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Immunotherapy for cancer treatment: CAR-T cells against pancreatic adenocarcinoma

Introduction

Pancreatic adenocarcinoma is a cancer with a very bad prognostic due to its usually late diagnosis. CAR-T cell therapy may be a promising option, though it has many problems against solid tumors.

Materials and methods

Bibliographical research



Interview with a professional researcher

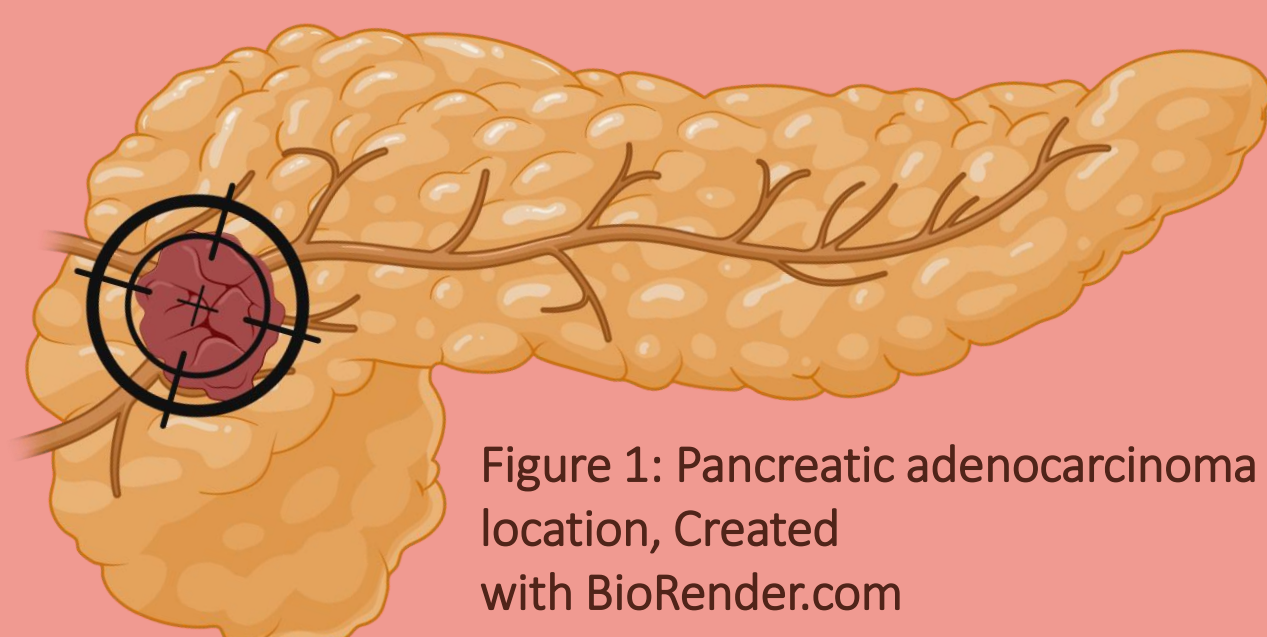
Manel Juan Otero, MD and PhD specialized in immunology

Objectives

- Make a brief introduction to pancreatic adenocarcinoma
- Explain CAR-T cell treatment theoretical framework and their application to treat cancer
- State solid tumors challenges to CAR-T cell treatment, proposed solutions and the actual situation for pancreatic adenocarcinoma treatment with CAR-T cells

Results: CAR-T cells challenges against solid tumors and possible solutions

Tumor location



Hard to locate :

- TAAs
- Antigen downregulation
- Low-affinity CARTs
- Dual CARTs

Tumor infiltration

Physical and chemical barriers

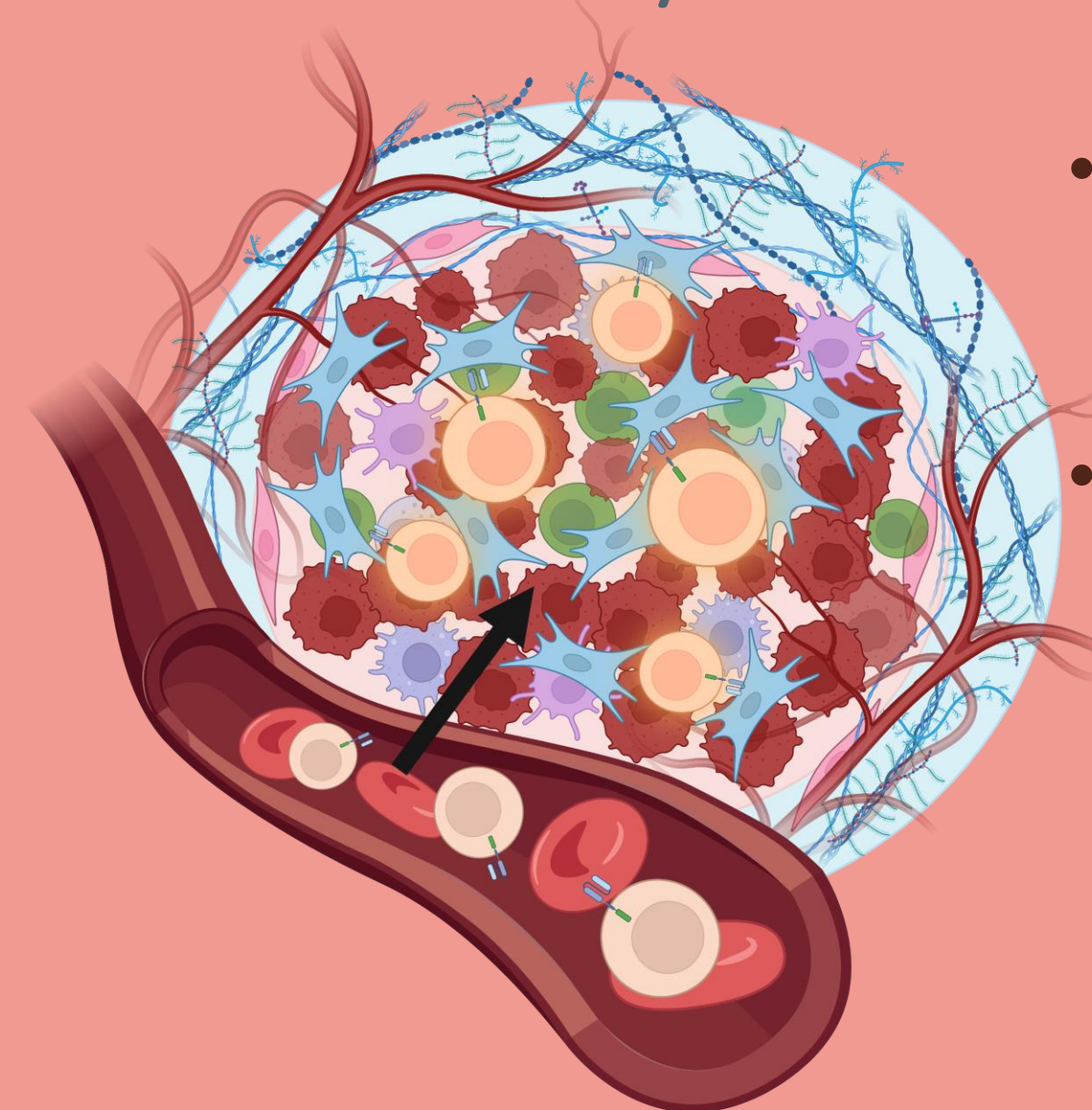


Figure 2: Tumor infiltration, Created with BioRender.com

- Direct CARTs/cytokines delivery
- CARTs against the TME

Survival and activity

Immunosuppressive TME

- TME-tolerant CARTs
- Checkpoint/transcription factor alteration
- Cytokine delivery
- Antiinflammatory cells depletion

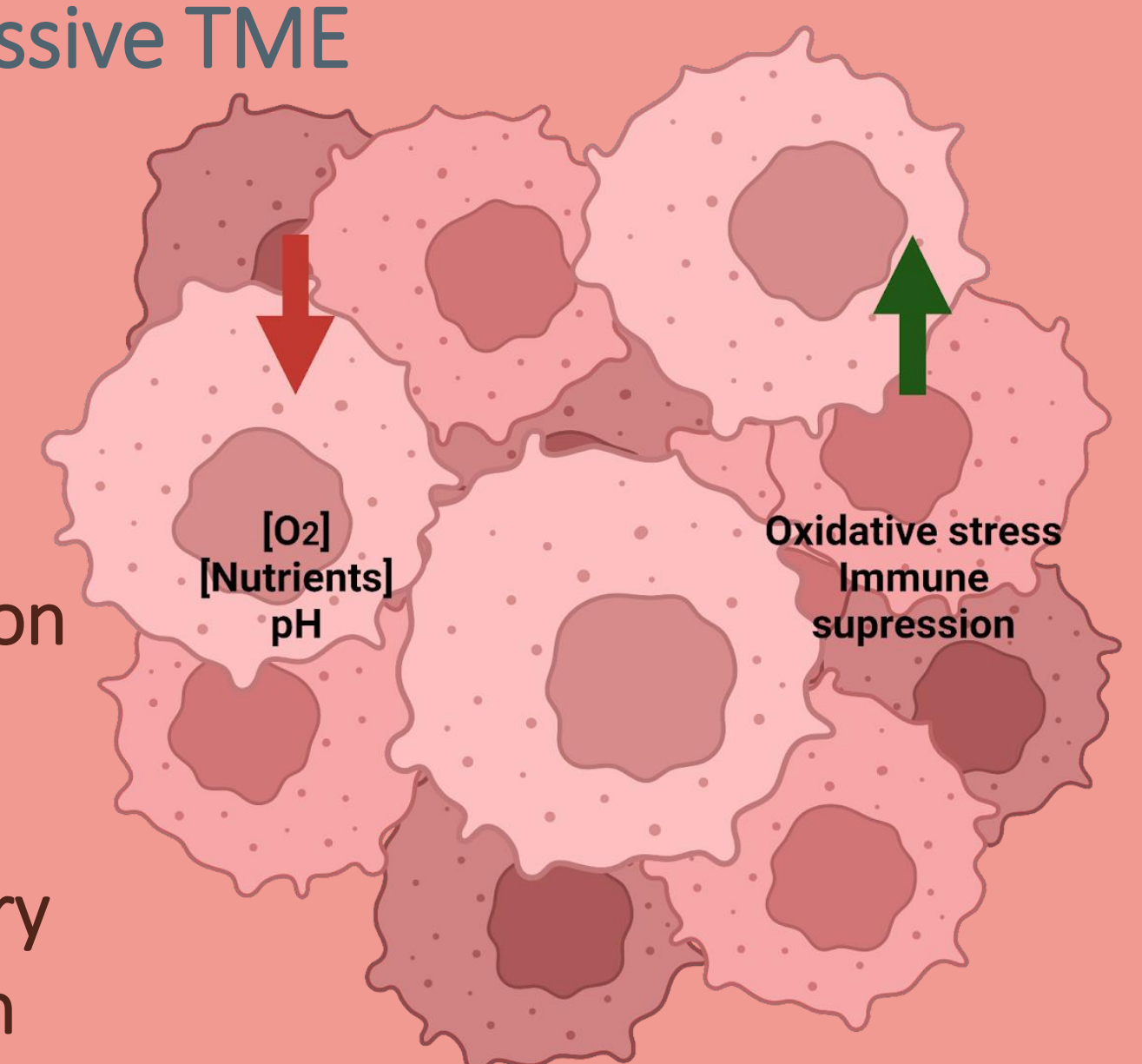


Figure 3: Tumor microenvironment (TME), Created with BioRender.com

Non-accurate animal models

Differences between animal models and human TME

Post-infusion safety methods

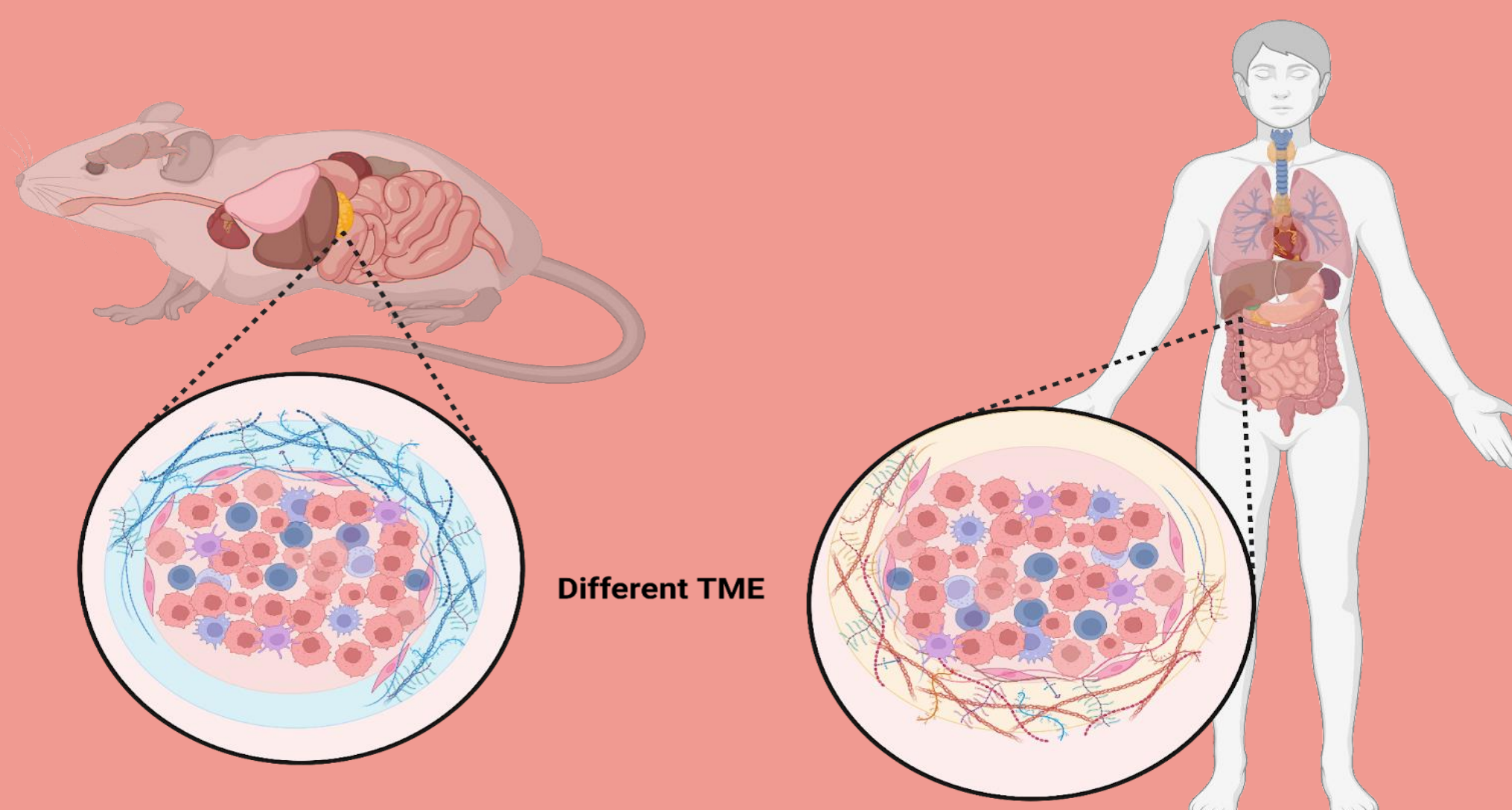


Figure 4: Human and mouse TME comparison, Created with BioRender.com

CAR-T cell toxicity

OTOT, CRS, ICANs

- CARTs fine-tuning/logic gating/direct delivery
- Supportive treatments

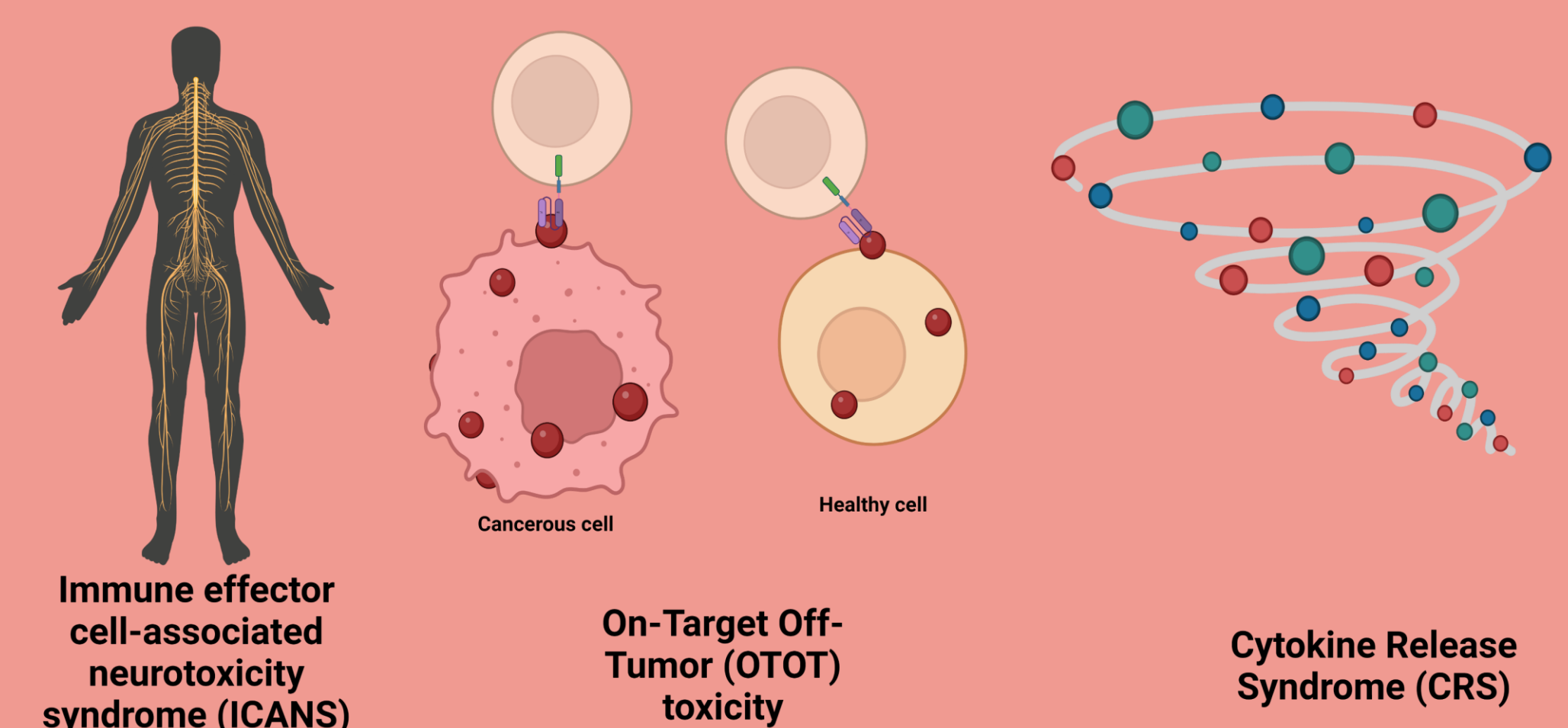


Figure 5: CAR-T cell treatment toxicities, Created with BioRender.com

Conclusions

Although promising, CAR-T cell treatment against pancreatic adenocarcinoma still has a long way to go before it overcomes its difficulties. However, there are many proposed solutions to the raised problems and it may be just a question of time.

Selected bibliography

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- Raj, D., Nikolaidi, M., Garces, I., Lorzio, D., Castro, N. M., Caiafa, S. G., Moore, K., Brown, N. F., Kocher, H. M., Duan, X., Nelson, B. H., Lemoine, N. R., & Marshall, J. F. (2021). CEACAM7 Is an Effective Target for CAR T-cell Therapy of Pancreatic Ductal Adenocarcinoma. *Clinical Cancer Research*, 27(5), 1538–1552. <https://doi.org/10.1158/1078-0432.ccr-19-2163>