ISSN. 2338-7475
E-ISSN. 2620-7869
Hearty
Jurnal Kesehatan Masyarakat
Beriman, Tulus, Sepenuh Hati,Berbesar Hati, Jujur, Sehat dan Kuat
Vol. 13 No. 3, June 2025, Hal. 592-601

UTILIZATION OF CHIMERIC ANTIGEN RECEPTOR-T (CAR-T) CELL THERAPY AS AN INNOVATIVE THERAPY FOR NON-SMALL LUNG CANCER (NSLC)

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Abstract

Non-Small Lung Cancer is one of the types of lung cancer with the highest prevalence in Indonesia. So that treatment is needed in an effort to reduce the prevalence rate. Chimeric Antigen Receptor-T (CAR-T) cell therapy is known to have the potential to be an alternative treatment for these types of cancer cells. This research is made with the hope that in the future this research can be further developed by researchers, especially in Indonesia. This literature study was made using the Systematic Literature Review (SLR) design to determine the effectiveness of CAR-T cell therapy targeted at several different genes and tested on mouse xenograft models. The journals used were obtained with a publication range of 2014-2024 and 7 journals were selected based on the results of inclusion and exclusion. Based on the results of the article review, it is known that CAR-T cell therapy targeting genes has good antitumor activity efficacy obtained from the test results by measuring the volume and weight of tumors in mouse xenograft models using a caliper and Bioluminescence Imaging (BLI) irradiation method.

Keywords: Therapy Cell CAR-T, Non-Small Lung Cancer, Targeting Gen

Introduction

Cancer is a disease characterized by the presence of uncontrolled cell growth and the ability of these cells to invade other biological tissues and spread to different parts of the body known as metastasis. The disease originates from genetic mutations in cells that cause abnormal growth and division. Cancer can affect almost all types of tissues and cells in the body, making it one of the most diverse and complex diseases (Prasetyo & Suprayitno, 2021). If this disease does not receive good therapeutic treatment, it can potentially cause death (Rahayuwati *et al*., 2020).

Based on WHO data in 2018, it explains that cancer is the second leading cause of death globally. It is estimated that there are cases of 9.6 million deaths with a global mortality ratio of 1: 6 lives (WHO, 2019) . According to other data in 2020, namely Global Cancer Statistics (GLOBOCAN), it is known that there are 19.3 million new cancer cases and 10 million cases of death due to cancer. Global Cancer Stastistics estimates that by 2040 there will be an increase in the number of new cancer cases by 47%, which is around 28.4 million cases, while in Indonesia there was also an increase in new cancer cases in 2020 compared to the addition of cases in 2018 of 396,914 people or an increase of 13.8%. Based on 2020 data, there are five types of cancer most experienced by the Indonesian population, namely breast cancer (16.6%), cervical cancer (9.2%), lung cancer (8.8%), colorectal cancer (8.6%) and liver cancer (5.4) (Sung *et al*., 2021).

It is known that lung cancer is the third highest incidence of cancer in Indonesia. Lung cancer is one of the most dangerous types of cancer and has the potential to cause death in sufferers. This disease occurs in the lung organ caused by genetic changes in airway epithelial cells that have the potential to

Submitted: May-2025 Received: May-2025 Available Online: June-2025

cause uncontrolled cell proliferation. Malignancy in this cancer can originate from the lung organ (primary) and from outside the lung organ known as metastatic (Buana & Harahap, 2022).

Cancer is a disease that consists of two main types, namely small cell lung cancer (SLC) and non-small cell lung cancer (non-SLC). SLC cancer tends to occur in less than 15% of all lung cancer cases, while non-SLC accounts for around 85% of cases (Duma *et al*., 2019). NSLC cancer itself is divided into several types of cancer types, namely Squamos Cell Carcinoma (SCC), Adenocarcinoma, Bronchoalveolar Carcinoma (BAC), and Large Cell Carcinoma (LCC) (Joseph & Rotty, 2019).

In Indonesia, the most common case is NSLC with an incidence prevalence of 95% of NSLC cases occurring in Regional Specialized Hospitals (RSKD) (Harahap *et al*., 2016). This is a major focus in the overall prevention, diagnosis and treatment of lung cancer. Lung cancer in Indonesia is often triggered by smoking, which is the biggest risk factor because cigarettes are known to contain carcinogenic substances that can trigger cell changes into cancer cells. The risk of developing lung cancer in active smokers can be up to 20 times higher than those who do not smoke. In addition, exposure to air pollution such as vehicle smoke, combustion smoke, and cigarette smoke from the surrounding environment can also increase the risk. Other factors such as heredity or genetics, dietary intake, and respiratory infections also play a role in causing an increase in incidence cases by 10-15% (Punamawati et al., 2020).

Seeing the high incidence of lung cancer cases that occur in Indonesia and globally, it is necessary to handle the therapy that needs to be done in an effort to reduce the percentage of the incidence rate. One of the cell therapies that can be done is Chimeric Antigen Receptor-T (CAR-T) cell therapy, an innovative approach in cancer treatment that involves the use of genetically modified T cells with the aim of strengthening the ability of target cells to fight cancer cells (Alnefaie *et al*., 2022).

Method

This research was conducted with the aim of conducting a literature review of several studies that discuss the use of Chimeric Antigen Receptor-T (CAR-T) cell therapy. The method in this literature review uses the Publish or Perish software version 8 as a medium in collecting data and information relevant to the journal review being done.

Table 1. Literature search results

SOURCE	KEY WORDS
Pubmed from Publish or Perish version 8	Therapy Cell CAR-T, Non Small Lung Cancer, Targeting gen

This literature review involved 293 literature studies obtained with a range of publication years between 2014-2024. In the initial stage, selection was carried out based on keywords that were adjusted to the title of the research journal review in accordance with the problems to be discussed. The next stage is filtering based on quality considerations and research relevance. Finally, a literature review was used with the criteria of using full data literature (Full text) and Original Research. So that 7 literature studies were selected that met the criteria set. The literature used is relevant to the issues to be discussed.

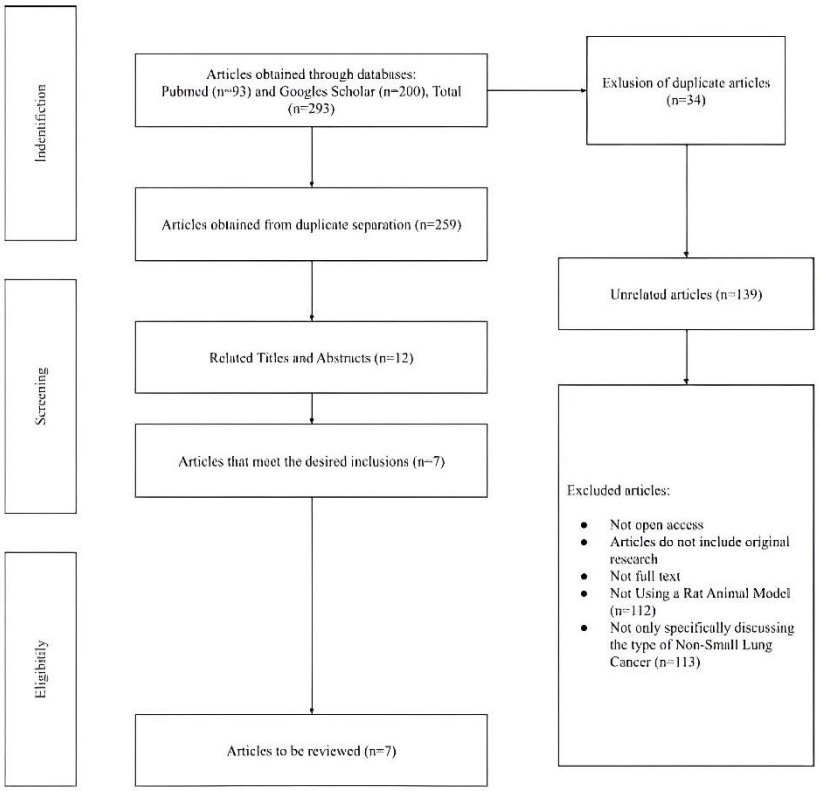

Figure 1. Prism diagram

PICO

Table 2. PICO

PICO	Inclusion Criteria	Exclusion Criteria
Participant	Mouse	Not mouse
Intervention	Therapeutic utilization of Chimeric Antigen Receptor-T (CAR-T) Cells for Non-Small Lung Cancer (NSLC) therapy	Not therapeutic utilization of Chimeric Antigen Receptor-T (CAR-T) cells for Non-Small Lung Cancer (NSLC) therapy
Comparator	No comparison factor	No comparison factor
Outcome	There is a successful therapeutic efficacy marked by a decrease in tumor size and weight in the test animals	There is no therapeutic efficacy marked by a decrease in tumor size and weight in the test animals

Results

	Target T Cells	Research Model	Gene Transfer Method	Country	Results	References
1	*EGFR*	Mouse	*System transposon piggy back non-viral*	China	The results showed that the development of CAR-T cell therapy targeting Epidermal Growth Factor Receptor (EGFR) in human lung cancer xenograft models in mice, where mice were inoculated with EGFR-positive lung cancer cells. The results obtained were that the engineered T cells showed significant anticancer efficacy in vitro. This can be seen from the decrease in the weight of the treated tumor compared to the control group which was monitored for 40 days using caliper measurements, Bioluminescence Imaging (BLI), and weighing of mouse.	(Li *et al*., 2018)
2	*B7-H3*	Mouse	Bicistronic vector	United States	The results showed that the development of CAR-T cell therapy targeting B7-H3 used the bicistronic vector method to insert the two genes into CAR-T cells. Then, cancer cells were inoculated into mice using xenograft. The results showed that the modified CAR-T cells showed significant anticancer efficacy in vitro which was tested by Bioluminescence Imaging (BLI) measurement. Testing of this efficacy was carried out for approximately 98 days.	(Liu et al., 2020)
3	*MUC1 & PSCA*	Mouse	Lentivirus vectors	China	The results showed that the development of CAR- T cell therapy with two antigen targets MUC1 and PSCA found in NSLC using lentivirus vector gene	(Wang et al., 2023)

					transfer method and xenogfraft method in mice. The results showed that CAR-T cells targeting MUC1 and PSCA, when combined with the use of anti-PD-1 antibodies, showed stronger antitumor activity compared to CAR-T targeting only one antigen. Testing was conducted for 24 days with tumor volume measurements every two days and mice body weight measurements.	
4	*LunX*	Mouse	Lentivirus vectors	China	The results showed that the development of Car-T cell therapy targeting LunX antigen found in NSLC using leviral vector method and mouse xenograft model can inhibit tumor growth and prolong mouse survival. The mice body weight was measured on day 15, using Bioluminescence Imaging (BLI) and tumor size was measured.	(Hu *et al*., 2020)
5	*FMR1NB*	Mouse	Lentivirus vectors	Japan	Based on this study, T cells found in humans were treated using 2-deoxy-glucose (2DG) to reduce glycosylation which was then transduced with CAR-T receptors targeting FMR1NB using lentivirus vector method and xenograft model showed to extend the survival of mice better. The measurement method performed was by Bioluminescence Imaging (BLI)	(Toyofuku *et al*., 2024)
6	*B7-H3*	Mouse	Lentivirus vectors	China	The results showed that the development of Car-T cell therapy with B7H3 target expressed in Lung Squamos-Cell Carcinoma (LUSC) which belongs to one	(Yu et al., 2024)

					class of NSLC using xenograft model and lentivirus vector gene transfer method showed significant cytotoxic effect against LUSC cells which was validated using measurement of tumor volume and weight in treated mouse.	
7	*EGFRvIII*	Mouse	Retrovirus vectors	China and America	The results showed that the development of Car-T cell therapy with EGFRvIII antigen target found in NSLC using xenograft model observed for 90 days and retrovirus vector method to infect T cells that have active lung cancer in mice. The results showed that EGFRvIII will specifically recognize and kill A549-EGFRvIII cells with an effector/target ratio of 10:1 by expressing and releasing cytokines, including perforin, granzyme B, IFN-γ, and TNF-α, so that it has potential as a therapeutic strategy in preventing recurrence and metastasis in lung cancer when patients after surgery. The test carried out is the measurement of the volume of mouse weight.	(Zhang et al., 2019)

Discussion

Gene Transfer Method into CAR-T Cells

CAR-T cells are T cells that have been genetically modified to express an artificial protein called CAR that allows them to recognize and attack cancer cells specifically. This process involves taking T cells from the patient, CAR proteins that have been designed to target specific respectors found on cancer cells. Then, the modified cells are multiplied, and finally the cells are injected into the test model (Li *et al*., 2018).

Gene transfer into T cells needs to be done first before CAR-T cells are inoculated into a mouse xenograft model. Gene transfer is necessary in modifying T cells to be able to recognize and target specific receptors found on cancer cells. In CAR-T therapy, the gene encoding CAR will be inserted into T cells to increase the cell's ability to recognize and destroy cancer cells. CAR-T cells that have

been modified by gene transfer can specifically recognize and interact with antigens expressed by cancer cells. Based on the mouse xenograft method, CAR-T cells that target human cancer antigens will be more effective in inhibiting tumor growth. This is to ensure that CAR-T cells have the appropriate receptors to recognize specific cancer cells. Without gene transfer, unmodified T cells will not have the specific ability to effectively recognize cancer cells (Ramos-Cardona *et al*., 2022).

The most widely used gene transfer method in research to insert genes into CAR-T cells is by using lentivirus vectors. In this article review, there are 4 articles that use the lentivirus vector method to transfer genes to T cells. The gene transfer method using lentivirus vectors has several advantages over other gene transfer methods such as bicistronic vectors, non-viral piggyBac transposon systems, and retrovirus vectors. Lentivirus vectors have the ability to integrate target genes into the host cell genome with high efficiency and long-term expression. This makes them highly effective in gene therapy and cell engineering (Milone & O'Doherty, 2018).

In the study of Li *et al*. (2018), a non-viral piggyback transposon system method was used to transfer the EGFR gene into the intended T cells. The mechanism of this method begins with the construction of plasmids containing CAR by including EGFR-specific scFv, transmembrane domain, and intracellular signaling domain. Then, human T cells are taken from peripheral blood and transduced with the plasmid using the piggyBac system. The transduced T cells will be propagated by stimulating anti-CD3/CD28 and interleukin-2 until they reach the desired number.

Meanwhile, based on the research of Li et al. (2022), the gene transfer was carried out using the bicistronic vector method. This experiment was carried out using bicistronic vectors to encode CARs that target B7-H3 and the CCL2 receptor, CCR2b. So that it can increase the expression of CCR2b in CAR-T cells which is important for increasing the migration ability of CAR-T cells towards CCL2 gradients which can potentially increase antitumor activity.

Mouse Xenograft Model

After CAR-T cells have been obtained from gene transfer into the target T cells, testing is performed using a mouse xenograft model. Based on the studies that have been conducted in this article, most of them use mouse xenograft models to evaluate the efficacy of new anticancer drugs in vivo. The xenograft model is based on the implantation of human tumor cells in mouse.

In the research of Wang et al., (2023) this experiment was carried out by first engineering the formation of A549 cancer cell tumors containing luciferase and GFP to be transplanted into the back of NCG mice so that it was possible to monitor tumor growth. T cells that have been modified with CAR-T were injected through the tail vein on days 0 and 7 after the tumor reached a certain volume. Afterward, the mice were treated with anti-PD-1 antibody on the 0th, 4th, 8th, and 12th days to increase the effectiveness of CAR-T. So that the volume and weight of the tumor can be measured.

Measurement of Mouse Volume and Weight

Based on the research that has been done in general, tumor cells that have been induced into mice through mouse xenograft models will be observed by researchers to determine the volume and weight of mice after treatment. This is the most important indicator to be carried out by researchers to be able to obtain conclusions whether the gene in CAR-T cells can have good effectiveness in cell therapy for patients with Non-Small Lung Cancer (NSLC). Measurements were made on tumors found in mice periodically.

In the research of Jie et al., (2021) the method of measuring tumor volume used is using calipers to monitor tumor growth by measuring the length and width of the tumor found in test mice. This tumor volume can be calculated using the formula V = 0.5 x Length x width2. This measurement was carried out for 60 days periodically and analyzed the data obtained to determine the efficacy of CAR-T PTK7-CAR2 cell therapy. Calipers or what is known as a caliper is a measuring instrument that has accuracy

exceeding the measuring ruler which consists of two main scales and a nonius scale (Mufarrih *et al*., 2022).

The measurement method carried out by researchers Zhang *et al*., (2019) is the measurement of lung weight in mice that have been injected with A549-EGFRvIII tumor cells through the mouse tail. Tumor weight data obtained using statistical testing, namely the One Way-ANNOVA test. This test is done by calculating the average of tumor weights in test mice.

Meanwhile, in the research of Toyofuku et al., (2024) the measurement method used was Bioluminescence Imaging (BLI) irradiation. This study uses BLI to measure the bioluminescence of tumor cells expressed by luciferase, which allows for non-invasive visualization and quantification of tumor growth. Tumor cells expressed by luciferase are incubated with a luciferin substrate, and the light emitted and measured using an imaging system such as IVIS (In Vivo Imaging System) spectrum. The intensity of the measured bioluminescence will correlate with the number of tumor cells present so that a determination can be made of the size and growth of the tumor present in the treated mice.

Mechanism of Action of CAR-T Cells

CAR-T (Chimeric Antigen Receptor T-cell) cell therapy is an immunotherapy approach that involves genetically engineering a patient's T cells to recognize and attack cancer cells. Generally, the process starts with T cells being harvested from the patient's blood. The T cells are then genetically engineered in the laboratory to express a chimeric antigen protein (CAR) on their surface. These CARs are specifically designed to recognize specific protein receptors expressed by cancer cells. One common example is the CD19 antigen, which is often found on blood cancer cells such as acute lymphoblastic leukemia (ALL). Once engineered, these altered T cells are multiplied in large numbers and then injected back into the patient or inoculated into animal models. The infused CAR-T cells will direct and bind to specific receptors on the cancer cells, triggering an immune response that destroys the cancer cells (Maude *et al*., 2018).

Conclusion

Based on the results of a literature review of 7 journals that have been used. It can be concluded that the use of CAR-T cell therapy has the potential for excellent efficacy against therapeutic treatment for Non-Small Lung Cancer (NSLC). This study uses several different target genes which will then be transferred into T cells to be expressed into CAR-T cells with specific targets. The gene transfer methods used were various including piggyback transposon system, bicistronic vector, leviral vector, lentivirus vector, and retrovirus vector.

This study was tested using a mouse model using the mouse xenograft method to inject the target CAR-T cells that had been made through the mouse tail. Indicators of the success of the test were obtained from the results of measuring the length and width of the tumor using calipers, measuring the weight by calculating the average weight of the mice with the help of one-way Annova statistical tests and Bioluminescence Imaging (BLI) irradiation to determine the size and growth of the tumor.

References

[1] Aljnefaie, A., Albogami, S., Asiri, Y., Ahmad, T., Alotaibi, S. S., Al-Sanea, M. M., & Althobaiti, H. (2022). Chimeric Antigen Receptor T-Cells: An Overview of Concepts, Applications, Limitations, and Proposed Solutions. *Frontiers in Bioengineering and Biotechnology*, *10*(June), 1–32. https://doi.org/10.3389/fbioe.2022.797440

[2] Buana, I., & Harahap, D. A. (2022). Asbestos, Radon Dan Polusi Udara Sebagai Faktor Resiko Kanker Paru Pada Perempuan Bukan Perokok. *AVERROUS: Jurnal Kedokteran dan Kesehatan Malikussaleh*, *8*(1), 1. https://doi.org/10.29103/averrous.v8i1.7088

[3] Duma, N., Santana-Davila, R., & Molina, J. R. (2019). Non–Small Cell Lung Cancer: Epidemiology, Screening, Diagnosis, and Treatment. *Mayo Clinic Proceedings*, *94*(8), 1623–1640. https://doi.org/10.1016/j.mayocp.2019.01.013

[4] Harahap, S. P., Sutandyo, N., Rumende, C. M., & Shatri, H. (2016). Perbandingan Rejimen Kemoterapi Cisplatin Etoposide dengan Cisplatin-Docetaxel dalam Hal Kesintasan 2 Tahun dan Progression-Free Survival Pasien Kanker Paru Stadium Lanjut Jenis Non-Small Cell. *Jurnal Penyakit Dalam Indonesia*, *3*(2), 67. https://doi.org/10.7454/jpdi.v3i2.11

[5] Hu, Z., Zheng, X., Jiao, D., Zhou, Y., Sun, R., Wang, B., Tian, Z., & Wei, H. (2020). LunX-CAR T Cells as a Targeted Therapy for Non-Small Cell Lung Cancer. *Molecular Therapy Oncolytics*, *17*(June), 361–370. https://doi.org/10.1016/j.omto.2020.04.008

[6] Jie, Y., Liu, G., Feng, L., Li, Y., Mingyan, E., Wu, L., Li, Y., Rong, G., Li, Y., Wei, H., & Gu, A. (2021). PTK7-Targeting CAR T-Cells for the Treatment of Lung Cancer and Other Malignancies. *Frontiers in Immunology*, *12*(August), 1–15. https://doi.org/10.3389/fimmu.2021.665970

[7] Joseph, J., & Rotty, L. W. A. (2019). Pulmonary Edema Occurring after Nitric Acid Exposure. *Case Reports in Emergency Medicine*, *2019*(1), 1–4. https://doi.org/10.1155/2019/9303170

[8] Li, H., Harrison, E. B., Li, H., Hirabayashi, K., Chen, J., Li, Q. X., Gunn, J., Weiss, J., Savoldo, B., Parker, J. S., Pecot, C. V., Dotti, G., & Du, H. (2022). Targeting brain lesions of non-small cell lung cancer by enhancing CCL2-mediated CAR-T cell migration. *Nature Communications*, *13*(1), 1–12. https://doi.org/10.1038/s41467-022-29647-0

[9] Li, H., Huang, Y., Jiang, D. Q., Cui, L. Z., He, Z., Wang, C., Zhang, Z. W., Zhu, H. L., Ding, Y. M., Li, L. F., Li, Q., Jin, H. J., & Qian, Q. J. (2018). Antitumor activity of EGFR-specific CAR T cells against non-small-cell lung cancer cells in vitro and in mice. *Cell Death and Disease*, *9*(2). https://doi.org/10.1038/s41419-017-0238-6

[10] Liu, H., Ma, Y., Yang, C., Xia, S., Pan, Q., Zhao, H., Fang, W., Chen, X., Zhang, Y., Zou, B., Li, Q., Wan, Y., Chen, H., Tang, Y., Zhao, J., Weng, D., Xia, L., Zhang, L., & Xia, J. (2020). Severe delayed pulmonary toxicity following PD-L1–specific CAR-T cell therapy for non-small cell lung cancer. *Clinical and Translational Immunology*, *9*(10), 1–11. https://doi.org/10.1002/cti2.1154

[11] Maude, S. L., Laetsch, T. W., Buechner, J., Rives, S., Boyer, M., Bittencourt, H., Bader, P., Verneris, M. R., Stefanski, H. E., Myers, G. D., Qayed, M., De Moerloose, B., Hiramatsu, H., Schlis, K., Davis, K. L., Martin, P. L., Nemecek, E. R., Yanik, G. A., Peters, C., … Grupp, S. A. (2018). Tisagenlecleucel in Children and Young Adults with B-Cell Lymphoblastic Leukemia. *New England Journal of Medicine*, *378*(5), 439–448. https://doi.org/10.1056/nejmoa1709866

[12] Milone, M. C., & O'Doherty, U. (2018). Clinical use of lentiviral vectors. *Leukemia*, *32*(7), 1529–1541. https://doi.org/10.1038/s41375-018-0106-0

[13] Mufarrih, A., Harijono, A., Qosim, N., & Gumono. (2022). Pelatihan Penggunaan Jangka Sorong Siswa Madrasah Aliyah Singosari. *Jurnal Pengabdian Masyarakat*, *1*(10), 1156–1163.

[14] Prasetyo, D. Y., & Suprayitno, E. (2021). Faktor Kualitas Hidup Pasien Kanker. *Care: Jurnal Ilmiah Ilmu Kesehatan*, *9*(2), 322–333. https://jurnal.unitri.ac.id/index.php/care

[15] Punamawati, Tandrian, C., Sumbayak, E. M., Kertadjaya, W., Anatomi, H., Kedokteran, F., Fkik, K., Krida, K., Ukrida, W., Kedokteran, F., Fkik, K., Kristen, U., & Wacana, K. (2020). Analisis Kejadian Kanker Paru Primer di Indonesia pada Tahun 2014-2019 Literature Review : Analysis of Primary Lung Cancer Incidence in Indonesia Data from 2014-2019. *Jurnal Kedokteran MEDITEK*, *27*(2), 164–172.

[16] Rahayuwati, L., Rizal, I. A., Pahria, T., Lukman, M., & Juniarti, N. (2020). Pendidikan Kesehatan tentang Pencegahan Penyakit Kanker dan Menjaga Kualitas Kesehatan. *Media Karya Kesehatan*, *3*(1), 59–69. https://doi.org/10.24198/mkk.v3i1.26629

[17] Ramos-Cardona, X. E., Luo, W., & Mohammed, S. I. (2022). Advances and challenges of CAR T therapy and suitability of animal models (Review). *Molecular and Clinical Oncology*, *17*(3), 1–11. https://doi.org/10.3892/mco.2022.2567

[18] Sung, H., Ferlay, J., Siegel, R. L., Laversanne, M., Soerjomataram, I., Jemal, A., & Bray, F. (2021). Global Cancer Statistics 2020: GLOBOCAN Estimates of Incidence and Mortality Worldwide for 36 Cancers in 185 Countries. *CA: A Cancer Journal for Clinicians*, *71*(3), 209–249. https://doi.org/10.3322/caac.21660

[19] Toyofuku, T., Ishikawa, T., Nojima, S., & Kumanogoh, A. (2024). Efficacy against Lung Cancer Is Augmented by Combining Aberrantly N-Glycosylated T Cells with a Chimeric Antigen Receptor Targeting Fragile X Mental Retardation 1 Neighbor Toshihiko. *The Journal of Immunology*, *212*, 917–927.

[20] Wang, A., Lv, T., & Song, Y. (2023). Tandem CAR-T cells targeting MUC1 and PSCA combined with anti-PD-1 antibody exhibit potent preclinical activity against non-small cell lung cancer. *Cellular Immunology*, *391–392*(June), 104760. https://doi.org/10.1016/j.cellimm.2023.104760

[21] Yu, T., Nie, F. Q., Zhang, Q., Yu, S. K., Zhang, M. L., Wang, Q., Wang, E. X., Lu, K. H., & Sun, M. (2024). Effects of methionine deficiency on B7H3-DAP12-CAR-T cells in the treatment of lung squamous cell carcinoma. *Cell Death and Disease*, *15*(1), 1–13. https://doi.org/10.1038/s41419-023-06376-w

[22] Zhang, Z., Jiang, J., Wu, X., Zhang, M., Luo, D., Zhang, R., Li, S., He, Y., Bian, H., & Chen, Z. (2019). Chimeric antigen receptor T cell targeting EGFRvIII for metastatic lung cancer therapy. *Frontiers of Medicine*, *13*(1), 57–68. https://doi.org/10.1007/s11684-019-0683-y