The SomaScan® Assay: **Cancer/Oncology Research Publication Highlights**

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High-Multiplex Aptamer-Based Serum Proteomics to Identify Candidate Serum Biomarkers of Oral Squamous Cell Carcinoma.

Blatt et al., *Cancer,* 15(7), 2071; 2023.
doi.org/10.3390/cancers15072071

Summary Abstract: Robust serological biomarkers are needed for early detection, risk stratification and treatment surveillance of patients with **oral squamous cell carcinoma (OSCC). SomaScan Assay 1305-plex** was used to identify distinct proteomic changes in patients with OSCC pre- vs. post-resection and compared to healthy controls. Significantly differentially expressed **serum proteins** discriminated OSCC from healthy controls with 100% accuracy, and others were significantly altered between pre- and post-resection. Twelve OSCC-associated proteins reversed to healthy control levels after resection and pathway analyses revealed potential pathophysiological mechanisms, indicating SomaScan proteomics **utility for biomarker assay development and to guide personalized therapies.**

Highly Multiplexed Proteomic Assessment of Human Bone Marrow in Acute Myeloid Leukemia.

Çelik, H. et al., *Blood Adv.* 4, 367-379, 2020.
doi.10.1182/bloodadvances.2019001124

Summary Abstract: Despite substantial evidence indicating the critical role of tumor–host interactions in **AML** pathogenesis and resistance to chemotherapy, little is known about the complex bone marrow (BM) microenvironment in which these occur. **SomaScan Assay** proteomic profiling of the noncellular compartment of the BM microenvironment in AML patients vs age- and sex-matched healthy controls showed superiority to blood and BM RNA-sequencing strategies to determine the true proteomic composition. The AML **BM microenvironment** was associated with differential protein abundance and a highly connected cytokine-chemokine signaling network. Significantly elevated levels and functional experiments of **CCL23 (myeloid progenitor inhibitory factor-1)** in both AML and myelodysplastic syndrome patients support its role in the suppression of normal hematopoiesis. This unique paired dataset provides **innovative mechanistic insights into AML** and healthy aging and serves as a useful public resource.

Associations Between Circulating Proteins and Risk of Breast Cancer by Intrinsic Subtypes: a Mendelian Randomization Analysis.

Shu, X et al., *Br J Cancer Nov*; 127(8):1507-1514, 2022.
doi:10.1038/s41416-022-01923-2

Summary Abstract: The aetiologic role of circulating proteins in the development of breast cancer subtypes is not clear. In this study five subtypes of **breast cancer** were studied (***luminal A-like*** *(ER+ and/or PR+, HER2−, Grades 1 and 2),* ***luminal B/ Her2-negative-like*** *(ER+ and/or PR+, HER2−, grade 3),* ***luminal B-like*** *(ER + and/or PR+, HER2+),* ***HER2-enriched-like*** *(ER− and PR−, HER2+),* ***and triple-negative*** *(ER−, PR−, HER2−)*) to identify the **potential causal effects of circulating proteins within the Mendelian randomization (MR) framework.** The authors identified 98 unique proteins significantly associated with the risk of one or more breast cancer subtypes. Of those, 51 were specific to luminal A-like subtype, 14 to luminal B/ Her2-negative-like, 11 to triple negative, 3 to luminal B-like, and 2 to Her2-enriched-like breast cancer. Associations for three proteins (ICAM1, PLA2R1 and TXNDC12) showed different associations depending on cancer subtype (proteins ICAM1 (intracellular adhesion molecule 1), PLA2R 1 (Phospholipase A2 Receptor 1) and TXNDC12 (Thioredoxin Domain Containing 12).

Activity of Ibrutinib Plus R-CHOP in Diffuse Large B-cell lymphoma: Response, Pharmacodynamic, and Biomarker Analyses of a Phase 1b Study.

Schaffer et al., *Cancer Treatment and Research Communications*, Volume 25, 2020.
doi:10.1016/j.ctarc.2020.100235

Summary Abstract: Prognosis and therapeutic response differ among diffuse **large B-cell lymphoma** (DLBCL) subtypes and ~40% of patients with initial response to modern chemoimmunotherapy will relapse or develop refractory disease. Association between molecular biomarkers and clinical response may inform most effective treatment strategies. **SomaScan Assay** proteomic profiling in DLBCL patients treated with ibrutinib plus rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP): differentiated responder groups, identified proteins / pathways related to more aggressive disease not reliant on BTK-mediation leading to poorer response, identified significant biological variation in progressive disease (PD) vs non-PD, and contributed to **molecular understanding** broadly relevant to BTK-targeted **mechanism of action.**

Siglec-7 is a Predictive Biomarker for the Efficacy of Cancer Vaccination Against Metastatic Colorectal Cancer.

Yamada et. al. *Oncol Lett.* 2021 Jan;21(1):10.
doi: 10.3892/ol.2020.12271

Summary Abstract: Biomarkers of response would improve identification of **colorectal cancer** (CRC) patients for which durable cancer immunotherapy efficacy is more likely. Comprehensive proteomic analysis with the **SomaScan Assay using tumor tissue lysates** from patients enrolled in a phase II study of five human leukocyte antigen (HLA) A*24:02 restricted peptides identified sialic acid binding immunoglobulin type lectin (Siglec) 7 as a potential predictive biomarker. Findings were validated on tissue samples and quantitative Siglec 7 expression was higher in peptide-treated patients with lower overall survival (OS) and in intratumoral macrophages, indicating **potential utility as a novel predictive efficacy biomarker for immunotherapy in metastatic CRC.**

Novel Cytokine-Mediated Mechanism of Action Identified by Quantitative Seroproteomics in Multiple Myeloma Patients Treated with Tagraxofusp, A Novel CD123-Directed Targeted Therapy.

Ray et. al. *Blood Vol.* 138, Supplement 1, 23. 2021.
doi.10.1182/blood-2021-153458

Summary Abstract: Plasmacytoid dendritic cells (pDCs) express CD123/IL-3Rα and promote tumor growth and immunosuppression in multiple myeloma (MM). Tagraxofusp is a novel FDA-approved CD123-targeted therapy that can also trigger anti-MM activity by reducing the viability of immunologically defective and tumor-promoting pDCs and enhance activity of anti-MM agents. **Serum** proteomic profiling with the **SomaScan Assay** and correlation with cellular studies identified underlying **therapeutic mechanisms and validated target specificity** in a recent phase 1/2 clinical trial demonstrating preliminary safety and efficacy of tagraxofusp with pomalidomide/dexamethasone in relapsed/refractory MM.

CARD10 Cleavage by Malt1 Restricts Lung Carcinoma Growth In Vivo.

Israël et al, *Oncogenesis*, 2021.
doi:10.1038/s41389-021-00321-2

Summary Abstract: Dysregulated cellular processes, such as uncontrolled NF-κB activation in humans, are associated with cancer pathogenesis. CARD-CC complexes involving BCL10 and MALT1 are major cellular signaling hubs. They govern NF-κB activation through their scaffolding properties as well as MALT1 paracaspase function, which cleaves substrates involved in NF-κB regulation. In human lymphocytes, gain-of-function defects in this pathway lead to lymphoproliferative disorders. CARD10, the prototypical CARD-CC protein in non-hematopoietic cells, is over expressed in several cancers and has been associated with poor prognosis. However, regulation of CARD10 remains poorly understood. Here, we identified CARD10 as the first MALT1 substrate in non-hematopoietic cells and showed that CARD10 cleavage by MALT1 at R587 dampens its capacity to activate NF-κB. Preventing CARD10 cleavage in the lung tumor A549 cell line increased basal levels of IL-6 and extracellular matrix components in vitro, and led to increased tumor growth in a mouse xenograft model, suggesting that CARD10 cleavage by MALT1 might be a built-in mechanism controlling tumorigenicity. This study has shown the inhibition of CARD10 cleavage accelerates tumor growth in vivo, alters gene expression, and increases IL-6 protein.

Comprehensive Apatamer-Based Screen of 1317 Proteins Uncovers Improved Stool Protein Markers of Colorectal Cancer.

Li, H. et. al., *J. Gastroenterol*, July; 56(7):659-672, 2021.
doi: 10.1007/s00535-021-01795-y

Summary Abstract: Considering **early detection of colorectal cancer** is essential for successful treatment, it is important to identify biomarker signature using non-invasive samples such as stool. 3 separate cohorts of CRC and healthy controls (HC) of Caucasian and Indian descent were enrolled in the study using **SomaScan 1.3K** and compared differences in protein level between CRC and HC. Through validation by ELISA, single-cell RNA seq database, literature search, and confirmation across different ethnicity cohorts, the investigators discovered 4 stool protein biomarkers that performed better than the current screening test FOBT (which uses stool hemoglobin) in predicting CRC. A total of 92 proteins were significantly elevated in CRC samples as compared to HCs in the discovery cohort. Among Caucasians, the 5 most discriminatory proteins among the 16 selected proteins, ordered by their ability to distinguish CRC from adenoma and healthy controls, were MMP9, haptoglobin, myeloperoxidase, fibrinogen, and adiponectin. Except myeloperoxidase, the others were significantly associated with depth of tumor invasion. The 8 stool proteins with the highest AUC values were also discriminatory in a second cohort of Indian CRC patients. Several of the stool biomarkers elevated in CRC were also expressed within CRC tissue, based on the single-cell RNA-seq analysis. Stool MMP9, fibrinogen, myeloperoxidase, and haptoglobin emerged as promising CRC stool biomarkers, outperforming stool Hemoglobin. Longitudinal studies are warranted to assess the clinical utility of these novel biomarkers in early diagnosis of CRC.

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