Mutanome

The term “mutanome” typically refers to the complete set of mutations present in the genome of a tumor. In the context of cancer research, understanding the mutanome of a tumor is crucial for studying the genetic alterations that drive cancer development and progression. The term is derived from the words “mutation” and “genome.”

Key points

Genetic Mutations in Cancer: Cancer is characterized by the accumulation of genetic mutations in the DNA of cells. These mutations can affect various genes, leading to uncontrolled cell growth, tumor formation, and the potential for metastasis.

Heterogeneity: Tumors are often genetically heterogeneous, meaning that different cells within the same tumor can have distinct sets of mutations. This heterogeneity poses challenges in terms of diagnosis, treatment, and understanding of the underlying biology of the cancer.

Next-Generation Sequencing (NGS): Advances in genomic technologies, particularly next-generation sequencing, have facilitated the comprehensive analysis of the mutanome. NGS allows researchers to sequence the entire genome or specific regions of interest in a cost-effective and high-throughput manner.

Neoantigens: Within the mutanome, researchers are particularly interested in identifying neoantigens. Neoantigens are peptides or proteins generated by tumor-specific mutations that can be recognized by the immune system. Understanding the neoantigen landscape is important in the context of cancer immunotherapy, where the goal is to enhance the immune system's ability to recognize and attack cancer cells.

Personalized Medicine: Knowledge of the mutanome is instrumental in the development of personalized cancer therapies. Targeted therapies and immunotherapies aim to exploit specific mutations or the immune response against neoantigens to treat cancer more effectively.

Tumor Mutational Burden (TMB): Tumor mutational burden is a measure of the number of mutations present in a tumor's DNA. High TMB is associated with a greater likelihood of responding to certain immunotherapies.

By studying the mutanome, researchers aim to uncover the genetic drivers of cancer, identify potential therapeutic targets, and develop more precise and effective treatments. This personalized approach to cancer research and treatment represents a significant shift in the paradigm of oncology, moving towards therapies tailored to the specific genetic characteristics of an individual's tumor.

Using the particular nature of melanoma mutanomes to develop medicines that activate the immune system against specific mutations is a game changer in immunotherapy individualization. It offers a viable solution to the recent rise in resistance to accessible immunotherapy alternatives, with some patients demonstrating innate resistance to these drugs despite past sensitization to these agents. However, various obstacles stand in the way of this method, most notably the practicality of

sequencing each patient's mutanome, selecting immunotherapy targets, and manufacturing specific medications on a large scale. With the robustness and advancement in research techniques, artificial intelligence (AI) is a potential tool that can help refine the mutanome-based immunotherapy for melanoma. Mutanome-based techniques are being employed in the development of immune-stimulating vaccines, improving current options such as adoptive cell treatment, and simplifying immunotherapy responses. Although the use of AI in these approaches is limited by data paucity, cost implications, flaws in AI inference capabilities, and the incapacity of AI to apply data to a broad population, its potential for improving immunotherapy is limitless. Thus, in-depth research on how AI might help the individualization of immunotherapy utilizing knowledge of mutanomes is critical, and this should be at the forefront of melanoma management [1)].

1)
Zakariya F, Salem FK, Alamrain AA, Sanker V, Abdelazeem ZG, Hosameldin M, Tan JK, Howard R, Huang H, Awuah WA. Refining mutanome-based individualised immunotherapy of melanoma using artificial intelligence. Eur J Med Res. 2024 Jan 5;29(1):25. doi: 10.1186/s40001-023-01625-2. PMID: 38183141.