edington HD, Rao UNM, et al.: Modulation of signal transducers and activators of transcription 1 and 3 signaling in melanoma by high-dose IFN alpha 2b. Clin Cancer Res 13:1523-1531, 2007

**Parameter: Autoantibodies and Clinical Manifestations of Autoimmunity**

**Setting: Adjuvant IFN-α Therapy - Melanoma** Gogas H, Ioannovich J, Dafni U, et al.: Prognostic significance of autoimmunity during treatment of melanoma with interferon. N Engl J Med: 354:709-18, 2006
Setting: Immuno (IL-2) Chemotherapy - Metastatic Melanoma
Liu DX, O’Day SJ, Yang DY, et al.: Impact of gene polymorphisms on clinical outcome for stage IV melanoma patients treated with biochemotherapy: An exploratory study. Clin Cancer Res 11:1237-1246, 2005
Parameter: IL-6, PPARG
Setting: BCG - Bladder Cancer
Leibovici D, Grossman HB, Dinney CP, et al.: Polymorphisms in inflammation genes and bladder cancer: From initiation to recurrence, progression, and survival. J Clin Oncol 23:5746-5756, 2005
C. Correlation between Immune Response and Clinical Outcome in Cancer Patients; Positive Studies
Examples
Parameter: Melan-A-tetramer+ Immunity
Setting: High Dose Poly-Epitope Vaccine - Metastatic Melanoma
Dangoo A, Lorigan P, Keiholz U, et al.: Clinical and immunological responses in metastatic melanoma patients vaccinated with a high-dose poly-epitope vaccine. Cancer Immunol Immunother 59:863-73, 2010
Parameter: High Interferon-gamma-associated Proliferative CD4+ T-cell Response and Broad Response of CD8+ Interferon-gamma T Cells
Setting: HPV-16 Vaccine Therapy - Vulvar Intraepithelial Neoplasia
Welters MJ, Kenter GG, de Vos van Steenwijk PJ, et al.: Success or failure of vaccination for HPV16-positive vulvar lesions correlates with kinetics and phenotype of induced T-cell responses. Proc Natl Acad Sci U S A. 107:11895-9, 2010
Parameter: High Interferon-gamma-associated Proliferative CD4+ T-cell Response and Broad Response of CD8+ Interferon-gamma T Cells
Setting: HPV-16 Vaccine Therap - Vulvar Intraepithelial Neoplasia
Kenter GG, Welters MJ, Valentijn AR, et al.: Vaccination against HPV-16 oncoproteins for vulvar intraepithelial neoplasia. N Engl J Med 361:1838-47, 2009
Parameter: Tumor Specific Immune Response (ELISPOT)
Setting: Tumor Multi-Epitope Vaccine - Metastatic Melanoma
Kirkwood JM, Lee S, Moschos SJ, et al.: Immunogenicity and antitumor effects of vaccination with peptide vaccine+-/-granulocyte-monocyte colony-stimulating factor and/or IFN-alpha2b in advanced metastatic melanoma: Eastern Cooperative Oncology Group Phase II Trial E1696. Clin Canc Res 15:1443-1451, 2009
Parameter: NY-ESO-1-specific B and T Cell Responses Setting: Anti CTLA-4 Immunotherapy - Metastatic Melanoma
Yuan J, Gnjatic S, Li H, Powel S, et al.: CTLA-4 blockade enhances polyfunctional NY-ESO-1 specific T cell responses in metastatic melanoma patients with clinical benefit. Proc Natl Acad Sci U S A. 105:20410-5, 2008
Parameter: Epitope Spreading
Setting: Adenovirus MART-1 Dendritic Cell Vaccination - Metastatic Melanoma
Butterfield LH, Comin-Anduix B, Vujanovic L, et al.: Adenovirus MART-1-engineered autologous dendritic cell vaccine for metastatic melanoma. J immunother 31:294-309, 2008
Parameter: Epitope Spreading
Setting: Dendritic Cell Based Vaccination - Stage II-IV Melanoma
Ribas A, Glaspy JA, Lee Y, et al.: Role of dendritic cell phenotype, determinant spreading, and negative costimulatory blockade in dendritic cell-based melanoma immunotherapy. J Immunother 27:354-367, 2004
Parameter: Epitope Spreading
Setting: Peptide-Pulsed Dendritic Cells Vaccination - Metastatic Renal Cell Carcinoma
Wierecky J, Müller MR, Wirths S, et al.: Immunologic and clinical responses after vaccinations with peptide-pulsed dendritic cells in metastatic renal cancer patients. Cancer Res 66:5910-8, 2006
Parameter: Epitope Spreading
Setting: Her2 Specific Vaccination - Stage III-IV Breast Cancer
Salazar LG, Goodell V, O’Meara M, et al: Persistent immunity and survival after immunization with a HER2/neu (HER2) vaccine. J Clin Oncol 27 (155):2010 (Meeting Abstract)
Parameter: Overall Immunity to MelAgs
Setting: Dendritic Cell Based Vaccination - Metastatic Melanoma
Banchereau J, Palucka AK, Dhodapkar M, et al. Immune and clinical responses in patients with metastatic melanoma to CD34(+) progenitor-derived dendritic cell vaccine. Cancer Res 64:51-8, 2001
Parameter: T-cell Response (ELISPOT)
Setting: 12-Peptide Vaccine - Stage IIB-IV - Melanoma
Slingluff CL, Jr., Petroni GR, Chianese-Bullock KA, et al.: Immunologic and clinical outcomes of a randomized phase II trial of two multipeptide vaccines for melanoma in the adjuvant setting. Clin Canc Res 13:6386-6395, 2007
Parameter: Tumor specific IFN-γ ELISPOT Response Setting: Adjuvant Autologous Tumor Lysate Vaccine - Colon Cancer
Barth RJ Jr, Fisher DA, Wallace PK, et al.: A randomized trial of ex vivo CD40L activation of a dendritic cell vaccine in colorectal cancer patients: tumor-specific immune responses are associated with improved survival. Clin Cancer Res 16:5548-56, 2010
Parameter: Delayed Type IV Hypersensitivity
Setting: Dendritic Cell Vaccine - Stage III-IV Melanoma Patients
López MN, Pereda C, Segal G, et al:
Prolonged survival of dendritic cell-vaccinated melanoma patients correlates with tumor-specific delayed type IV hypersensitivity response and reduction of tumor growth factor beta-expressing T cells. J Clin Oncol 27:945-52, 2009

**Parameter: Delayed Type IV Hypersensitivity**

**Setting: Adjuvant Autologous Tumor Cell Vaccination - Stage III-IV Melanoma Patients** Baars A, Claessen AM, van den Eertwegh AJ et al.: Skin tests predict survival after autologous tumor cell vaccination in metastatic melanoma: experience in 81 patients. Ann Oncol 11:965-70, 2000

**Parameter: Delayed Type IV Hypersensitivity**

**Setting: Allogeneic GM-CSF - Stage I-III Pancreatic Cancer** Jaffee EM, Hruban RH, Biedrzycki B, et al.: Novel allogeneic granulocyte-macrophage colony-stimulating factor-secreting tumor vaccine for pancreatic cancer: a phase I trial of safety and immune activation. J Clin Oncol 19: 45-56, 2000

**Parameter: Delayed Type IV Hypersensitivity**

**Setting: Dendritic Cell Vaccination - Stage IV Melanoma** de Vries IJ, Bernsen MR, Lesterhuis WJ, et al: Immunomonitoring tumor-specific T cells in delayed-type hypersensitivity skin biopsies after dendritic cell vaccination correlates with clinical outcome. J Clin Oncol 23:5779-87, 2005

### 3. Gene Expression Profiling in Cancer Immunotherapy

**Examples**

Gajewski TF, Fuertes M, Spaapen R et al.: Molecular profiling to identify relevant immune resistance mechanisms in the tumor microenvironment. Curr Opin Immunol 23:286-92, 2011

Bedognetti D, Wang E, Sertoli MR, Marincola FM: Gene-expression profiling in vaccine therapy and immunotherapy for cancer. Expert Rev Vaccines 6:555-65, 2010

Worschech A, Chen NH, Yu YA et al.: Systemic treatment of xenografts with vaccinia virus GLV-1h68 reveals the immunologic facet of oncolytic therapy. BMC Genomics 10, 2009

Harlin H, Meng Y, Peterson AC et al.: Chemokine expression in melanoma metastases associated with CD8 (+) T-cell recruitment. Cancer Res 69:3077-3085, 2009

Wang E, Miller LD, Ohnmacht GA et al.: Prospective molecular profiling of melanoma metastases suggests classifiers of immune responsiveness. Cancer Res 62:3581-3586, 2002

Panelli MC, Stashower ME, Slade HB et al.: Sequential gene profiling of basal cell carcinomas treated with imiquimod in a placebo-controlled study defines the requirements for tissue rejection. Genome Biol 8:R8, 2007

Sullivan RJ, Hoshida Y, Brunet J et al.: A single center experience with high-dose (HD) IL-2 treatment for patients with advanced melanoma and pilot investigation of a novel gene expression signature as a predictor of response. J Clin Oncol 27:9003, 2009 (Meeting Abstract)

Gajewski TF, Zha Y, Thurner B et al.: Association of gene expression profile in metastatic melanoma and survival to a dendritic cell-based vaccine. J Clin Oncol 27:9002, 2009 (Meeting Abstract)

Louahed J, Gruselle O, Gaulis S et al.: Expression of defined genes identified by pretreatment tumor profiling: Association with clinical responses to the GSK MAGE-A3 immunotherapeutic in metastatic melanoma patients (EORTC 16032-18031). J Clin Oncol 26:9045, 2008 (Meeting Abstract)

Vansteenkiste JF, Zielinski, M, Dahabreh IJ et al.: Association of gene expression signature and clinical efficacy of MAGE-A3 antigen-specific cancer immunotherapeutic (ASCI) as adjuvant therapy in resected stage IB/II non-small cell lung cancer (NSCLC). J Clin Oncol 26:7501, 2008 (Meeting Abstract)

Mandruzzato S, Callegaro A, Turcatel G et al.: A gene expression signature associated with survival in metastatic melanoma. J Transl Med. 4:50, 2006

Panelli MC, Wang E, Phan G et al.: Gene-expression profiling of the response of peripheral blood mononuclear cells and melanoma metastases to systemic IL-2 administration. Genome Biol 3, 2002

### 4. Useful Reviews

Marincola FM: The trouble with translational medicine. J Intern Med. 2011 May 16. [Epub ahead of print]

Kirkwood JM, Butterfield LH, Tarhini AA, Zarour H, Kalinski P, Ferrone S: Immunotherapy of Cancer in 2011 CA: A Cancer Journal for Clinicians [in press]

Ascierto ML, De Giorgi V, Liu Q et al.: An immunologic portrait of cancer. Journal of Translational Medicine, 2011, (in press).

Gajewski TF, Fuertes M, Spaapen R et al.: Molecular profiling to identify relevant immune resistance mechanisms in the tumor microenvironment. Curr Opin Immunol 23:286-92, 2011

Disis ML: Immunologic biomarkers as correlates of clinical response to cancer immunotherapy. Cancer Immunol Immunother. 60:433-42, 2011

Szol M: Molecular markers of response to treatment for melanoma Cancer J 17:127-33, 2011

Bedognetti D, Wang E, Sertoli MR, Marincola FM. Gene-expression profiling in vaccine therapy and immunotherapy for cancer. Expert Rev Vaccines 6:555-65, 2010

Slota M, Lim JB, Dang Y, Disis ML: ELISpot for measuring human immune responses to vaccines. Expert Rev Vaccines 10:299-306, 2011

Gogas H, Eggermont AM, Hauschild et al: Biomarkers in melanoma. Ann Oncol. 20 Suppl 6:vi8-13, 2009
5. Bioinformatics for Biomarkers Discovery

Zhao Y, Simon R: Development and validation of predictive indices for a continuous outcome using gene expression profiles. Cancer Inform 9:105-114, 2010

Chaussabel D: Data management: it starts at the bench. Nat Immunol. 10:1225-7, 2009

Chaussabel D, Quinn C, Shen J, et al.: A modular analysis framework for blood genomics studies: Application to systemic lupus erythematosus. Immunity 29:150-164, 2008

Bredel M, Scholtens D, Harsh GR, et al.: Model of a cooperative genetic landscape in gliomas. Neuro-Oncology 11:606, 2009

Simon R: The use of genomics in clinical trial design. Clin Cancer Res 14:5984-5993, 2008

Simion R: Development and validation of biomarker classifiers for treatment selection. J Stat Plan Infer 138:308-320, 2008

Nucu S, Critchley-Thorne R, Lee P, et al.: Gene expression network analysis and applications to immunology. Bioinformatics 23:850-858, 2007

Dupuy A, Simon RM: Critical review of published microarray studies for cancer outcome and guidelines on statistical analysis and reporting. J Natl Cancer Inst 99:147-57, 2007

6. New Technologies for Biomarkers Discovery

Linnarsson S: Recent advances in DNA sequencing methods - general principles of sample preparation. Exp Cell Res 316:1339-1343, 2010

Metzker ML: Sequencing technologies - the next generation. Nat Rev Genet 11:31-46, 2010

McAecker HT, Nolan GP, Fathman CG: New technologies for autoimmune disease monitoring. Curr Opin Endocrinol Diabetes Obes 17:322-328, 2010

Ornatsky O, Bandura D, Baranov V, et al.: Highly multiparametric analysis by mass cytometry. J Immunol Method 361:1-20, 2010

Newell EW, Klein LO, Yu W, Davis MM: Simultaneous detection of many T-cell specificities using combinatorial tetramer staining. Nat Methods 6:497-9, 2009

Hadrup SR, Bakker AH, Shu Cj, et al.: Parallel detection of antigen-specific T-cell responses by multidimensional encoding of MHC multimers. Nat Methods 6:520-6, 2009

Lugli E, Roederer M, Cossarizza A: Data analysis in flow cytometry: the future just started. Cytometry A 77:705-713, 2010

Ryan BM, Robles AI, Harris CC: Genetic variation in microRNA networks: the implications for cancer research. Nat Rev Cancer 10:389-402, 2010

Collas P: The current state of chromatin immunoprecipitation. Mol Biotechnol 45:87-100, 2010

Espina V, Wulfkuhle J, Liotta LA: Application of laser microdissection and reverse-phase protein microarrays to the molecular profiling of cancer signal pathway networks in the tissue microenvironment. Clin Lab Med 29:1-13, 2009

Luchini A, Longo C, Espina V, et al.: Nanoparticle technology: Addressing the fundamental roadblocks to protein biomarker discovery. J Mater Chem 19:5071-5077, 2009

Park PJ: ChiP-seq: advantages and challenges of a maturing technology. Nat Rev Genet 10:669-680, 2009

Hanash SM, Pitteri SJ, Faca VM: Mining the plasma proteome for cancer biomarkers. Nature 452:571-579, 2008

Wang E, Marincola FM: Bottom up: a modular view of immunology. Immunity 2:9-11, 2008

Gulmann C, Sheehan KM, Kay EW, et al.: Array-based proteomics: mapping of protein circuitries for diagnostics, prognostics, and therapy guidance in cancer. J Pathol 208:595-606, 2006

DeAngelis JT, Farrington WJ, Tollefsbol TO: An overview of epigenetic assays. Mol Biotechnol 38:179-183, 2008

Gilad Y, Borevitz J: Using DNA microarrays to study natural variation. Curr Opin Genet Dev 16:553-558, 2006

Speer R, Wulfkuhle JD, Liotta LA, et al.: Reverse-phase protein microarrays for tissue-based analysis. Curr Opin Mol Ther 7:240-245, 2005

Perfetto SP, Chattopadhyay PK, Roederer M: Seven-colour flow cytometry: unravelling the immune system. Nat Rev Immunol 4:648-655, 2004

Hanash S: Disease proteomics. Nature 422:226-232, 2003

7. Standardization and Harmonization of Sample Collection and Use of Immunological Assays

A. Processing, Storage and Shipping of Blood Samples and Serum for Immunological Studies - Technical Considerations Examples

Disis ML, dela Rosa C, Goodell V, et al.: Maximizing the retention of antigen specific lymphocyte function after cryopreservation. J Immunol Methods 308:13-18, 2006
Bull M, Lee D, Stucky J, et al.: Defining blood processing parameters for optimal detection of cryopreserved antigen-specific responses for HIV vaccine trials. J Immunol Methods 322:57-69, 2007
Kierstead LS, Dubey S, Meyer B, et al.: Enhanced rates and magnitude of immune responses detected against an HIV vaccine: effect of using an optimized process for isolating PBMC. AIDS Res Human Retroviruses 23:86-92, 2007
Ruitenbergen JJ, Mulder CB, Maino VC, et al.: VACUTAINER CPT and Ficoll density gradient separation perform equivalently in maintaining the quality and function of PBMC from HIV seropositive blood samples. BMC Immunol 7:11, 2006
Tree TI, Roep BO, Peakman M.: Enhancing the sensitivity of assays to detect T cell reactivity: the effect of cell separation and cryopreservation media. Ann N Y Acad Sci 1037:26-32, 2004
Smith JG, Joseph HR, Green T, et al.: Establishing acceptance criteria for cell-mediated immunity assays using frozen peripheral blood mononuclear cells stored under optimal and suboptimal conditions. Clin Vaccine Immunol 14:527-37, 2007
McKenna KC, Beatty KM, Vicetti Miguel R, Bilonick RA: Delayed processing of blood increases the frequency of activated CD11b+ CD15+ granulocytes which inhibit T cell function. J Immunol Method 341:68-75, 2009
B. Cellular Immunotherapy: Characterization of Cellular Products
Examples
Jin P, Han TH, Ren J, Saunders S, et al.: Molecular signatures of maturing dendritic cells: implications for testing the quality of dendritic cell therapies. J Transl Med 8:4, 2010
Sheikh NA, Jones LA: CD54 is a surrogate marker of antigen presenting cell activation. Immunol Immunother 57:1381-1390, 2008
Higano CS, Schellhammer PF, Small EJ, et al.: Integrated data from 2 randomized, double-blind, placebo-controlled, phase 3 trials of active cellular immunotherapy with Sipuleucel-T in advanced prostate cancer. Cancer 115:3670-3679, 2009
Butterfield LH, Gooding W, Whiteside TL: Development of a potency assay for human dendritic cells: IL-12p70 production. J Immunother 31:89-100, 2008
Ayache S, Panelli M, Marincola FM, et al.: Effects of storage time and exogenous protease inhibitors on plasma protein levels. American Journal of Clinical Pathology 126:174-184, 2006
C. Assay Standardization and Harmonization
Examples
Clinical Laboratory Improvement Amendments (CLIA) Guideline: http://www.cms.hhs.gov/CLIA/
International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) - common platform of Europe, Japan and United States authorities: http://www.ich.org/products/guidelines.html
Attig S, Price L, Janetzki S, Kalos M, Pride M, McNeil L, Clay T, Yuan J, Ondrus K, Hoos A, Romero P, Britten CM, Assay Working Group CC. A critical assessment for the value of markers to gate-out undesired events in HLA-peptide multimer staining protocols. J Transl Med, 9:108, 2011
Maecker HT, Hassler J, Payne JK, et al.: Precision and linearity targets for validation of an IFNGamma ELISPOT, cytokine flow cytometry, and tetramer assay using CMV peptides. BMC Immunol 9:9, 2008
Nomura L, Maino VC, Maecker HT: Standardization and optimization of multiparameter intracellular cytokine staining. Cytometry A 73:984-991, 2008
Afonso G, Scotto M, Renand A, et al.: Critical parameters in blood processing for T-cell assays: validation on ELISPOT and tetramer platforms. J Immunol Methods 359:28-36, 2010
Britten CM, Gouttefangeas C, Welters M, et al.: Harmonization guidelines for HLA-peptide multimer assays derived from results of a large scale international proficiency panel of the Cancer Vaccine Consortium. Cancer Immunol Immunother 57:289-302, 2008
Britten CM, Janetzki S, Ben Porat L, et al.: Toward the harmonization of immune monitoring in clinical trials: quo vadis? Cancer Immunol Immunother 57:285-288, 2008
Mander A, Gouttefangeas C, Ottensmeier C, et al.: Serum is not required for ex vivo IFN-gamma ELISPOT: a collaborative study of different protocols from the European CIMT Immunoguiding Program. Cancer Immunol Immunother 59:619-627
Fahey JL, Aziz N, Spritzler J, et al.: Need for an external proficiency testing program for cytokines, chemokines, and plasma markers of immune activation. Clin Diagn Lab Immunol 7:540-548, 2000
Denny TN, Gelman R, Bergeron M, et al.: A North American multilaboratory study of CD4 counts using flow cytometric panLeukogating (PLG): a NIAID-DAIDS Immunology Quality Assessment Program Study. Cytometry B Clin Cytom 74 Suppl 1: S52-S64, 2008
Boaz MJ, Hayes P, Tarragona T, et al.: Concordant proficiency in measurement of T-cell immunity in human immunodeficiency virus vaccine clinical trials by
peripheral blood mononuclear cell and enzyme-linked immunospot assays in laboratories from three continents. Clin Vaccine Immunol 16:147-155, 2009

Smith SG, Joosten SA, Verscheure V, et al.: Identification of major factors influencing ELISpot-based monitoring of cellular responses to antigens from Mycobacterium tuberculosis. PLoS One 4:e7972, 2009

Hanekom WA, Dockrell HM, Ottenhoff TH, et al.: Immunological outcomes of new tuberculosis vaccine trials: WHO panel recommendations. PLoS Med 5:e145, 2008

Schloot NC, Meierhoff G, Karlsson Faresjö M, et al.: Comparison of cytokine ELISpot assay formats for the detection of islet antigen autoreactive T cells. Report of the third immunology of diabetes society T-cell workshop. J Autoimmun 21:365-76, 2003

Moodie Z, Price L, Gouttefangeas C, et al.: Response definition criteria for ELISPOT assays revisited. Cancer Immunol Immunother 59:1489-501, 2010

D. Assays for Determination of Antitumor Immune-Response in Clinical Trials

Examples

ELISPOT Quast S, Zhang W, Shive C, et al.: IL-2 absorption affects IFN-gamma and IL-5, but not IL-4 producing memory T cells in double color cytokine ELISPOT assays. Cell Immunol 237:28-36, 2005

Granzyme B ELISPOT Shafer-Weaver K, Rosenberg S, Strobl S, et al.: Application of the granzyme B ELISPOT assay for monitoring cancer vaccine trials. J Immunother 29:328-335, 2006

Modified ELISPOT Malyguine A, Strobl SL, Shafer-Weaver KA, et al.: A modified human ELISPOT assay to detect specific responses to primary tumor cell targets. J Trans Med 2:9, 2004

FACS-based Cytotoxicity Assay Kim GG, Donnenberg VS, Donnenberg AD, et al.: A novel multiparametric flow cytometry-based cytotoxicity assay simultaneously immunophenotypes effector cells: comparisons to a 4 h 51Cr-release assay. J Immunol Methods 325:51-66, 2007

Devevere E, Romero P, Mahnkne YD: LiveCount Assay: concomitant measurement of cytolytic activity and phenotypic characterisation of CD8(+) T-cells by flow cytometry. J Immunol Methods 311:31-46, 2006

Zaritskaya L, Shafer-Weaver KA, Gregory MK, et al.: Application of a flow cytometric cytotoxicity assay for monitoring cancer vaccine trials. J Immunother 32:186-194, 2009

Maecker HT, Dunn HS, Suni MA, et al.: Use of overlapping peptide mixtures as antigens for cytokine flow cytometry. J Immunol Methods 255:27-40, 2001

FACS/ELISPOT/TETRAMERS Whiteside TL, Zhao Y, Tsukishiro T, Elder EM, Gooding W, Baar J: Enzyme-linked immunospot, cytokine flow cytometry, and tetramers in the detection of T-cell responses to a dendritic cell-based multipeptide vaccine in patients with melanoma. Clin Cancer Res, 2003

8. Reporting Biomarkers Data in Publications Examples

REMARK Recommendations
(accepted by most major journal included those published by the American Society of Clinical Oncology and the American Association for Cancer Research)

McShane LM, Altman DG, Sauerbrei W, et al.: Reporting recommendations for tumor marker prognostic studies (REMARK). J Natl Canc Inst 97:1180-1184, 2005

MIBBI Project - Guidelines Promotion
http://www.mibbi.org

Taylor CF, Field D, Sansone SA, et al.: Promoting coherent minimum reporting guidelines for biological and biomedical investigations: the MIBBI project. Nat Biotechn 26:889-896, 2008

MIAME - Microarray Experiment
Brazma A, Hingamp P, Quackenbush J, et al.: Minimum information about a microarray experiment (MIAME)-toward standards for microarray data. Nat Genet 29:365-371, 2001

MIATA - T Cell Assays
http://www.miataproject.org

Janetzki S, Britten CM, Kalos M, et al.: “MIATA”-minimal information about T cell assays. Immunity 31:527-528, 2009

Britten CM, Janetzki S, van der Burg SH, et al: Minimal information about T cell assays: the process of reaching the community of T cell immunologists in cancer and beyond. Cancer Immunol Immunother 60:15-22, 2011

MIFlowCyt - Flow Cytometry
Lee JA, Spidlen J, Boyce K, et al.: MIFlowCyt: the minimum information about a Flow Cytometry Experiment. Cytometry A 73:926-930, 2008

Data File for Flow Cytometry
Spidlen J, Moore W, Parks D, et al.: Data file standard for flow cytometry, version FCS 3.1. Cytometry A 77:97-100, 2010

Part II. High Throughput and New Technologies for Biomarker Discovery: Arrays, Platforms, Tools for The Bench and Online Resources

1. Genomic Biomarkers Discovery
A. Single Nucleotide Polymorphisms (SNPs) Arrays

Examples

Name: Affymetrix Genome-Wide Human SNP Array 6.0

Comment: 1.8 million genetic markers, including more than 906,600 single nucleotide polymorphisms (SNPs)
and more than 946,000 probes for the detection of copy number variation.

**Website:** [http://www.affymetrix.com/browse/products.jsp?productId=131533&navMode=34000&navAction=jump&aid=productsNav#1_1](http://www.affymetrix.com/browse/products.jsp?productId=131533&navMode=34000&navAction=jump&aid=productsNav#1_1)

**Name:** Affymetrix DMET Plus Premier Pack  
**Comment:** Drug metabolism studies. Coverage of a wide range of genetic variations, including common and rare SNPs, insertions, deletions, tri-alleles, and copy number. 1,936 drug metabolism markers in 225 genes.

**Website:** [http://www.affymetrix.com/browse/products.jsp?productId=131412&navMode=34000&navAction=jump&aId=productsNav#1_1](http://www.affymetrix.com/browse/products.jsp?productId=131412&navMode=34000&navAction=jump&aId=productsNav#1_1)

**Name:** Illumina Omni Microarray  
**Comment:** Next generation genome-wide association studies. The Omni family of microarrays will soon allow researchers to assay up to 5 million markers per sample, including comprehensive coverage of both common and rare variants identified by 1000 Genomes Project. As novel SNP sets are released into the public database, researchers using Omni products will have exclusive access to supplemental arrays that build up to the full 5 million variants.

**Website:** [http://www.illumina.com/landing/gwas.html?scid=2011110PPC1&gclid=CJij6ffe26kCFQPC4AodcmxEZQ](http://www.illumina.com/landing/gwas.html?scid=2011110PPC1&gclid=CJij6ffe26kCFQPC4AodcmxEZQ)

**Name:** Fluidigm Dynamic Array for SNP Genotyping  
**Comment:** The Fluidigm Dynamic Arrays allow you to use your existing TaqMan® SNP Genotyping assays in a flexible and cost effective fashion. Each dynamic array allows you to setup up to 9,216 individual TaqMan reactions in a single experiment.

**Website:** [http://www.expressionanalysis.com/services/category/fluidigm_dna-focused_set_snp](http://www.expressionanalysis.com/services/category/fluidigm_dna-focused_set_snp)

**Name:** TaqMan® Pre-Designed SNP Genotyping Assays  
**Comment:** Includes over 4.5 million SNP assays, including 3.5 million HapMap, and ~70,000 coding SNP assays. This collection now includes ~160,000 validated assays with associated minor allele frequency data available.

**Website:** [https://products.appliedbiosystems.com/ab/en/US/adirect/ab?cmd=catNavigate2&catId=600769&tab=TechSpec](https://products.appliedbiosystems.com/ab/en/US/adirect/ab?cmd=catNavigate2&catId=600769&tab=TechSpec)

**B. Comparative Genomic Hybridization (CGH) Arrays**

**Examples**

**Name:** Agilent Human Genome CGH Microarrays  
**Comment:** High-resolution tool for genome-wide DNA copy number variation profiling. Comprehensive probe coverage is enhanced with emphasis on known genes, promoters, miRNAs, pseudoautosomal, and telomeric regions.

**Website:** [http://www.genomics.agilent.com/Collection-Subpage.aspx?PageType=Product&SubPageType=ProductDetail&PageID=1463](http://www.genomics.agilent.com/Collection-Subpage.aspx?PageType=Product&SubPageType=ProductDetail&PageID=1463)

**Name:** Nimblegen Cytogenetics (CGX) Arrays  
**Comment:** Genome-wide analysis of DNA copy number changes with a subset of probes focused in disease-associated regions.

**Website:** [http://www.nimblegen.com/products/cgh/human.html#cyto](http://www.nimblegen.com/products/cgh/human.html#cyto)

**C. Mitochondrial Genome Arrays**

**Example**

**Name:** Affymetrix GeneChip® Human Mitochondrial Resequencing Array 2.0  
**Comment:** Detection of germ line and heteroplasmic mutations by delivering the complete mitochondrial genome with minimal PCR in only 48 hours.

**Website:** [http://www.affymetrix.com/support/technical/byproduct.affx?product=humitoreseq](http://www.affymetrix.com/support/technical/byproduct.affx?product=humitoreseq)

2. Epigenomic Biomarkers Discovery

**A. Methylation Arrays**

**Examples**

**Name:** Agilent Human DNA Methylation Microarrays  
**Comment:** The array is specifically designed for analysis of methylated DNA derived from affinity-based isolation methods such as methylated DNA immunoprecipitation (MDIP).

**Website:** [http://www.genomics.agilent.com/Collection-Subpage.aspx?PageType=Product&SubPageType=ProductDetail&PageID=2157](http://www.genomics.agilent.com/Collection-Subpage.aspx?PageType=Product&SubPageType=ProductDetail&PageID=2157)

**Name:** Nimblegen 2.1 M Whole-Genome Tiling Set  
**Comment:** Whole-genome formats are available in two versions: a 10-array set at 100 bp probe interval or a 4-array set at > 200 bp probe interval.

**Website:** [http://www.nimblegen.com/products/methylation/whole_genome.html](http://www.nimblegen.com/products/methylation/whole_genome.html)

**Name:** Illumina 450 K Infinium Methylation Bead-Chip Kit  
**Comment:** This assay allow to interrogate > 450,000 methylation sites per sample at single-nucleotide resolution.

**Website:** [http://www.illumina.com/products/methylation_450_beadchip_kits.ilmn](http://www.illumina.com/products/methylation_450_beadchip_kits.ilmn)

**B. microRNA (miRNA) Arrays**

**Examples**

**Name:** Illumina MicroRNA Universal Array Matrix  
**Comment:** miRNA analysis

**Website:** [http://www.illumina.com/products/microRNA_universal_array_matrix.ilmn](http://www.illumina.com/products/microRNA_universal_array_matrix.ilmn)

**Name:** Affymetrix GeneChip miRNA Array  
**Comment:** miRNA analysis

**Website:** [http://www.affymetrix.com/store/browse/products.jsp?sessionid=7386716AB0BD679701B518044AD58F5?navMode=34000&productId=131473&navAction=jump&aid=productsNav](http://www.affymetrix.com/store/browse/products.jsp?sessionid=7386716AB0BD679701B518044AD58F5?navMode=34000&productId=131473&navAction=jump&aid=productsNav)

**Name:** Exiqon’s miRCURY LNA microRNA Array  
**Comment:** miRNA analysis
C. Chromatin Immunoprecipitation (ChIP) Arrays (ChIP on chip)

[ChIP-on-chip, also known as Location Analysis (LA), is a high throughput (genome-wide) identification and analysis of DNA fragments that are bound by specific proteins such as histones, transcriptional factors and polymerases]

Examples

Name: Nimblegen 2.1 M ChIP-Chip Array
Comment: ChIP-chip analysis
Website:http://www.nimblegen.com/products/chip/index.html

Name: Agilent SurePrint G3 Human Promoter Microarray
Comment: ChIP-chip analysis
Website:http://www.genomics.agilent.com/CollectionSubpage.aspx?PageType=Product&SubPageType=ProductDetail&PageID=1487

Name: Affymetrix GeneChip Tiling Arrays
Comment: ChIP-chip analysis
Website:http://www.affymetrix.com/estore/browse/level_three_category_and_children.jsp?parent=35808&expand=true&category=35818&fromAccordionMenu=true&subCategory=35818

3. Transcriptomic Biomarkers Discovery

A. Expression Arrays

Examples

Name: Affymetrix Gene Chip Human Exon 1.0 ST Array
Comment: Whole genome microarray. With approximately four probes per exon and roughly 40 probes per gene, the GeneChip Human Exon 1.0 ST Array enables two complementary levels of analysis—gene expression and alternative splicing
Website:http://www.affymetrix.com/estore/browse/products.jsp?navMode=34000&productId=131453&navAction=jump&ald=productsNav#1_1

Name: Agilent SurePrint G3 Human GE 8 × 60 K Kit
Comment: Whole genome microarray. The SurePrint G3 Human GE 8 × 60 K Microarrays and Human GE 4 × 44 K v2 Microarrays are based on updated transcriptome databases for mRNA targets, while the SurePrint G3 arrays also include probes for lincRNAs (long intergenic non-coding RNAs). With the combination of mRNA and lincRNAs, it is possible to perform two experiments on a single microarray, confidently predicting lincRNA function
Website:http://www.genomics.agilent.com/CollectionSubpage.aspx?PageType=Product&SubPageType=ProductDetail&PageID=1515

Name: Illumina HumanHT-12 v4 Expression BeadChip Kits

Comment: The HumanHT-12 v4 Expression BeadChip provides high throughput processing of 12 samples per BeadChip. Each array on the HumanHT-12 v4 Expression BeadChip targets more than 31,000 annotated genes with more than 47,000 probes
Website:http://www.illumina.com/products/humanht-12_expression_beadchip_kits_v4.ilmn

B. Quantitative Assays

Examples

Name: QuantiGene® Plex 2.0 Reagent System (Luminex Assay)
Comment: Quantitatively measure 3-36 RNA targets simultaneously
Website:http://www.panomics.com/index.php?id=product_6

Name: Procarta Transcription Factor Profiling Kits (Luminex Assay)
Comment: Quantitate the DNA binding activity of up to 44 different transcription factors (TFs) in a single well using nuclear extracts or whole cell lysates
Website:http://www.panomics.com/index.php?id=product_17

Name: TaqMan® Probe-Based Gene Expression Analysis
Comment: Quantitatively measure 1-384 RNA targets simultaneously
Website:http://www.appliedbiosystems.com/absite/us/en/home/applications-technologies/qpcr-real-time-pcr/taqman-probe-based-gene-expression-analysis.html

Name: Fluidigm Dynamic Array for Single Cell Gene Expression
Comment: The Fluidigm Dynamic Array enables you to test up to 96 individual cells against 96 genes in a single experiment. The dynamic array assembles the cDNA material from individual cells and reagents to create individual qPCR reactions
Website:http://www.fluidigm.com/docs/Application>Note_Dynamic_Array_for_Single-Cell_GE_Analysis.pdf

Name: Nanostring nCounter Analysis System for digital gene expression analysis
Comment: The nCounter Analysis System utilizes a novel digital technology that is based on direct multiplexed measurement of gene expression and offers high levels of precision and sensitivity (< 1 copy per cell). The technology uses molecular “barcodes” and single molecule imaging to detect and count hundreds of unique transcripts in a single reaction.
Website: http://www.nanostring.com/applications/technology/

4. Proteomic Biomarkers Discovery

A. Protein and Phosphoprotein Assays

Examples

Name: Nodality Bedognetti et al. Journal of Translational Medicine 2011, 9:155 http://www.translational-medicine.com/content/9/1/155
Comment: Single-cells network profiling (SCNP): advanced multiparametric quantitative flow cytometry to measure compound effects on multiple signaling cascades in a cell-type-specific manner

Website: http://www.nodalityinc.com/

Name: NanoPro Immunoassay

Comment: Characterization of proteins in extremely small and precious samples. Unlike traditional protein analysis techniques which require thousands to millions of cells, these assays require as few as 25 cells per assay.

Website: http://www.cellbiosciences.com/nanopro.html

Name: Invitrogen Immunoassays

Comment: Wide range of immunoassays using antibody pairs for single-analyte (ELISA kits) as well as multi-analyte (Lumibex assays) analysis or accurate quantitation of intracellular or extracellular proteins.

Website: http://www.invitrogen.com/site/us/en/home/Products-and-Services/Applications/Cell-and-Tissue-Analysis/Immunoassays.html

Name: Procarta Cytokine Profiling Assays (Luminex Assay)

Comment: Quantitatively measure 3-30 cytokine proteins simultaneously from a variety of matrices including cell culture supernatants, serum or plasma.

Website: http://www.panomics.com/index.php?id=products_luminexAssays

Name: SearchLight Multiplex Immunoassay Kits

Comment: As many as 16 proteins (4 x 4 array in each well) can be measured per well simultaneously with each 50 μl sample.

Website: http://www.aushon.com/Products-and-Services.php

Name: MSD Multiplex Cytokines and Chemokines

Comment: 96-well; multiplex cytokine/chemokine kits for up to ten (10) analytes per well. 384-well: Order multiplex cytokine/chemokine kits for up to four (4) analytes per well.

Website: http://www.illumina.com/products/veracode_carboxyl_bead_sets.ilmn

Name: Procarta SH2 Domain Plex Profiling Kits (Luminex Assay)

Comment: Profile phosphotyrosine protein interactions against 30 SH2 binding in a single well using treated and untreated cell lysates. Protein-Protein interaction.

Website: http://www.panomics.com/downloads/13_A_SH2UM_2_V1.pdf

Name: Proto-Array

Comment: Advanced, high-content, functional protein microarray enables to scan thousands of proteins (> 9000) in as little as one day. Highly sensitive results for protein-protein interaction, kinase substrate identification, and serum profiling studies.

Website: http://www.invitrogen.com/protoarray

Name: Metal Nanoparticle Probes and Dynamic Light Scattering

Comment: This assay is based on the use of gold nanoparticle probes combined with dynamic light scattering (DLS) technique, named nanoDLSAY, a highly sensitive, fast and convenient one-step homogeneous immunoassay for monitoring and detecting biotargets, including cancer biomarkers.

Website: http://tt.research.ucf.edu/LinkClick.aspx?fileticket=6p5A2nGSYzA%3d&tabid=119

B. Multicolor Cytometric Systems

Examples

Name: BD LSRFortessa™ Cell Analyzer

Comment: Up to 4 lasers to detect up to 18 colors simultaneously.

Website: http://www.bdbiosciences.com/instruments/lsr/index.jsp

Name: The MACSQuant® Analyzer

Comment: Three lasers, up to 8 colors, compact benchtop flow cytometer that is small in size; MACSQuant® Analyzer allows researchers to perform sensitive rare cell analysis using magnetic separation.

Website: http://www.miltenyi-biotec.com/downloads/6760/6764/18602/MQ_brochure.pdf

Name: CyAn ADP Analyzer

Comment: Up to 11 standard parameters and 9 colors.

Website: http://www.coulterflow.com/bciflow/instrumentsus.php

Name: Partec CyFlow® ML

Comment: 3-laser configuration to detect up to 16 colors.

Website: http://www.partec.com/cms/front_content.php?idcat=13

Name: Accuri C6
Comment: Standard 2-laser configuration, 4-color system

Website: http://www.accuricytometers.com/products/

5. Next Generation Sequencing: Whole Genomic and Transcriptomic Sequencing Systems

Next generation sequencing, possible applications: Whole Genome and Transcriptome Sequencing-Based analysis, Gene Regulation Analysis, SNP Discovery and Structural Variation Analysis, Cytogenetic Analysis, DNA-Protein Interaction Analysis (ChIP-Seq), Sequencing-Based Methylation Analysis, Small RNA Discovery and Analysis

Examples
- Name: Illumina - several systems, examples: HiSeq 2000 (Sequencing); HiScanSQ (Sequencing + Arrays) and MiSeq
  Comment: Next generation sequencing
  Website: http://www.illumina.com/systems.ilmn
- Name: Roche - several systems, examples: Genome Sequencer FLX System and GS Junior System (454 Sequencing)
  Comment: Next generation sequencing
  Website: http://www.454.com/
- Name: Applied Biosystems - several systems, examples: Solid 4 System and Solid PI System (Solid System)
  Comment: Next generation sequencing
  Website: http://www.appliedbiosystems.com/absite/us/en/home/applications-technologies/solid-next-generation-sequencing.html
- Name: Ion Torrent PGM
  Comment: Next generation sequencing: semiconductor technology allows runs in about 2 hours.
  Website: http://www.iontorrent.com/products-ion-pgm/
- Name: PacBio RS
  Comment: Third generation sequencing: Long read-lengths, single molecule sequencing
  Website: http://www.pacificbiosciences.com/products

6. Software and Tools for Data Analysis

A. Microarrays/Sequencing Data Analysis

Examples:
- Name: BRB - ArrayTools
  Comment: Microarray/array CGH analysis. BRB-ArrayTools Development Team, NCI, NIH. The program can be used for non-commercial purposes free-of-charge
  Website: http://linus.nci.nih.gov/pilot/index.htm
  License needed: No
- Name: Partek
  Comment: Next generation sequencing technologies, including gene expression and DGE, RNA-seq and alternative splicing, copy number and association, ChIP-chip, ChIP-seq, microRNA and SNP association study
  Website: http://www.partek.com/
  License needed: Yes
- Name: Nexus Copy Number
  Comment: aCGH and SNP copy number analysis
  Website: http://www.biodiscovery.com/index/nexus
  License needed: Yes
- Name: Nexus Expression
  Comment: Microarray gene expression analysis
  Website: http://www.biodiscovery.com/index/nexus-expression
  License needed: Yes
- Name: mAdb (aka Mad Bee)
  Comment: Microarray gene expression analysis
  Website: http://madb.nci.nih.gov/
  License needed: No
- Name: Bioconductor
  Comment: Tools for the analysis and comprehension of high-throughput genomic data. Bioconductor uses the R statistical programming language
  Website: http://www.bioconductor.org/
  License needed: No
- Name: MATLAB 7.11
  Comment: MATLAB is a high-level technical computing language and interactive environment for algorithm development, data visualization, data analysis, and numeric computation
  Website: http://www.mathworks.com/products/matlab/
  License needed: Yes
- Name: GeneSifter® Analysis
  Comment: Software microarray and next generation sequencing analysis
  Website: http://www.geospiza.com/Contact/genesifter-trial_ng.shtml
  License needed: Yes
- Name: ADaCGH
  Comment: Web tool for the analysis of aCGH data sets
  Website: http://adacgh.bioinfo.cnio.es/
  License needed: No
- Name: ArrayStar
  Comment: Gene expression analysis software package that includes visualization tools to help analyze microarray data, including Venn diagrams, a scatter plot, heat maps and line graphs for clustering, and a gene ontology tree
  Website: http://www.dnastar.com/t-products-arraystar.aspx
  License needed: Yes
- Name: GeneSpring GX
  Comment: Statistical tools for fast visualization and analysis of expression and genomic structural variation data
  Website: http://www.dnastar.com/t-products-arraystar.aspx
  License needed: Yes
B. Next Generation Sequencing Data Analysis

Blog

Name: SEQanswers
Comment: SEQanswers is a blog founded to be an information resource and user-driven community focused on all aspects of next-generation genomics. A reasonably thorough table of next-gen-seq software available in the commercial and public domain is provided.
Website: http://seqanswers.com/forums/shoutthread.php?t=43

Note:
Examples

Name: Cufflinks
Comment: Cufflinks assembles transcripts, estimates their abundances, and tests for differential expression and regulation in RNA-Seq samples. It accepts aligned RNA-Seq reads and assembles the alignments into a parsimonious set of transcripts, free of charge.
Website: http://cufflinks.cbcb.umd.edu/
License needed: No

Name: Bowtie
Comment: Bowtie is an ultrafast, memory-efficient short read aligner. It aligns short DNA sequences (reads) to the human genome at a rate of over 25 million 35-bp reads per hour. Bowtie indexes the genome with a Burrows-Wheeler index to keep its memory footprint small: typically about 2.2 GB for the human genome (2.9 GB for paired-end).
Website: http://bowtie-bio.sourceforge.net/index.shtml
License needed: No

Name: TopHat
Comment: TopHat is a program that aligns RNA-Seq reads to a genome in order to identify exon-exon splice junctions. It is built on the ultrafast short read mapping program Bowtie. TopHat runs on Linux and OS X.
Website: http://tophat.cbcb.umd.edu/
License needed: No

Name: Oases
Comment: Oases is a de novo transcriptome assembler designed to produce transcripts from short read sequencing technologies, such as Illumina, SOLiD, or 454 in the absence of any genomic assembly.
Website: http://www.ebi.ac.uk/~zerbino/oases/
License needed: No

Name: Genomatix Genome Analyzer (GGA) and Genomatix Software Suite (GSS)
Comment: GGA comprehensive second-level analysis of Next Generation Sequencing (NGS) data from ChIP-Seq, RNA-Seq or genotyping experiments. GSS conducts a scientific analysis of genomic data in gene regulation, networks, pathways and genome annotation visualization.
Website: http://www.genomatix.de/en/index.html
License needed: yes

Name: ALLPATHS-LG
Comment: genome assembly algorithms recommended by the Broad Institute
Website: http://www.broadinstitute.org/science/programs/genome-biology/computational-rd/computational-research-and-development
License needed: no

C. Multicolor Cytometric Data-Analysis

Examples

Name: FlowJo
Comment: FlowJo is designed around the structure of flow data and the researcher’s experiments. Through FlowJo’s patent-pending Groups structure, for example, gates can be applied to many samples as easily as one.
Website: http://www.treestar.com
License needed: Yes

Name: WinList/FCOM
Comment: Load FCS files from instruments and do FACS data analysis with a full set of region tools and gates. The algorithms allow for rapid generation of registers with frequencies/numbers of all possible supheno-type combinations. Can be used to input data for cluster analysis and heat maps, allowing rapid visualization of numerous complex data sets.
Website: http://www.vsh.com/
License needed: Yes

Name: FCSPress
Comment: FCSPress is an easy-to-use Macintosh program that produces presentation quality graphics and generates statistics from flow-cytometric data.
Website: http://www.fcspress.com/
License needed: Yes
Name: FCS Express
Comment: FCS Express is designed to bring the power sophisticated analysis protocols to users in an intuitive, easy to grasp manner.
Website: http://www.denovosoftware.com/
License needed: Yes
Name: GemStone
Comment: GemStone is software for analysis of high-dimensional, flow cytometry data. Based on patented Probability State Modeling technology, GemStone eliminates some problems that have faced flow cytometry. Subjective gating and associated errors are eliminated. Population overlaps in multidimensional data are accounted for. Multiple samples may be combined into one coherent analysis.
Website: http://www.vsh.com/
License needed: Yes
Name: SPICE
Comment: SPICE is a data mining software application that analyzes large FLOWJO data sets from polychromatic flow cytometry and organizes the normalized data graphically. SPICE enables users to discover potential correlations in their experimental data within complex data sets.
Website: http://exon.niaid.nih.gov/spice/
License needed: Yes

7. Software and Tools for Function and Pathway Analysis
Examples
Name: Ingenuity Pathway Analysis (IPA)
Comment: User friendly software that allows analysis of biological and chemical systems.
Website: http://www.ingenuity.com/
License needed: Yes
Name: GeneGo MetaCore
Comment: User friendly software that allows analysis of biological and chemical systems.
Website: http://www.genego.com/about.php
License needed: Yes
Name: Ariadne Pathway Studio
Comment: Analysis of biological system with an interactive software interface and the computational approach to generating database content from the literature.
Website: http://www.ariadnegenomics.com/
License needed: Yes
Name: DAVID
Comment: Analysis of biological system.
Website: http://david.abcc.ncifcrf.gov/content.jsp?file=-functional_annotation.html#intro
License needed: No
Name: KEGG Pathway
Comment: Collection of manually drawn pathway maps representing knowledge on the molecular interaction and reaction networks, free of charge.
Website: http://www.genome.jp/kegg/pathway.html
License needed: No
Name: BioCarta pathway
Comment: BioCarta pathway provides displays of gene interactions within pathways for human cellular processes, such as apoptosis and signal transduction.
Website: http://cgap.nci.nih.gov/Pathways/BioCarta_Pathways
License needed: No
Name: Interactive Genomics Viewer
Comment: The Integrative Genomics Viewer (IGV) is a high-performance visualization tool for interactive exploration of large, integrated datasets. It supports a wide variety of data types including sequence alignments, microarrays, and genomic annotations.
Website: http://www.broadinstitute.org/igv/home
License needed: No
Name: GSEA
Comment: Gene Set Enrichment Analysis (GSEA) is a computational method that determines whether an a priori defined set of genes shows statistically significant, concordant differences between two biological states (e.g., phenotypes).
Website: http://www.broadinstitute.org/gsea/
License needed: No
Name: GOMiner
Comment: A tool for biological interpretation of ‘omic’ data - including data from gene expression microarrays. Omic experiments often generate lists of dozens or hundreds of genes that differ in expression between samples.
Website: http://discover.nci.nih.gov/gominer/index.jsp
License needed: No
Name: MatchMiner
Comment: Set of tools that enables the user to translate between disparate ids for the same gene. It uses data from the UCSC, LocusLink, Unigene, OMIM, Affymetrix and Jackson data sources to determine how different ids relate. Supported id types include, gene symbols and names, IMAGE and FISH clones, GenBank accession numbers and UniGene cluster ids.
Website: http://discover.nci.nih.gov/matchminer/index.jsp
License needed: No
Name: PANTHER Classification System
Comment: Panther is a resource that classifies genes by their functions, using published scientific experimental data.
evidence and evolutionary relationships to predict function even in the absence of direct experimental evidence. Proteins are also classified

**Website:** [http://www.pantherdb.org/](http://www.pantherdb.org/)

**License needed:** Yes

### 8. siRNA Libraries

**Examples**

- **Name:** Ambion siRNA Libraries
  **Comment:** siRNA Libraries  
  **Website:** [http://www.ambion.com/techlib/116/11.html](http://www.ambion.com/techlib/116/11.html)

- **Name:** Thermo Scientific siRNA Libraries  
  **Comment:** siRNA Libraries  
  **Website:** [http://www.dharmacon.com/catalog/catalogtemplate.aspx?id=1435&imageid=1882](http://www.dharmacon.com/catalog/catalogtemplate.aspx?id=1435&imageid=1882)

- **Name:** siRNA Libraries  
  **Website:** [http://genome.duke.edu/cores/rnaI/libraries/qiagen/](http://genome.duke.edu/cores/rnaI/libraries/qiagen/)

### 9. Public Databases

**Name:** NCBI Databases  
**Comment:** Gene/Protein/SNP/Nucleotide and several other databases  
**Website:** [http://www.ncbi.nlm.nih.gov/gquery/](http://www.ncbi.nlm.nih.gov/gquery/)

**Name:** Gene Expression Omnibus (GEO)  
**Comment:** Public functional genomics data repository supporting MIAME-compliant (Minimum information about a microarray experiment) data submissions. Array- and sequence-based data are accepted. Tools are provided to help users query and download experiments and curated gene expression profiles  
**Website:** [http://www.ncbi.nlm.nih.gov/geo/](http://www.ncbi.nlm.nih.gov/geo/)

**Name:** Catalogue Of Somatic Mutations In Cancer (COSMIC)  
**Comment:** COSMIC is designed to store and display somatic mutation information and related details and contains information related to human cancers  
**Website:** [http://www.sanger.ac.uk/genetics/CGP/cosmic/](http://www.sanger.ac.uk/genetics/CGP/cosmic/)

**Name:** The Cancer Genome Atlas (TCGA)  
**Comment:** The Cancer Genome Atlas (TCGA) Data Portal provides a platform for researchers to search, download, and analyze data sets generated by TCGA. Launched in 2006 as a partnership between the National Cancer Institute and the National Human Genome Research Institute, both NIH components, The Cancer Genome Atlas (TCGA) has developed a comprehensive strategy for comparing the genome of cancer cells to the genome of normal cells from the same patient  
**Website:** [http://cancergenome.nih.gov/](http://cancergenome.nih.gov/)

**Name:** The Human Protein Atlas  
**Comment:** The Human Protein Atlas portal is a publicly available database with millions of high-resolution images showing the spatial distribution of proteins in 46 different normal human tissues and 20 different cancer types, as well as 47 different human cell lines. The data is released together with application-specific validation performed for each antibody. The database was developed in a gene-centric manner with the inclusion of all human genes predicted from genome efforts  
**Website:** [http://www.proteinatlas.org](http://www.proteinatlas.org)

**Name:** DIP (Database of Interacting Proteins)  
**Comment:** The DIP database catalogs experimentally determined interactions between proteins. It combines information from a variety of sources to create a single, consistent set of protein-protein interactions  
**Website:** [http://dip.doe-mbi.ucla.edu/dip/Main.cgi](http://dip.doe-mbi.ucla.edu/dip/Main.cgi)

**Name:** MINT (Molecular INTeraction Database)  
**Comment:** MINT focuses on experimentally verified protein-protein interactions mined from the scientific literature by expert curators. The curated data can be analyzed in the context of the high throughput data and viewed graphically with the ‘MINT Viewer’  
**Website:** [http://mint.bio.uniroma2.it/mint/Welcome.do](http://mint.bio.uniroma2.it/mint/Welcome.do)

**Name:** Human Protein Reference Database  
**Comment:** The Human Protein Reference Database represents a centralized platform to visually depict and integrate information pertaining to domain architecture, post-translational modifications, interaction networks and disease association for each protein in the human proteome  
**Website:** [http://www.hprd.org](http://www.hprd.org)

**Name:** Cancer Genome Anatomy Project (CGAP)  
**Comment:** The NCI’s Cancer Genome Anatomy Project sought to determine the gene expression profiles of normal, precancer, and cancer cells, leading eventually to improved detection, diagnosis, and treatment for the patient. Resources generated by the CGAP initiative are available to the broad cancer community  
**Website:** [http://cgap.nci.nih.gov/cgap.html](http://cgap.nci.nih.gov/cgap.html)

**Name:** caBIG  
**Comment:** caBIG stands for the cancer Biomedical Informatics Grid. caBIG is an information network enabling members of the cancer community - researchers, physicians, and patients - to share data and knowledge  
**Website:** [https://cabig.nci.nih.gov/](https://cabig.nci.nih.gov/)

**Name:** mirbase  
**Comment:** Searchable database of published miRNA sequences and annotation  
**Website:** [http://www.mirbase.org](http://www.mirbase.org)

**Name:** deepBase  
**Comment:** deepBase is a database for annotating and discovering small and long ncRNAs (microRNAs,
siRNAs and piRNAs) from high-throughput deep sequencing data

**Website:** http://deepbase.sysu.edu.cn/miRDeep.php

**Name:** Gene Ontology Annotation (UniProtKB-GOA) Database

**Comment:** The UniProtKB-GOA project aims to provide high-quality Gene Ontology (GO) annotations to proteins in the UniProt Knowledgebase (UniProtKB) and International Protein Index (IPI) and is a central dataset for other major multi-species databases; such as Ensembl and NCBI

**Website:** http://www.ebi.ac.uk/GOA/

**Name:** ProtFun

**Comment:** The ProtFun 2.2 server produces *ab initio* predictions of protein function from sequence

**Website:** http://www.cbs.dtu.dk/services/ProtFun/

**Name:** TRANSFAC 7.0 Public 2005

**Comment:** Data on transcription factors, their experimentally-proven binding sites, and regulated genes. Its broad compilation of binding sites allows the derivation of positional weight matrices

**Website:** http://www.gene-regulation.com/pub/databases.html

**Name:** OptiTope

**Comment:** OptiTope aims at assisting immunologists in designing epitope-based vaccines. It is an easy-to-use tool to determine a provably optimal set of epitopes with respect to overall immunogenicity in a specific individual or a target population, free of charge

**Website:** http://www.epitoolkit.org/optitope

**Name:** Cancer Central Clinical Database (C3D)

**Comment:** Cancer Central Clinical Database (C3D) is a clinical trials data management system. C3D collects clinical trial data using standard case report forms (CRFs) based on common data elements (CDEs)

**Website:** https://cabinb.nci.nih.gov/tools/c3d

**Name:** UCSC Genome Browser

**Comment:** Provides a large database of publicly available sequence and annotation data along with an integrated tool set for examining and comparing the genomes of organisms, aligning sequence to genomes, and displaying and sharing users' own annotation data

**Website:** http://genome.ucsc.edu/

**Name:** Next Bio

**Comment:** Exhaustive collection of public microarray data. NextBio's platform combines powerful tools with unique correlated content. With NextBio you can search tens of thousands of studies containing billions of data points spanning different experimental platforms, organisms and data types

**Website:** http://www.nextbio.com/b/corp/faq.nb

**Name:** SYFPEITHI

**Comment:** SYFPEITHI is a database comprising more than 7,000 peptide sequences known to bind class I and class II MHC molecules. The entries are compiled from published reports only

**Website:** http://www.syfpeithi.de/

**Name:** Melanoma Molecular Map Project

**Comment:** Systematic collection of the scientific knowledge regarding the development of targeted therapy for melanoma

**Website:** http://www.mmmp.org

10. Tools for the Bench and Other Useful Websites

A. Primer Design Software

**Examples**

**Name:** Primer3

**Comment:** Primer3 is a free online tool to design and analyze primers for PCR and real time PCR experiments. Primer3 can also select single primers for sequencing reactions and can design oligonucleotide hybridization probes

**Website:** http://frodo.wi.mit.edu/primer3

**Name:** Oligo Analyzer 3.0

**Comment:** Software developed by IDT (Integrated DNA Technologies) that analyzes physical properties of a specific oligo sequence. The results show a complementary sequence, oligo length, GC content, melting temperature, extinction coefficient, molecular weight, μg/OD, and nmoles/OD.

**Website:** http://www.idtdna.com/analyzer/applications/oligoanalyzer

**Name:** MethPrimer

**Comment:** MethPrimer is a program for designing bisulfite-conversion-based methylation PCR Primers. It can design primers for Methylation-Specific PCR (MSP), Bisulfite-Sequencing PCR (BSP) and Bisulfite-Restriction PCR

**Website:** http://www.urogene.org/methprimer/index1.html

B. Transcription Factors Binding Sites Prediction Software

**Examples**

**Name:** TFSEARCH

**Comment:** TFSEARCH predicts transcription factors binding sites from a given sequence. It does simple correlation calculation with binding site profile matrices

**Website:** http://www.cbrc.jp/research/db/TFSEARCH.html

C. Design of Antisense Oligonucleotides, Nucleic Acid Probes, siRNA Software

**Examples**

**Name:** Sfold
Comment: Sfold predicts RNA duplex thermodynamics for rational siRNA design. It supports target accessibility prediction and rational design of antisense oligonucleotides (ASO) and nucleic acid probes. It can design an ASO for a gene of interest based on the mRNA sequence.

Website: http://sfold.wadsworth.org/cgi-bin/soligo.pl

D. miRNA Prediction

Examples

Name: TargetScan
Comment: Prediction of biological targets of miRNAs
Website: http://www.targetscan.org/
License needed: No
Name: microRNA.org
Comment: A resource for predicted microRNA targets and expression, free of charge
Website: http://www.microrna.org/microrna/home.do
License needed: No
Name: DIANA Lab
Comment: miRNA computational predictive models.
Experimental supported databases
Website: http://diana.cslab.ece.ntua.gr/?sec=home
License needed: No
Name: R2A2
Comment: This software first finds putative microRNA binding sites in the sequence of interest, then identifies the targeting microRNA
Website: http://cbcsrv.watson.ibm.com/rna22.html
Name: PicTar
Comment: PicTar provides combinatorial microRNA target predictions
Website: http://pictar.mdc-berlin.de
Name: miRanda
Comment: miRanda is an algorithm for finding genomic targets for microRNAs
Website: http://www.microrna.org/microrna/home.do

E. Alternative Splicing Analysis

Example

Name: SpliceCenter
Comment: The SpliceCenter applications are user-friendly tools that provide information on the target location of probesets, primers, or siRNAs within the known splice variants of a gene
Website: http://www.tigerteamconsulting.com/SpliceCenter/
License needed: No

F. Linkage Disequilibrium Analysis

Examples

Name: PhAT
Comment: It analyzes SNP data, showing pairwise Linkage Disequilibrium of various types (r^2, r, D' and abs(D)) and producing graphical matrices of obtained results
Website: http://pharmgat.org/Tools/pbtoldplotform

G. Analysis Support, Laboratory Optimization and Other Useful Websites

Examples

Name: Immuneering
Comment: Computer Model. Development of computer models that aim to predict the response to biological therapies in cancer patients
Website: http://www.immuneering.com/
Name: Cellumen CellCiphr Patient Sample Profiling
Comment: To use the cellular systems biology approach to improve patient stratification for clinical trial enrollments. Cellumen is collaborating with the Mayo Clinic and Foundation to create panels of cellular biomarkers using multiplexed fluorescence to apply to patient cells and tissues, starting with breast cancer
Website: http://www.cellumen.com/solutions/patient.php
Name: Biotracker
Comment: Lab Management. Biotracker is a specialty Lab Information Management Solution (LIMS) for enhancing productivity and effectiveness in life sciences research laboratories
Website: http://www.ocinumbio.com/lims2/products/
Name: Gene's Logic Expression Array Analysis
Comment: Array analysis support; team dedicated to statistical and bioinformatic analyses of microarray data, ranging from basic quality control and differential gene expression analysis
Website: http://www.genelogic.com/services/bioinformatic-analysis
Name: Microsoft Word Add-In for the GenePattern Reproducible Research Document (GRRD)
Comment: To facilitate publishing reproducible results, GenePattern automatically captures the history of any computational work being done, allowing scientists to easily generate pipelines to reproduce computational methods
Website: http://www.broadinstitute.org/cancer/software/genepattern/grrd/AddIn.html
License needed: No
Name: IIIBio Archive
Comment: Archive of biology data and software, established in 1989 to promote public access to freely available information, primarily in the field of molecular biology and bioinformatics
Website: http://iubio.bio.indiana.edu/
Name: Labome
Comment: Tools for searching antibodies, siRNA/shRNA, ELISA, cDNA clones, proteins/peptides, microRNA, and biochemicals from all suppliers
Website: http://www.labome.com/
License needed: No

H. Nanotechnology

Examples
I. Clinical Trials Registries

Example

Name: Clinical Trial Registries
Comment: The five clinical trials registries approved by the International Committee of Medical Journal Editors (ICMJE)
Website: http://ClinicalTrials.gov, http://www.actr.org.au, http://www.ISRCTN.org, http://www.umin.ac.jp/ctr/index.htm, http://www.trialregister.nl

Conclusion

Immune biomarkers are playing an increasingly important role in the successful development, clinical evaluation, and immune monitoring of cancer immunotherapies. The references, products and online resources in this Cancer Immunotherapy Biomarkers Resource Document were identified by the authors and the STIC/ISBtc Taskforce on Immunotherapy Biomarkers to support the discovery, evaluation and application of biomarkers for cancer immunotherapy. These selected references and links serve as a compass to point investigators to useful resources in this ever growing, and important field of cancer immunotherapy biomarkers. Emerging issues surrounding cancer immunotherapy biomarker discovery and clinical application will continue to be addressed in upcoming STIC Annual Meetings and Associated Programs [13].

Acknowledgements

The authors wish to acknowledge the members of the STIC/ISBtc Taskforce on Immunotherapy Biomarkers, Working Group 2 who reviewed these resources as part of the planning for the Symposium on Immuno-Oncology Biomarkers, 2010 and Beyond. This working group includes: Francesco Marincola, Peter P. Lee, Damien Chausabel, George Coukos, Bernard Fox, John Kirkwood, Leif Häkansson, Michele Maio, Antoni Ribas, Dolores Schendel, Barbara Selinger, Senthilvel Selvan, Wennu Song, Howard Steicher, Madgalena Thurn, Giorgio Trinchieri, Ena Wang, Xifeng Wu, Ben Zeskind, Yingdong Zhao. The authors also wish to acknowledge all colleagues who reviewed and commented on previous versions of this document, including: Pietro Blandini, Enrico Lugli, Stefania Santamaria, Tim Greten, Sylvia Janetzki, Janet Siebert, Wenji Zhang and Gabriele Zoppoli. Davide Bedognetti is a participant in the NIH Graduate Partnership Program and a graduate student at University of Geneva. Davide Bedognetti’s fellowship is supported by the Conquer Cancer Foundation of the American Society of Clinical Oncology (2011 Young Investigator Award).

Author details

1Society for Immunotherapy of Cancer, Milwaukee, WI, USA. 2Infectious Disease and Immunogenetics Section (IDIS), Department of Transfusion Medicine, Clinical Center and Trans-NIH Center for Human Immunology (CHI), National Institutes of Health, Bethesda, MD, USA. 3Department of Internal Medicine (DIMI), University of Genoa, and Department of Medical Oncology, National Cancer Research Institute of Genoa, Genoa, Italy. 4Tumor Vaccine Group, Division of Oncology, University of Washington, Seattle, WA, USA. 5Department of Medicine, University Medical Center of the Johannes Gutenberg-University, and Ribologib GmbH, Mainz, Germany. 6Department of Internal Medicine, University Medical Center of the Johannes Gutenberg-University, and Clinical Development, BioNTech AG, Mainz, Germany. 7University of Sassari, Department of Drug Sciences, Sassari, Italy. 8Division of Surgical, Molecular and Ultrastructural Pathology, Department of Oncology, University of Pisa and Pisa University Hospital, Pisa, Italy. 9Laboratory of Molecular and Tumor Immunology, Earle A. Chiles Research Institute, Robert W. Franz Cancer Center, Providence Portland Medical Center, Portland, OR, USA. 10Section of Hematology/Oncology, Department of Pathology and Department of Medicine, University of Chicago, Chicago, IL, USA. 11Departments of Medicine, Surgery and Immunology, University of Pittsburgh, Pittsburgh, PA, USA.

Authors’ contributions

DB and JB prepared the manuscript. EW, MLD, CMV, LGD, ST, BAF, TFG, FMM and LHB provided substantive editing and critical review. All authors read and approved the final manuscript.

Competing interests

DB, JB, EW, MLD, CMV, LGD, ST, TFG, LHB and FFM declare that they have no competing interests. BAF is co-founder of Ubivac, LLC and serves on the scientific advisory boards of Micromet, Inc. and MannKind Corporation.

Received: 9 August 2011 Accepted: 19 September 2011 Published: 19 September 2011

References

1. Symposium on Immuno-Oncology Biomarkers, 2010 and Beyond: Perspectives from the ISBtc Biomarker Task Force. [http://www.sitcancer.org/meetings/am10/biomarkers10/]
2. STIC/ISBtc-FDA-NCI Workshop on Prognostic and Predictive Immunologic Biomarkers in Cancer. [http://www.sitcancer.org/meetings/am09/workshop09/]
3. Immune Monitoring Workshop I. [http://www.sitcancer.org/meetings/am04/workshop.php]
4. Workshop on Cancer Biomarkers: Identifying Biomarkers and Surrogates of Tumors in Patients. [http://www.sitcancer.org/meetings/am03/biomarkers.php]
5. Immune Monitoring Workshop. [http://www.sitcancer.org/meetings/bethesda/immune_monitoring_workshop.php]
6. Butterfield LH, Palucka AK, Britten CM, Dhadapkar MV, Hakansson L, Janetzki S, Kawakami Y, Kleen TO, Lee PP, Maccaill C, Maeker HT, Maino VC, Maio M, Maly-Herort A, Masucci G, Pawelec G, Potter DM, Rivoltini L, Salazar LG, Schendel DJ, Slungluff CL Jr, Song W, Stromeck DF, Tahara H, Thurn T, Trinchieri G, van Der Burg SH, Whiteside TL, Wiggington JM, Marincola F, Khiev S, Fox BA, Diss ML: Recommendations from the ISBtc-
SITC/FDA/NCI Workshop on Immunotherapy Biomarkers. Clin Cancer Res 2011, 17:3064-3076.

7. Butterfield LH, Disis ML, Khleif SN, Balwit JM, Marincola FM. Immu
Oncology Biomarkers 2010 and Beyond: Perspectives from the iSBTc/SITC Biomarker Task Force. J Transl Med 2010, 8(1):130.

8. Butterfield LH, Disis ML, Fox BA, Lee PP, Khleif SN, Thrun M, Trinchieri G, Wang E, Wegginton J, Chauvabbel D, Coukos G, Dhodapkar M, Häkansson L, Janetzki S, Kleen TO, Kirkwood JM, Maccalli C, Maecker H, Maio M, Malyguine A, Marucci G, Palucka AK, Potter DM, Ribas A, Rivoltini L, Schendel D, Seliger B, Selvan S, Stingleff CL Jr, Stromeck DF, Streicher H, Wu X, Zeskind B, Zhao Y, Zocca MB, Zwerina H, Marincola FM. A systematic approach to biomarker discovery; Preamble to “the iSBTc-FDA taskforce on immunotherapy biomarkers”. J Transl Med 2008, 6:81.

9. Lotze MT, Wang E, Marincola FM, Hanna N, Bugelski PJ, Burns CA, Coukos G, Damle N, Godfrey TE, Howell WM, Panelli MC, Petriconi MA, Petricoin EF, Sauter G, Scheibenbogen C, Shivers SC, Taylor DL, Weinstein JN, Whiteside TL. Workshop on cancer biometrics: identifying biomarkers and surrogates of cancer in patients. J Immunother 2005, 28:79-119.

10. Keilholz U, Weber J, Finke J, Gabrilovich D, Kast WM, Disis N, Kirkwood JM, Scheibenbogen C, Schlom J, Maino VC, Lyerly HK, Lee PP, Storkus W, Marincola F, Worobec A, Atkins MB. Immunologic monitoring of cancer vaccine therapy: results of a Workshop sponsored by the Society of Biological Therapy. J Immunother 2002, 25:37-138.

11. Brazas MD, Yamada JT, Ouellette BFF. Providing web servers and training in Bioinformatics: 2010 update on the Bioinformatics Links Directory. Nucleic Acids Res 2010, 38(Web Server):W3-W6.

12. Bioinformatics Links Directory. [http://bioinformatics.ca/links_directory/journals/nar/2010].

13. SITC 2011 Annual Meeting and Associated Programs. [http://www.sitcancer.org/meetings/].

Cite this article as: Bedognetti et al. SITC/iSBTc Cancer Immunotherapy Biomarkers Resource Document: Online resources and useful tools - a compass in the land of biomarker discovery. Journal of Translational Medicine 2011 9:155.