Dean&Francis
ISSN 2959-409X

Can Targeted Drugs Developed from the Study of Human Endogenous Retrovirus K Replace Traditional Chemotherapy in terms of Colorectal Tumors?

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Abstract:

Cancer remains a leading cause of death worldwide, with colorectal cancer (CRC) being one of the most prevalent forms. Traditional chemotherapy, while effective, often comes with significant side effects and limitations, prompting the need for more targeted and less toxic therapeutic strategies. This dissertation explores the potential of Human Endogenous Retrovirus K (HERV-K) as a novel target for cancer treatment, particularly in CRC. HERV-K, a retroviral element embedded in the human genome, has been linked to various cancers due to its reactivation in malignant tissues. The study reviews existing literature on HERV-K's role in carcinogenesis, its protein expression in tumors, and the development of therapeutic strategies targeting HERV-K, such as CRISPR-based gene editing, immune activation, and autoantibody therapies. These emerging strategies are compared with traditional chemotherapy in terms of efficacy, side-effect profiles, and economic feasibility. While HERV-K-based therapies show promise due to their precise targeting and potential for long-term immune protection, they are still in early stages of development and face challenges such as high costs and limited clinical trials. The dissertation concludes that HERV-K-targeted therapies, while promising, cannot currently replace traditional chemotherapy due to certain limitations. Future research should focus on expanding the understanding of HERV-K's role in different cancers and optimizing these therapies for broader application.

Keywords: Human Endogenous retrovirus type-K (HERV-K), Colorectal cancer (CRC), Chemotherapy, Active immunity, Monoclonal antibodies, Clustered Regulatory Interspaced Short Palindromic Repeats (CRISPR), Taxane, Topoisomerase inhibitors, Cisplatin, Carcinogenic transcripts of HERV-K.

ISSN 2959-409X

1. Introduction

Cancer, as the second leading cause of death globally, has become a major global concern (WHO, 2024). Given the increasing number of newly diagnosed cancer cases, the development of new therapeutic strategies has become an urgent matter. Fortunately, research on Human Endogenous Retrovirus (HERVs) has achieved certain breakthroughs, providing new insights into cancer treatment.

Previous studies on cancer treatment mainly focused on chemotherapies, including the mechanisms of drugs at the intracellularly level under *in vivo* conditions. However, most papers that introduce a particular type of drug do not include the analysis drug intake's impact on organisms in a macroscopic perspective. Additionally, existing research lacks a systematic comparison in the efficacy of anti-cancer drugs. Against this background, this study will first examine what types of cancer drugs have been developed based on the study of HERV-K, and compare the impact of these new drugs and the impact of chemotherapy drugs on organisms. Secondly, this research will evaluate the efficacy of these two treatment methods in terms of their universality in treating different cancers, the size of the patient population eligible for these treatments, and the side-effects by applying these drugs (i.e., symptoms after/during treatment)

2. Literature Review

2.1 What are HERVs

2.1.1 An introduction into the HERV family

HERVs are viruses that hide in our DNA. In the human body, there are fragments of genetic information that are not derived from human DNA, and these genetic fragments are called Human Endogenous Retrovirus (HERVs) (IHGSC, 2001).

Gene sequencing and analysis conducted in 2001 revealed that 8% of the human genome comprises various HERVs. (IHGSC, 2001). A hypothesis suggests that HERVs were originally the genomes of prehistoric exogenous retroviruses. (Cold Spring Harbor, 1997). These viruses fused their genomes with our ancestors' via retro transcription and these modified genetic codes have been inherited by ancient humans from generation to generation (Cold Spring Harbor, 1997).

The structure of HERVs is highly similar to that of exogenous retroviruses: both are composed of two long terminal repeats (LTRs) and *Gag, Pol, Pro*, *Env* regions between the LTRs. Different regions of the genetic code of HERVs are responsible for manufacturing different parts of a complete virus. The *Env* gene codes for *Env* protein that is composed of two subunits: cell surface domain (SU) and the transmembrane domain (TM) (Posso-Osorio, Tobón & Cañas, 2021).

2.1.2 HERV-K (HML-2) – a branch of HERV family

HERV-K, the youngest member of the HERV family, has been repressed in ordinary states, similar to other HERVs, as their proviral DNA is highly defective due to mutations (i.e., frameshift mutations, deletions) over generations and the presence of methylation sites. However, several external stimuli could lead to the re-activation of HERV-K expression, including UV radiation, cytokines that amplify during immune responses, and exogenous viral products (Villesen et al., 2004). As a result, there is evidence indicating HERV products have a positive correlation with multiple tumors. In cancer studies, a pattern of HERV-K protein expression and the location of malignant region was investigated. The result shows that there is an enhanced expression of HERV-K proteins in the tissue samples collected from the malignant regions. Additionally, a study published in Frontiers in Microbiology suggests that HERV *Env* proteins promote tumorigenesis by increasing cellular fusogenicity and immunosuppression (Grandi & Tramontano, 2018). What's more, the study revealed that the SU subunit is responsible for binding with the host cell receptors in order to make the somatic cells stick together for intercellular fusion, whereas the TM subunit is known to participate in immune modulatory activities (Grandi & Tramontano, 2018). (Figure 1)

Recent clinical studies have observed immune responses triggered by HERV-K Gag and Env proteins in patients with seminoma, lymphoma, thrombocytopenia, prostate cancer, breast cancer, lung cancer, and gastrointestinal cancers (Müller, Holst & Nielsen, 2022) (Figure 2). Consequently, there is sufficient evidence that HERV-K protein-based targeted drugs are feasible in clinical trials since HERV-K related proteins act as a relatively common antigen in multiple categories of tumor cells.

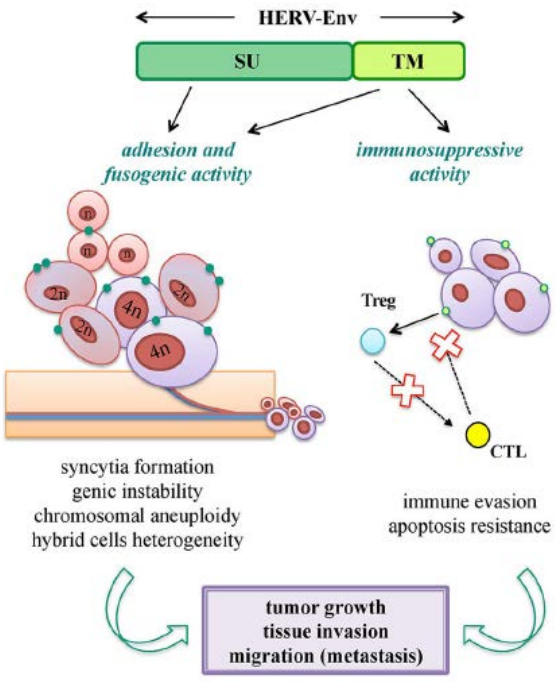

Figure 1 |Subunits SU and TM of HERV-*Env* causing two types of somatic cell dysfunctions (fusogenicity and immunosuppression) (Grandi, N. et al., 2018)

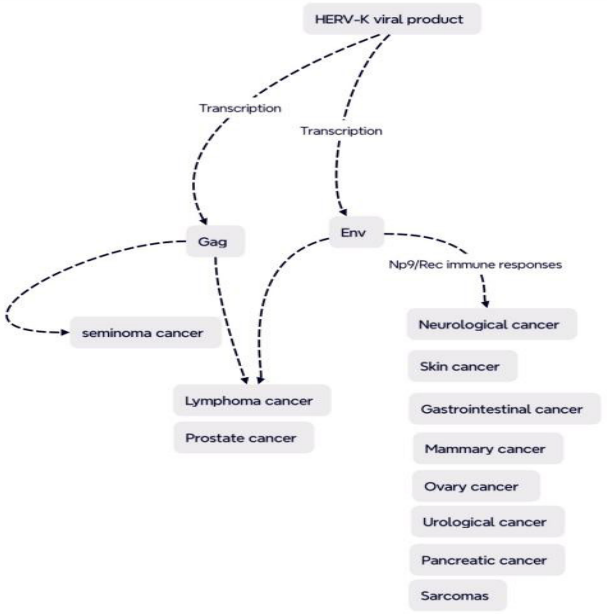

Figure 2 | *Gag* and *Env* implicating multiple tumors, using immune respond lead by monoclonal antibody to assess the presence of viral proteins

2.2 Colorectal tumors

Colorectal cancer, with 100,000 new cases per year, is known as the third most common cancer around the globe, while the first two are breast cancer and lung cancer respectively.

In 2024, there was a total of 152,810 new CRC cases added in the United States of America, which increased by 3.7% compared with the figure in 2023. (Figure 3) Apart from that, according to the bar chart, it is clear to notice that colon cancer contributes higher figures than rectal cancers. The general trend of the number of the new CRC cases is increasing, and this trend is expected to continue in the next half decade, which raise concerns about public health (CA: a cancer journal for clinicians, 2020-2024).

In general, most colorectal cancers originate from colon polyps, which are abnormal growths in the mucosal layer. 95% of CRC is derived from neoplastic polyps, and the conversion from neoplastic polyps to adenocarcinoma usually takes 5 to 15 years. The development of neoplastic polyps could be result by multiple factors, including diet habits, inflammatory physical inactivity, and smoking (Siegel et al., 2024).

Research conducted by International Agency for Research on Cancer Groups in 2021 showed that red meat and proceeded meat are potential carcinogens. It suggested that some toxic substances may be formed under the high temperature condition during cooking. For instance, heterocyclic amines, polycyclic aromatic hydrocarbons are genotoxic substances that are likely to be form under cooking condition. These two chemicals have been proven to be implicatedin point mutations of DNA acting as stimuli that promote carcinogenesis (Sawicki et al., 2021). In this case, they may act as external stimuli to activate HERV-K expression, which Catalyzes the carcinogenic process.

Smoking and physical inactivity are two supplement factors other than dietary factors that would promote carcinogenesis. Undoubtebly, being physically active is beneficial for promoting metabolism, thus toxic substances will be expelled from the body in a faster rate, blocking the pathway of carcinogens to diffuse into somatic cells and repress actions carried out by the tumor suppression genes such as the mismatch repair mechanism of DNA. In contrast, chemicals inhaled from the cigarettes are likely to initiate carcinogenesis. Besides angiogenesis in colon cancer under the action of nicotine, other carcinogenic molecules could be formed by the conversion of a cytochrome *p*450s. Since these carcinogenic molecules are generally electrophiles, they are likely to form DNA adducts that methylate the *p53* tumor suppressor gene (Chen et al., 2011)

Overall, these papers reveal that the ultimate mechanism

ISSN 2959-409X

of most carcinogens people encounter in life is to act on the gene level, for example, tumor suppressor genes suppression or oncogenes activation. Therefore, this conclusion provides insight for developing HERV-K-targeting therapies.

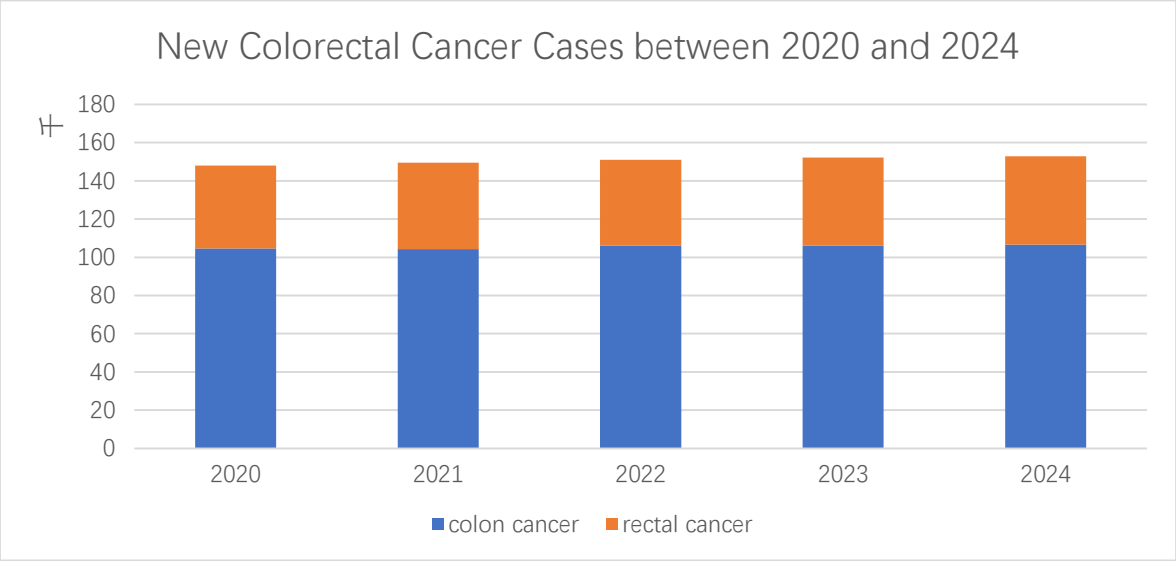

Figure 3| statistic data of the trend and number of cases added between 2020 and 2024 (CA: a cancer journal for clinicians, 2020-2024).

2.3 Therapeutic methods developed based on HERV-K study

Overall, there are three strategies being developed during the study of HERV-K: Direct disruption of HERV-K expression, active immunity activators, and autoantibodies that targets HERV-K *Env* protein to attack. Although HERV-K viral products are not direct prodrugs used to develop new therapeutic methods, they are promising as targets for targeted therapeutic strategies since HERV-K viral products are mainly distributed around tumor. Up to now, there are multiple progresses being made in HERV-K study in prostate cancer, breast cancer, and colorectal cancers. Two potential therapeutic targets were identified: HERV-K gene and its viral products.

The method of disturbing HERV-K gene expression can be separated into two branches. Firstly, since the target is now fixed, it is feasible to use Clustered Regulatory Interspaced Short Palindromic Repeats (CRISPR) technology to switch off the expression of HERV-K. (Ibba et al., 2018) Whereas another insight was observed during an investigation: it was noticed that CuSO4 could regulate the expression of HERV-K: A negative correlation between the concentration of CuSO4 and HERV-K expression level.(Karimi, Sheervalilou & Kahroba, 2019) Therefore, this founding suggests that studying HERV may provide more insights to develop a richer approach to chemotherapy.

Another insight of therapy is achieved by initiating the active immunity of an individual. Since the viral protein itself could be modelled as a target for the immune system. Two common virus vectors, the adenovirus (type 5 and 19a/64) (Ragonnaud et al., 2022) and the modified vaccinia virus Ankara (MVA) were used to practice this theory. Both viruses activate the immune response successfully, leading to the production of antibodies by B lymphocytes. (Kraus et al., 2013 & 2014)

The third insight derived from research on systemic lupus erythematosus (SLE). Since a highly precise autoantibody was observed with a relatively high concentration in SLE patients. This type of autoantibody targets HERV-K-Env as a target to for immune cells to attack, inducing antibody-dependent cell-mediated cytotoxicity (ADCC), a process that activates immune effector cells injecting cytotoxins into the autoantibody-binding cells leading to cell apoptosis. which eliminates carcinogens inside the patients' body and mediate tumor progression. (Gong et al., 2024) Therefore, culturing and harvesting this type of autoantibody provide an insight for cancer treatment.

2.4 Traditional chemotherapies

Chemotherapies were first investigated in World War I. It was observed that soldiers who were exposed to mustard gas would experience sever leukopenia, and dysfunction of bone marrow and lymph nodes (Krumbhaar & Krumbhaar, 1919). This phenomenon was quickly noticed by lymphoma researchers and eventually provide new insight

to develop strategies in cancer treatment.

Taxane is a drug generally that release the effects in the interphase of the cell cycle. The overall actions were exerted on the microtubule organizing centre (MTOC), impeding the formation of centrioles by binding with microtubules to interfere with microtubule dynamic balance. Eventually, it terminates the abnormal cell proliferation by halting the cell cycle in G0 and G1 phase (Krens McLeod & Hertz, 2013).

During S phase of the cell cycle, interfering the replication related enzymes is another feasible strategy via several chemicals. For instance, Topoisomerase (TOPO) are enzymes that play critical roles during DNA replication, transcription, and chromosome condensation. Therefore, inhibitors of TOPOs such as Irinotecan were developed. This chemical added on TOPO will form a TOPO I-DNA-camptothecin ternary complex. This complex would act as an obstacle by blocking the DNA replication pathway and collide with the DNA replication fork, causing a permanent conformational damage of DNA, which would eventually lead to cell death. (Jang, Kim & Kim, 2023)

Comparatively, aside from inhibiting enzymes, modification on their substrate is a viable plan too. Platinum-mixture drugs are platiniferous drug compounds used to treat the vast majority of solid tumors and leukemia. Cisplatin, an example of platinum-mixture drug could act as an adduct on the DNA strand, which changes the conformation of DNA double-stranded structure, making it unable to combine with replication-related enzymes. Therefore, impeding proliferation of cancer cells (Tchounwou et al., 2021).

3. Methodology

3.1 Analytical framework of the research questions

The methodology of this dissertation is based on secondary research, and the dissertation can be divided into two major parts. Firstly, the literature review part concludes four subparts:

1. The introduction of HERV family, including their common structures, hypothesis of their origins, and a more detailed overview in HERV-K, such as their mechanisms in carcinogenesis and the identification of multiple cancers that correlate with their viral products during HERV-K expression.
2. The introduction of CRC, including trend concluded from the number of new cases added in the US in past half decade and the lifestyle factors that promotes CRC with the outline of simple mechanism explanations.
3. An overview of chemotherapy and the classification of different chemotherapy strategies based on their drug mechanism. One representative drug of each kind of drug is identified with the mechanisms and actions that particular drug acts intracellularly.
4. New possible therapeutic strategies developed based on HERV-K studies were identified. It was discovered that the HERK-K coding region and HERV-K viral proteins have the potential to become promising targets for targeted drugs.

Secondly, the Discussion and Result part is mainly comparing the advantages and limitations of two types of therapeutic strategies, their efficacy comparison, their side effects, and the affordability of two type of strategies to the public is concluded in this part. A table is illustrated to list out all evaluation events to make visually clearer comparison. Eventually, a final judgement is made to justify whether the newly developed strategies have the potential to fully replace the traditional chemotherapy strategies.

3.2 Data source and the reliability assessing

Due to a lack of access to laboratories, all data were derived from secondary resources. For statistical data (new colorectal cancer cases from 2020 to 2024), are cited from CA: A Cancer Journal for Clinicians, an authorized journal that counts cancer data and updates annually. The reason for choosing this particular time interval is because it's up to date and considers the impacts on immune system resulted by COVID-19.

Articles published by Cold Spring Harbor Frontiers in Microbiology, Journal of oncology, and Virus were used in this dissertation. Articles published by Cold Spring Harbor, International Journal of Molecular Sciences, etc. are used to illustrate and identify the carcinogenesis of HERV-K proteins and outline the mechanisms of how these proteins that lead to the formation of oncology. Articles published on PloS One, and Virus journals are used to interpret and identify the potential therapeutic strategies used to against multiple tumors (including colorectal tumor).

Most of the articles cited in this paper were published after 2018, however, there are some exceptions. For instance, some fundamental articles published in the study of this topic and the information in these articles are still reliable nowadays, since researchers in recent years are still citing these articles. Another reason to cite an older article is because it records factual data observed during that period instead of hypothesis-based statements such as the discovery of chemical-based therapy could be used to treat leukemia in 1919.

ISSN 2959-409X

4. Result and Discussions

This section would mainly focus on the comparison between the pros and cons of the two therapeutic strategies, since the traditional and innovative therapies actually have their own advantages in comparison. Therefore, it is critical to discuss and make a fair judgement based on their efficacy, limitations during treatment, and which treatment would minimize the pain experienced by the patient during and after the cycle.

4.1 Advantages of Chemotherapy

Overall, there are three main advantages of chemotherapy: a mature and well-developed drug system, its wide applicability in the treatment of various cancer type, and a relatively affordable price.

Firstly, as chemotherapy has been developed for more than a hundred years, it consists of many branches of drug that target and interfere with different organelles. Thus, it is feasible for two or more than two parallel branches of drug to interact with each other, achieving the effect of synergy. For instance, in the treatment of colorectal cancer, the effect of mono-chemotherapy, such as using cisplatin or 5-fluorouracil (a DNA replication enzyme inhibitor) singularly is smaller than the efficacy achieved by combining these two drugs together in the treatment of metastatic colorectal tumor.

Secondly, since the mechanism of the most proportion of chemotherapy is to avoid the cell from finishing the cell cycle. For instance, interfering the replication of centrioles in G1 phase (a phase for organelle replication). Or restricting the replication of DNA in the S phase of the cycle. Hence there are no specific binding sites required for chemotherapy drugs to exert their actions, since their only targets are DNA related molecules in every single cell. Therefore, chemotherapy could be used to eliminate KRAS-mutated colorectal cancer cells that lack targeted drug binding sites. This feature allows chemotherapies to maintain efficacy across diverse cancer types, especially in the treatment of cancers that lack all the targets available for existing targeted drugs to bind (i.e., Triple Negative Breast Cancer).

Last but not least, since most chemotherapy drugs could be covered by health insurance, the financial pressure to treat cancer is extremely low compared with that of targeted drugs. For instance, according to the data published by National Healthcare Security Administration of China and the website of the Central People's government of the PRC, there are 241 drugs related to cancer treatment are covered by the medical insurance of China, and the reimbursement of chemotherapy treatment for malignant tumors is about 90% of the total amount. Therefore, the audience that can afford chemotherapy financially remains at a relatively high number, which is a significant advantage of chemotherapy compared with the treatment of monoclonal antibodies, antigen vaccines, and CRISPR gene therapies.

4.2 Drawbacks of Chemotherapy

Limitations of chemotherapies mainly originated from three aspects, the presence of cell efflux pumps (CEPs) and non-cell to cell targeting feature.

CEPs are generally plasma membrane transporters. These types of membrane proteins are responsible to pump out the foreign substances inside the cell. Since the chemicals used during chemotherapies are likely being marked as "anomalous", therefore this particular cell Self-protection mechanism is likely to be activated. For instance, there are breast cancer studies indicating that these pumps would pump out taxane and cisplatin since these has the conformation that fits the binding site of organic cation transporters, an example of CEP, thus would be pump out of the cell (Muley et al., 2020).

Another disadvantage of traditional monotherapy, its widespread indiscriminate cytotoxicity trait and the compulsive implantation of intravenous infusion port for transfusion needs. Since most chemicals applied in chemotherapy are non-biologically active cytotoxic metabolites, these metabolites have significant chance to act on healthy somatic cells which leads to tissues/organs damage that results in defective biological systems. Consequently, it interrupts patients' daily life and inflicts unnecessary pain on their body physically and mentally. In clinical trials, patients who had applied chemotherapy can be easily recognized. Since the impacts result by chemotherapy drugs seems more significant on metabolically active cells: hair matrix cells, which are responsible for androgenic hair growth would likely to be affected by cell metabolic activity inhibitors such as cisplatin and TOPO inhibitors. Consequently, the function of cells would be mediated, and patients who took chemotherapy are generally bareheaded. Additionally, stem cells in bone marrow which have the potential to divide and differentiate into different blood corpuscle would also be inhibited by chemotherapy inhibitors. As a result, there would be a decline in the ability of immune response and blood clotting after injury. Apart from that, injection of toxic and foreign chemicals would increase metabolic stress on the liver and kidneys, with an increasing risk of hepatic and renal damage.

4.3 Advantages of HERV-K study based therapeutic strategies

There are three advantages that were noticed during the

application of HERV-K study-based medicines: the precise targeting feature, the long-term immune protection, and a fixed target in colorectal cancer.

Firstly, since most drugs were developed to target the specific HERV-K related antigens (i.e., HERV-K viral gene and viral protein), which is not presented in normal tissues. Therefore, it minimizes the lethality of the drug to normal tissue cells by eliminating carcinogens, *Env* proteins via antibodies or using a protein-to-gene technology to utilize a type of protein that recognizes and destroys targeted HERV-K genes (i.e., CRISPR tech). All these strategies show great efficacy in cancer cells but nearly no side effects in normal cells, which improve patients' quality of life during and after treatment, as HERV-K targeted drug treatment won't cause significant tissue/organ damages that interrupt the body systems from functioning.

Apart from that, once the immune cells that are sensitive to HERV-K Env protein have been activated, they are now able to produce massive number of antibodies that lock HERV-K *Env* proteins as targets. This process could eliminate carcinogens and inhibit the colorectal cancer cell growth. What's more, since the body has experienced an active immune response, part of the immune cells that were involved in this immune response will be transformed into memory cells of *Env* proteins, which promised a greater rate in the next immune response caused by *Env* proteins. To summarize, formation of the memory cells after an active immune response could act as a defensive shield that ensures the elimination of the HERV-K Env in the long run and reduce the promotion of colorectal cancer by this particular carcinogen.

Another remarkable advantage of these particular HERV-K viral protein hunter is that there aren't any recent publications that report the absence of HERV-K proteins in any type of colorectal cancer. Therefore, compared with other targeted drugs which are used in the treatment colorectal cancers, the targets for HERV-K hunters always exist in malignant tissues. As a result, targeted therapy by locating the HERV-K proteins will avoid the situation that happened in Triple Negative Breast Cancer, since HERV-K proteins can always be promising as targets for targeting drugs.

4.4 Limitations of HERV-K study based therapeutic strategies

On the other hand, drawbacks of the HERV-K targeting drugs still exist. For instance, the absence of clinical trials, lack of ability to treat untargeted cancers, unavailable to patients with defective immune system, and a relative expensive price of drug.

Firstly, these drugs haven't conducted any clinical trial that guarantees its safeness and efficacy. All investigation were conducted on lab mice, and there is currently no literature on the impacts of specific dose and concentration changes. Therefore, clinical application of these newly developed targeted drugs still needs more time to assess its toxicity, efficacy, and to explore the appropriate dosage of the drug for human use.

Secondly, since one of the therapeutic strategies is to activate the active immune response of patients through injecting modified virus that carries the *Env* protein or *Gag* protein to stimulate the immune cells inside the host body, therefore if the host does not have an intact immune system that could conduct the immune response, then this strategy would unlikely to perform its efficacy during treatment. This restricts the audience of this type of strategy, for instance, the patients who infects HIV lacks CD4 immune cells are a group of people who cannot benefits from this strategy.

Last but not least, compared with traditional chemotherapy medicines, the HERV-K targeted drugs are relatively high in price, there are three likely reason to explain this phenomenon. Firstly, R&D costs of HERV-K gene/protein targeted drugs are much higher than broad-spectrum anticancer drug (drugs used in chemotherapy), since these targeted drugs need to be developed based on a specific target (i.e., HERV-K Env gene, HERV-K Env protein, HERV-K Gag gene and protein.), which has a high failure rate. What's more, since the audience of a particular targeted drug is less than that of chemotherapy's due to less flexibility in cancer treatment, there is likely to have a greater cost of production, as the producer cannot benefits from scale economy. Eventually, during the patient's drug selection stage, despite the fact that more than 74 cancer-targeting drugs have been included in Chinese medical insurance as of January 2025 (published by Chinese medical insurance in April, 2024), some imported targeted drugs with better efficacy are still not included in the reimbursement list of the medical insurance of China.

4.5 Can Targeted Drugs from Human Endogenous Retrovirus K Replace Traditional Chemotherapy for Colorectal Tumors?

A systematic comparison between conventional cisplatin-based chemotherapy and the HERV-K study-derived targeted drug revealed significant differences in therapeutic and economic parameters (Figure 4). Cisplatin, a broad-spectrum chemotherapeutic agent, demonstrated a shorter treatment cycle (3–6 months) and a substantially lower cost of 320–480 RMB/800 mg per m^3 (after social health insurance reimbursement). In contrast, the HERV-K-targeted drug, which remains in preclinical

ISSN 2959-409X

development, showed a markedly higher reference price of 1,416,000 RMB/800 mg per m^3. This estimate was derived from an analogous Env protein-targeting drug with a similar mechanism of action, as the HERV-K therapeutic is not yet commercially available.

Key distinctions included efficacy prerequisites: the targeted drug required a specific molecular target and an intact immune system for optimal function, whereas cisplatin exhibited no such dependencies. Clinically, cisplatin caused significant tissue damage but remained widely accessible due to insurance coverage and compatibility with combination therapies. Conversely, the HERV-K-targeted agent offered potential advantages such as long-term protection and minimal tissue toxicity, albeit contingent on rigorous biomarker screening and unresolved insurance eligibility. These findings underscore the trade-offs between cost, accessibility, and precision in current versus emerging therapeutic strategies for oncology.

Evaluation

Overall, this dissertation summarized and compared the two therapeutic strategies in the aspect of colorectal cancer, which is a relatively new field in cancer treatment with no previous studies that compares the new HERV-K targeted drug therapy with traditional chemotherapy. And clearly discussed the feasibility of the replacement of traditional chemotherapy by the new HERV-K targeted drugs in different aspects, for instance, there is a detailed comparison of pros and cons for both therapies. However, some limitations still exist, for instance, although most articles are referenced from authorized institutions, for instance researches published by Cold Spring Harbor lab, several exceptions that are preprints and aren't been peer-viewed published on BioRxiv were used. Additionally, due to publication bias, there might be articles that indicate the situation that the case of colorectal cancer that absent the HERV-K Env exists. If this situation happens, then the HERV-K Env target would lose its advantage in targeted drug treatment, making this new targeted drug narrower in cancer treatment. Apart from that, due to practical factors, there aren't any HERV-K Env targeted drug issued on the market yet, therefore detailed efficacy and side-effects are still unavailable to be discovered so far. And the referenced price of the new targeted drug that plots in figure 4 may be inaccurate, due to the drug is not yet commercially available, therefore this article inferred its possible price based on existing drug with similar mechanisms, *Ibalizumab,* monoclonal antibody-based drug, function as a non competitve inhibitor that changes the conformation of the T cell receptors, therefore blocking the attachment between *Env* protein and receptors on the cell surface. Lastly, the word count requirement limits the content and detailed that could be mentioned and discussed in this dissertation, making this dissertation lacks case support or pharmacological explanation for certain arguments.

Conclusion

Cancer remains one of the most significant threats to human health, with traditional chemotherapy often causing severe side effects that impact patients‘ quality of life. This dissertation has explored the potential of a novel therapeutic approach targeting Human Endogenous Retrovirus K (HERV-K) as an alternative to conventional chemotherapy, particularly in the treatment of colorectal cancer (CRC).

Based on existing research, HERV-K-based therapies, such as vaccines that activate the host‘s immune response and autoantibodies derived from systemic lupus erythematosus (SLE) patients, have shown promise in targeting HERV-K proteins. These studies have demonstrated the feasibility of using HERV-K molecules as a therapeutic target, leading to the development of new drugs by institutions like Avalon GloboCare Corp. However, it is important to note that all HERV-K-targeted therapies are currently in the early stages of clinical trials (Phase I), and detailed information regarding their efficacy and safety in larger populations remains unavailable.

Given the current state of research, it is clear that HERV-K-targeted therapies are not yet ready to fully replace traditional chemotherapy. While they offer advantages such as precise targeting and reduced side effects, their limited broad-spectrum applicability and high costs pose significant challenges. Traditional chemotherapy, despite its well-documented drawbacks, remains a widely accessible and effective treatment option for a variety of cancers, including CRC.

Looking ahead, future research should focus on further understanding the role of HERV-K in different cancer types and stages. Establishing a comprehensive HERV-K expression database could help identify specific patterns and potential new targets within the HERV family. This would enable the development of more tailored and effective therapies, moving away from a „one-size-fits-all“ approach. Additionally, optimizing the cost and accessibility of HERV-K-targeted drugs will be crucial for their widespread adoption.

In conclusion, while HERV-K-targeted therapies hold significant potential, they are not yet a viable replacement for traditional chemotherapy. Continued research and development in this field are essential to unlock the full potential of HERV-K as a therapeutic target, ultimately improving cancer treatment outcomes and reducing the burden on patients.

Conclusion of the Comparison

Parameter	Chemotherapy (Cisplatin)	HERV-K-Targeted Drug
Treatment cycle	3-6 months (NHSA, 2024)	N/A
Insurance coverage	90% reimbursement in China (NHSA, 2024)	N/A
Cost (RMB per 4 weeks)	300-700 (NHSA, 2024)	182,840 (Drugs, 2024)
Target specificity	Broad spectrum (Krens McLeod & Hertz, 2013).	HERV-K Env protein (Gong et al., 2024)
Immune requirement	None	Requires intact immune system (Kraus et al., 2014)
Tissue toxicity	Significant	N/A
Clinical trial status	Availiable in the market	Phase I (Spinger, 2024)

Figure 4| An overall comprehensive comparison between two therapeutic methods.

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