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George Vasmatzis

Mayo Clinic, USA

Biomarker discovery facilitated by next generation sequencing

Radical improvement in cancer care will be accomplished by individualizing patient management via the integration of genomics and functional model systems. A process that uses comprehensive genomics to discover biomarkers will be presented and followed by a representative example. The hypothesis was that chromosomal rearrangements (CRs) could separate low-risk of progression (LRP) from an intermediate and high risk of progression (IHRP) prostate cancer (PCa). The number of abnormal junctions did not distinguish LRP from IHRP. Loci corresponding to genes implicated in PCa were more frequently altered in IHRP. Integrated analysis of CNVs and microarray data yielded six potential markers that were more frequently detected in the GP3 of a Gleason score of 7 (GS7) PCa compared to GP3 in a GS6 PCa. Five of those were cross-validated in an independent sample-set with statistically significant AUCs. Recent breakthroughs in immunotherapy and targeted therapies are now becoming cancer agnostic (i.e. NTRK inhibitors) arguing for a more individualized approach to patient care. A process that uses that a combination of comprehensive genomics with 3D organoid-type functional model systems to guide treatments will be presented followed by a representative example. We tested the hypothesis in a triple negative breast cancer (TNBC) patient with metastatic. Comprehensive genomic information derived from the patient's tumor cells was integrated with the purpose of deciphering the activated molecular pathways in her tumor. The results of the genomic analysis were then used to functionally validate drug sensitivity and predict response to therapy in 3D micro cancer preclinical model systems grown from the patient's tumor cells. The patient was subsequently treated with the recommended drug and showed a near complete response as observed by radiographic and blood-marker testing.

Biography

George Vasmatzis is a Consultant in the Department of Molecular Medicine and a member of the Mayo Clinic Cancer Center, as well as the co-director of the Biomarker Discovery Program, within the Center for Individualized Medicine. His research program consists of bioinformatics specialists, molecular biologists, epidemiologists, and pathologists. His team has demonstrated success in discovery and translation of several biomarkers as well as developing evidence-based models that should help clinicians stratify (cancer) patients in order to provide each individual with the appropriate care. With the recent advances in Next Generation Sequencing (NGS) technologies his laboratory has been engaging in massive sequencing to scan the genome of cancer cells for abnormalities that can be used for clinical purposes such as diagnosis and stratification of patients for optimal treatment. Published papers in Journal of Clinical Oncology, Cancer Research and BLOOD further demonstrate their discovery, validation, and translation capabilities.

Vasmatzis.george@mayo.edu

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