Commentary

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British Biomedical Bulletin
ISSN 2347-5447

2022
Vol.10 No.5:002

Description of the Evolution of International Public Cancer Genome Projects and Related Databases

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Received date: September 06, 2022, Manuscript No. IPBBB-22- 15112; **Editor assigned date:** September 08, 2022, PreQC No. IPBBB-22- 15112 (PQ); **Reviewed date**: September 15, 2022, QC No IPBBB-22- 15112; **Revised date:** September 22, 2022, Manuscript No. IPBBB-22- 15112 (R); **Published date:** October 05, 2022, DOI: 10.36648/2347-5447.10.5.2

Citation: Outram SM (2022) Description of the Evolution of International Public Cancer Genome Projects and Related Databases. Br Biomed Bull Vol. 10 Iss No.5:002

Description

Genomic research has fundamentally altered our understanding of cancer biology over the past ten years, making it possible for large-scale studies of various cancer types to conduct in-depth analyses of mutations, copy number alterations, structural variants, gene expression, and DNA methylation profiles. Public databases that provide scientists all over the world with access to meticulously curated data have been extensively utilized as a tool for further hypothesis-driven research on a variety of aspects of cancer biology. Initiatives such as The Cancer Genome Atlas (TCGA) and the International Cancer Genome Consortium (ICGC) have facilitated international collaborations for cancer genomic analyses. In parallel, some of these findings are being used to provide cancer patients with specific clinical advantages. The evolution of international public cancer genome projects and related databases, as well as their impact on general cancer research, are briefly discussed in this review.

Systematic Description and Identification of Various Types of Genetic Alterations

During the early stages of tumor development, the cancer genome sequencing also revealed the frequent presence of catastrophic single events that affected clustered regions of the genome. Numerous clustered structural aberrations are produced during chromothripsis, which typically results in DNA Copy Number Alterations (CNA), such as the amplification of genes associated with cancer. The systematic description and identification of various types of genetic alterations (such as substitutions, indels, gene fusions, and CNAs) that lead to human cancer is one example of how genome sequencing efforts have contributed to improving our fundamental understanding of cancer. In addition, these projects investigated how DNA alterations in human cancer complement aberrations at the protein, transcriptional, and epigenetic levels that produce distinct functional effects. Analyses of microRNAs and long-non-coding RNAs (lncRNAs) in the epigenetic and transcriptional domains have improved our comprehension of the development of intricate regulatory networks in healthy tissues and the role that changes in these networks play in the development of cancer. A comprehensive analysis of cancer cells' functional biological pathways and the discovery of mutational signatures were made possible by the identification of this multitude of aberrations in the cancer genome. This gave researchers a better understanding of how these pathways might be acting in concert during the development of cancer.

Combination of Synchronized Clinical Data with Genomic Data and Patient Follow-Up

How we classify and comprehend the early stages of tumor development may be profoundly affected by fundamental insights into the cellular origin of cancer and modifications of common biological pathways. In this regard, a better classification of cancer has been proposed as a result of the discovery of tumors from distinct anatomical sites that share common genomic alterations. These tumors are biologically more similar to one another than tumors from the same tissue but do not share common genetic aberrations. Tumors may be better divided into biological and clinical entities if they have specific genomic alterations. Gene silencing, overexpression, the presence of fusion transcripts, and aberrations in alternative splicing are just some of the RNA alterations that have been associated with human cancer. In 1,188 cases, the TCGA and ICGC/PCAWG projects included paired genome and RNA sequencing in addition to DNA sequencing. This made it possible to look into fundamental questions like how DNA changes affect RNA expression and how aberrations in RNA expression are explained on the genomic level. Despite the fact that cancer genomics analyses are already present in the clinical setting, particularly in areas such as the application of targeted gene panels and NGS approaches for the detection of actionable somatic mutations and tumor subtyping based on RNA expression. The knowledge and information produced by massive sequencing cancer projects are vastly separated in this setting. Genomic testing will become an essential component of the clinical decision-making process as a result of technological advancements and the decreasing costs of nucleic acid sequencing. Current initiatives, such as the ICGC-ARGO, that combine synchronized clinical data with genomic data and patient follow-up will undoubtedly contribute to realizing the potential of genomics for cancer patients.