

A short Review of Human Epidermal Growth Factor Receptor 2

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Abstract

Human epidermal growth factor receptor 2 (HER2), also known as ErbB2, is a transmembrane protein that belongs to the epidermal growth factor receptor family. It plays a crucial role in regulating cell growth, division, and differentiation. HER2 is of significant interest in the field of cancer research due to its involvement in various malignancies, particularly breast cancer. HER2 is a proto-oncogene, and when it is overexpressed or amplified, it can lead to uncontrolled cell proliferation and tumor formation. The overexpression of HER2 is observed in approximately 20-30% of breast cancers and is associated with more aggressive disease progression. It has become a vital biomarker for breast cancer diagnosis and treatment. In recent years, targeted therapies such as trastuzumab (Herceptin) and pertuzumab (Perjeta) have been developed to specifically inhibit HER2 signaling in breast cancer patients with HER2-positive tumors. These treatments have shown significant clinical benefits and have improved the prognosis for many patients. Understanding the biology and signaling pathways of HER2 has led to the development of innovative strategies for diagnosing and treating HER2-positive cancers. Ongoing research continues to explore new therapeutic approaches and better understand the role of HER2 in various cancer types, offering hope for improved outcomes and personalized treatment options for patients with HER2-driven malignancies.

Keywords: HER2; Epidermal growth factor; Breast cancer

Introduction

The human epidermal growth factor receptor 2 (HER2), also known as ErbB2, is a pivotal protein in the context of cellular growth, proliferation, and differentiation. It belongs to the epidermal growth factor receptor (EGFR) family, which consists of four closely related members, including EGFR (ErbB1), HER2 (ErbB2), HER3 (ErbB3), and HER4 (ErbB4). These receptors play crucial roles in various cellular processes by transducing extracellular signals into intracellular responses. HER2, in particular, has garnered significant attention in the fields of cancer research and clinical oncology due to its pivotal role in cancer development and progression. This transmembrane receptor is encoded by the ERBB2 gene and is characterized by an extracellular ligand-binding domain, a transmembrane domain, and an intracellular tyrosine kinase domain. Unlike some of the other EGFR family members, HER2 has no known ligand that directly activates it. Instead, it often forms heterodimers (pairs) with other EGFR family members, enhancing their signaling capabilities [1].

One of the most critical aspects of HER2 is its association with cancer. In certain malignancies, notably breast cancer, HER2 can be overexpressed or amplified, resulting in an excessive number of HER2 receptors on the cell surface. This overexpression of HER2 is associated with more aggressive disease behavior and poorer prognosis. HER2-positive breast cancer represents a distinct subtype, accounting for approximately 20-30% of all breast cancer cases. The discovery of HER2 overexpression in breast cancer led to a paradigm shift in cancer treatment. It became the first oncogene-directed therapeutic target in cancer therapy. Monoclonal antibodies, such as trastuzumab (Herceptin) and pertuzumab (Perjeta), were developed to specifically inhibit HER2 signaling. These targeted therapies have significantly improved the clinical outcomes and survival rates of HER2-positive breast cancer patients [2].

In addition to breast cancer, HER2 overexpression has been observed in other cancer types, including gastric cancer and certain types of lung cancer. The study of HER2 biology and its role in cancer continues to be a vibrant area of research, with ongoing efforts

to develop new treatments and diagnostic tools for HER2-driven malignancies. Understanding HER2 and its signaling pathways has not only revolutionized cancer treatment but has also paved the way for personalized medicine approaches tailored to the specific molecular characteristics of a patient's tumor.

Methodology

The methodology employed in researching and studying the human epidermal growth factor receptor 2 (HER2) involves a multifaceted approach that encompasses various experimental and clinical techniques. Researchers have employed a combination of in vitro and in vivo methods to gain insights into the structure, function, and significance of HER2, especially in the context of cancer. Below, we outline some of the key methodologies used:

Cell culture studies: Researchers commonly use human cell lines, including breast cancer cell lines, to investigate HER2 biology. These studies involve growing cells in controlled laboratory conditions, manipulating HER2 expression, and observing how it affects cell behavior, such as proliferation, migration, and apoptosis [3].

Immunohistochemistry (IHC) and immunofluorescence (IF): To assess HER2 expression in patient tumor samples, researchers utilize IHC and IF techniques. These methods involve staining tissue sections with specific antibodies against HER2, allowing for the visualization and quantification of HER2 protein levels.

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Fluorescence in situ hybridization (FISH): FISH is a molecular technique used to detect HER2 gene amplification in tumor samples. By labeling specific DNA sequences, researchers can identify and quantify gene amplification, a hallmark of HER2-positive cancers [4, 5]. Preclinical studies often involve the use of animal models, such as mice with HER2-driven tumor xenografts. These models allow researchers to evaluate the efficacy of HER2-targeted therapies and gain insights into tumor biology.

Molecular biology techniques: Techniques like polymerase chain reaction (PCR) and western blotting are employed to assess HER2 mRNA and protein levels, as well as downstream signaling pathways. In the clinical setting, HER2 status is routinely determined in cancer patients using IHC and FISH. Patients with HER2-positive tumors may be eligible for HER2-targeted therapies as part of clinical trials or standard of care. Researchers use imaging techniques like positron emission tomography (PET) and magnetic resonance imaging (MRI) to assess treatment responses in HER2-positive cancers [7, 8].

Genomic analysis: High-throughput sequencing technologies, such as next-generation sequencing (NGS), are used to study the genetic alterations associated with HER2-positive cancers, helping to identify potential therapeutic targets and mechanisms of resistance. Researchers analyze clinical data from patient cohorts to assess the impact of HER2 status on treatment outcomes, survival, and disease progression. Structural studies, including X-ray crystallography and cryo-electron microscopy, have provided insights into the three-dimensional structure of the HER2 receptor and its interactions with other proteins and inhibitors. In summary, the methodology for studying HER2 involves a diverse array of laboratory and clinical techniques, ranging from cell culture experiments to clinical trials and molecular analyses. This comprehensive approach has deepened our understanding of HER2's role in cancer and has led to the development of targeted therapies that have revolutionized the treatment of HER2-positive malignancies [9].

Results and Discussion

The research on the human epidermal growth factor receptor 2 (HER2) has yielded significant findings that have both advanced our understanding of HER2 biology and had a substantial impact on cancer treatment strategies. In this section, we will discuss some key results and their implications.

HER2 overexpression in cancer:

One of the central findings is the discovery of HER2 overexpression in various cancer types, most notably breast cancer. HER2-positive breast cancer is characterized by elevated levels of HER2 receptors on the cell surface due to gene amplification. This overexpression is associated with more aggressive tumor behavior, increased metastatic potential, and poorer prognosis.

Targeted therapies:

The development of HER2-targeted therapies, such as trastuzumab (Herceptin) and pertuzumab (Perjeta), has been a groundbreaking result in HER2 research. These monoclonal antibodies specifically inhibit HER2 signaling and have revolutionized the treatment of HER2-positive breast cancer. Clinical trials have demonstrated significant improvements in survival rates and quality of life for patients receiving these targeted therapies.

Resistance mechanisms:

Research has also unveiled mechanisms of resistance to HER2-targeted therapies. Some patients initially respond well but later develop resistance. Studies have identified various mechanisms, including alterations in downstream signaling pathways, alternative receptor dimerization, and genetic mutations. Understanding these resistance mechanisms is crucial for developing strategies to overcome treatment resistance [10].

Personalized medicine:

The identification of HER2 as a critical biomarker has paved the way for personalized medicine in oncology. HER2 status is routinely assessed in cancer patients, and treatment decisions are tailored based on the presence or absence of HER2 overexpression. This approach has led to more precise and effective cancer treatments, minimizing side effects for patients without HER2-positive tumors.

Structural insights:

Structural biology studies have provided detailed insights into the three-dimensional structure of the HER2 receptor and its interactions with targeted therapies. This knowledge has guided the design of new HER2 inhibitors and improved our understanding of drug-resistance mechanisms. HER2 status has proven to be a valuable prognostic and predictive marker. It not only informs treatment decisions but also helps predict patient outcomes. Patients with HER2-positive tumors tend to benefit significantly from HER2-targeted therapies, leading to extended survival and better disease control. In conclusion, research on HER2 has transformed our understanding of cancer biology and treatment. The identification of HER2 as a key player in cancer development has led to the development of targeted therapies, improved patient outcomes, and provided valuable insights into the mechanisms of resistance. This body of research continues to evolve, with ongoing efforts to refine treatments, identify novel therapeutic targets, and further our understanding of HER2's role in cancer.

Conclusion

The study of human epidermal growth factor receptor 2 (HER2) has profoundly influenced both our understanding of cancer biology and the treatment of HER2-associated malignancies, most notably breast cancer. The culmination of extensive research and clinical investigations has resulted in several pivotal conclusions:

HER2 as a key biomarker:

HER2 has emerged as a critical biomarker in various cancers, with HER2 overexpression being a hallmark of aggressive tumor behavior. It has not only provided a diagnostic tool for identifying HER2-positive cancers but also serves as a prognostic indicator, guiding treatment decisions and predicting patient outcomes.

Targeted therapies transforming cancer treatment:

The development and implementation of HER2-targeted therapies, such as trastuzumab (Herceptin) and pertuzumab (Perjeta), represent a groundbreaking achievement in cancer therapeutics. These monoclonal antibodies specifically inhibit HER2 signaling, leading to improved response rates, prolonged survival, and enhanced quality of life for HER2-positive cancer patients.

Personalized medicine advancements:

HER2-directed treatment has set the stage for personalized medicine in oncology. The evaluation of HER2 status has become a routine part of cancer diagnosis, allowing for tailored therapeutic

approaches that maximize treatment efficacy while minimizing side effects for patients with HER2-negative tumors. Research has shed light on the mechanisms of resistance to HER2-targeted therapies, revealing challenges in the long-term management of HER2-positive cancers. Understanding these mechanisms is vital for developing strategies to overcome treatment resistance and improve patient outcomes.

Structural and molecular understanding:

Structural and molecular studies have provided detailed insights into the architecture of the HER2 receptor and its interactions with therapeutic agents. This knowledge has facilitated the design of new HER2 inhibitors and deepened our understanding of the complex signaling pathways involved. In essence, the exploration of HER2 has not only revolutionized the treatment landscape for HER2-positive cancers but has also enriched our knowledge of cancer biology and the intricacies of targeted therapy. As research in this field continues to evolve, it holds the promise of further refining treatments, discovering novel therapeutic targets, and ultimately enhancing the lives of patients affected by HER2-driven malignancies. The journey from HER2's discovery to the development of precision therapies underscores the remarkable progress achieved in the realm of cancer research and treatment.

Acknowledgment

None

Conflict of Interest

None

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