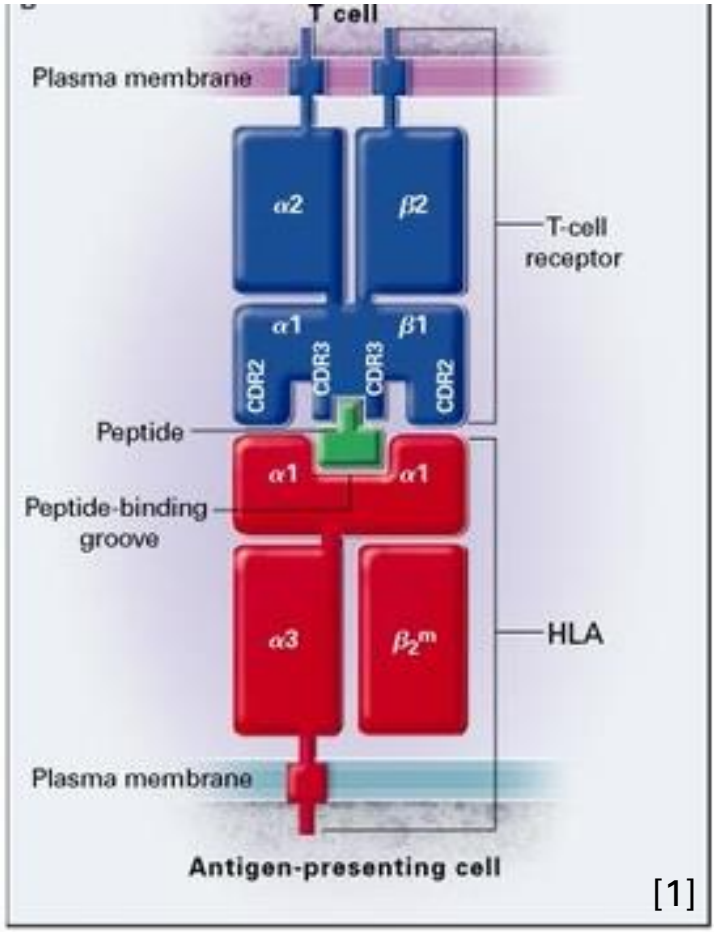
CAR T-cell Therapy for Lung Cancer

JOSEPH BUBAK

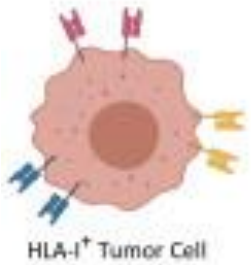
New Receptor Target for CAR T-cell Therapy

Human leukocyte antigen (HLA) Loss of Heterozygosity (LOH)



[1]

Genetic defects in HLA expression



LOH at Chromosome 6

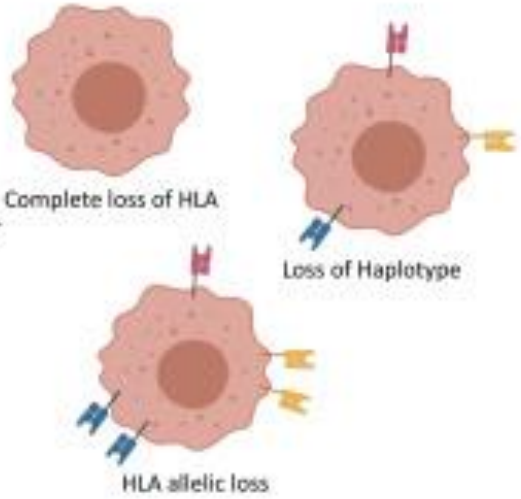
LOH at Chromosome 15

HLA-I heavy chain mutations

B2M mutations

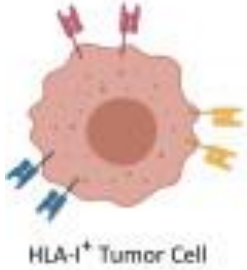
IFN pathway defects

Mutations in any gene involved in antigen presentation



HLA-I expression not recoverable by conventional pharmacological interventions (hard mutations)

Non-genetic defects in HLA expression



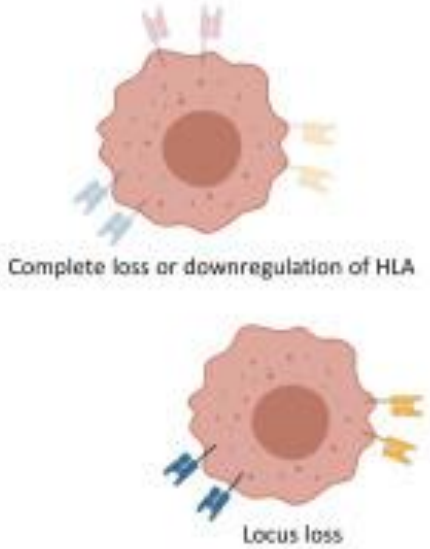
Transcriptional downregulation of HLA-I genes

Downregulation of APM

Hypermethylation, deacetylation

Autophagy degradation

Stress and hypoxia



Cytokine treatment

DNA Methyltransferase inh.

Transcriptional regulators

Autophagy inhibitors

HLA-I expression potentially recoverable with drugs or cytokines (soft mutations)

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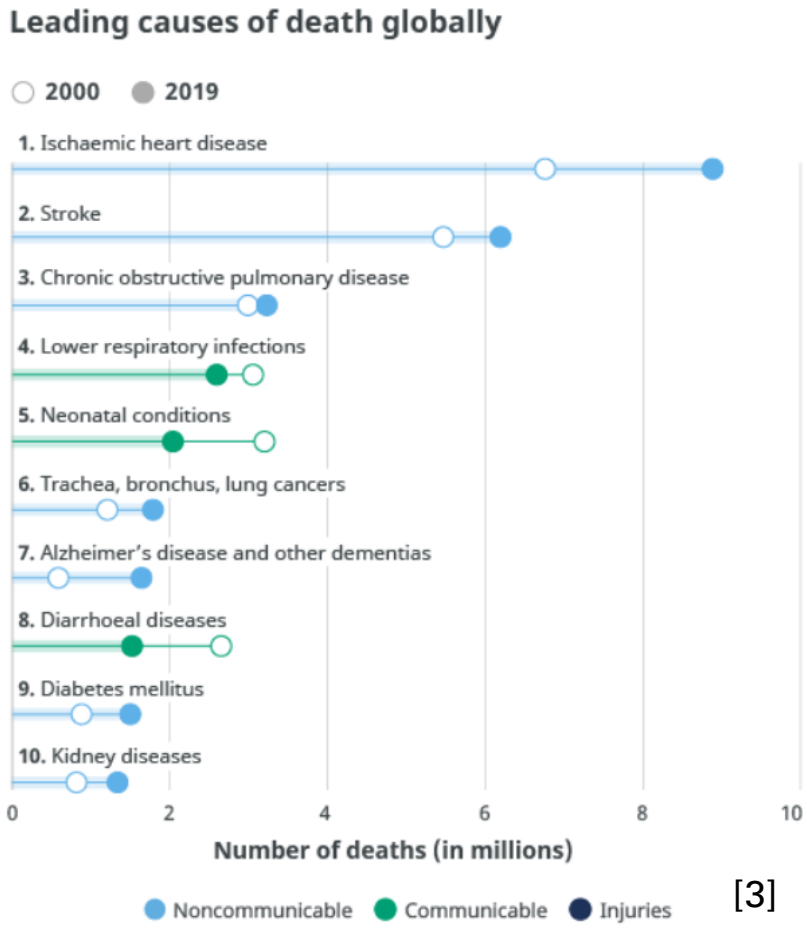
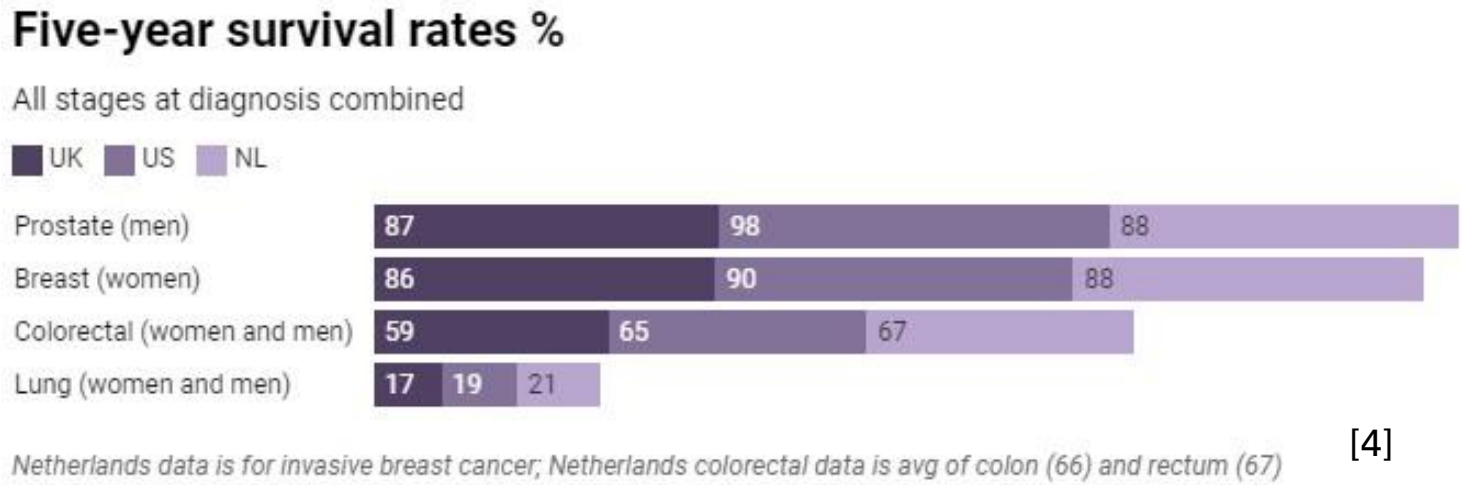
Why is Lung Caner such a Problem?



[3]

2^{nd} most common cancer in the world



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Motivation to use CAR T-cell Therapy

Target population in first-world countries

Rough estimate of 6-7 million people with lung cancer

Approximately $400,000 per year

Current Solutions for Lung Cancer

Surgery

Radiotherapy

Chemotherapy

Osimertinib

Immune checkpoint inhibitors (ICIs)

Gaps in Coverage

Late-stage lung cancer

Low response rate

Design Criteria

Tumor reduction

Manufacturability

Efficacy

Prevalence of receptors

CAR T-cell toxicity

Will the Therapy Work?

Mice models show tumor reduction

Pre-clinical study shows manufacturing time can be 1 day

Clinical trials of combination therapy

Observational clinical trial

Cells with non-functioning HLA undergo apoptosis

Validation

Report Coverage	Details
Market Size	US$ 21.0 Billion by 2030
Growth Rate	CAGR of 31.2% from 2022 to 2030
Largest Market	North America
Fastest Growing Market	Asia Pacific
Base Year	2021
Forecast Period	2022 to 2030
Segments Covered	Product Type, Indication,End-user, Target Antigen and Region,
Companies Mentioned	Pfizer, Inc., Novartis AG, Bristol-Myers Squibb, Amgen, Inc., Sorrento Therapeutics, Inc., Johnson & Johnson Services, Inc., Gilead Sciences, Inc., Merck & Co., Inc., and bluebird bio, Inc.

[5]

Sources

[1] Klein, Jan, and Akie Sato. “The HLA System.” *New England Journal of Medicine*, vol. 343, no. 10, 2000, pp. 702–709., https://doi.org/10.1056/nejm200009073431006.

[2] Hazini, Ahmet, et al. “Deregulation of HLA-I in Cancer and Its Central Importance for Immunotherapy.” *Journal for ImmunoTherapy of Cancer*, vol. 9, no. 8, 2021, https://doi.org/10.1136/jitc-2021-002899.

[3] “The Top 10 Causes of Death.” *World Health Organization*, World Health Organization, 9 Dec. 2020, https://www.who.int/news-room/fact-sheets/detail/the-top-10-causes-of-death.

[4] “Cancer Survival Statistics: World Cancer Research Fund International.” *WCRF International*, 11 July 2022, https://www.wcrf.org/cancer-trends/cancer-survival-statistics/.

[5] “Car T-Cell Therapy Market (Product Type: Axicabtagene CILOLEUCEL, Tisagenlecleucel, Brexucabtagene Autoleucel, Lisocabtagene Maraleucel, Idecabtagene Vicleucel, and Others; Indication: Acute Lymphocytic Leukemia, Diffuse Large B-Cell Lymphoma, Mantle Cell Lymphoma, Follicular Lymphoma, Multiple Myeloma, and Others; and End-User: Hospitals and Cancer Treatment Centers) - Global Industry Analysis, Size, Share, Growth, Trends, and Forecast, 2022-2030.” *CAR T-Cell Therapy Market to Exceed Valuation of US$ 21 Bn by 2030*, Nova One Advisor, 3 May 2022, https://www.novaoneadvisor.com/report/car-t-cell-therapy-market.