



LUND UNIVERSITY

Potential immunoregulatory role of T and dendritic cells in cancer

Investigations based on transcriptional analysis

Abolhalaj, Milad

2021

Document Version:
Other version

[Link to publication](#)

Citation for published version (APA):

Abolhalaj, M. (2021). *Potential immunoregulatory role of T and dendritic cells in cancer: Investigations based on transcriptional analysis*. Department of Immunotechnology, Lund University.

Total number of authors:

1

General rights

Unless other specific re-use rights are stated the following general rights apply:

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal

Read more about Creative commons licenses: <https://creativecommons.org/licenses/>

Take down policy

If you believe that this document breaches copyright please contact us providing details, and we will remove access to the work immediately and investigate your claim.

LUND UNIVERSITY

PO Box 117
221 00 Lund
+46 46-222 00 00

Popular science summary

Cancer is a complex disease which may be caused by different factors such as genetic background and lifestyle. Immune cells are responsible for accurate recognition and killing of cancer cells. Some cancer treatments such as chemotherapy cause unwanted side-effects, as they target all dividing cells no matter if they are cancer cells or normal cells. Additionally, treatments like chemotherapy are often not able to fully eradicate all cancer cells as some cancer cells evolve to develop resistance and cause tumor reoccurrence. Therefore, the accuracy of our immune system has been used to treat cancer, what we today know as immunotherapy.

There are several immune cells that are critical for combating cancer cells. For instance, so-called *T cells* are responsible for the direct killing of cancer cells and so-called *dendritic cells* help *T cells* identify cancer cells by presenting cancer cell molecules to *T cells*. These communications among different immune cells within the tumors occur through many complicated molecular interactions where one cell type communicates a signal to the other type. We also know that cancer cells can evolve to escape the immune response by using these molecules which can communicate negative signals to immune cells. For example, cancer cells can take advantage of a surface molecule and communicate a suppressing signal to T cells via a complimentary molecule on their surface, thus, inhibiting their killing function. Therapy using so-called *immune checkpoint blockade* blocks this type of interaction and as a result, *T cells* can evade the suppression imposed by cancer cells. This type of therapy has shown very outstanding clinical results in the treatment of some cancer patients and two of the pioneer researchers in this field have won a Noble Prize in 2018 for their contribution to this therapy. However, thanks to decades of research, we now know that inhibitory mechanisms vary among tumor types and this is the major underlying reason why only a portion of cancer patients benefit from prolonged clinical benefits of targeted therapy.

This thesis's objective is to extend current knowledge on *T cells* and *dendritic cell* subsets in head and neck cancers, acute myeloid leukaemia, and bladder cancer with the aim to understand if they are present in these tumors, they properties, and the mechanisms affecting their immune duties. As a result, this thesis shows presence of four populations of *dendritic cells* in head and neck tumors. Additionally, it also shows that some of the *dendritic cells* may be hijacked by cancer settings and help cancer cells escape immune response while others can contribute to promotion of immune response against cancer cells. These

differences highlight the importance of selective targeting of different *dendritic cell* subpopulations. In this theme, investigation of active genes in different subpopulations of *dendritic cells* in head and neck cancer suggests several different molecules on the surface of each *dendritic cell* subpopulation. These molecules may be used to either activate *dendritic cells* or facilitate delivery of tumor molecules by targeted therapy so that they can present them to *T cells*. This presentation can subsequently enable *T cells* to specifically recognize tumor cells and kill them. For example, selective presence of two of these molecules on a subpopulation of *dendritic cells* in head and neck cancer is shown by this thesis, suggesting a possibility for specific targeting of this subpopulation in such tumors for delivery of tumor molecules. Additionally, further investigation of active genes in *dendritic cells* in head and neck cancers provided by this thesis may uncover additional inhibitory mechanism in these tumors, paving the way for new therapeutic interventions which may restore immunity.

T cells in acute myeloid leukaemia and bladder tumors is another focus of this thesis. This thesis shows that the economy of energy in anticancer *T cells* is negatively affected in acute myeloid leukemia and bladder cancer, which may be one the reasons why they are not able to kill cancer cells. In contrast, a type of *T cell* with inhibitory roles was shown to have increased abilities to produce energy in acute myeloid leukemia patients. Thus, contributing factors to such differences in the management of energy between suppressive *T cells* and the *T cells* that can kill cancer cells may be investigated further as a ground for more novel therapeutic approaches. Furthermore, several inhibitory molecules on the surface of anticancer *T cells* of acute myeloid leukemia and bladder cancer patients were identified which may be explored as drug targets for reactivation of such *T cells*. It was also observed that these molecules are higher in anticancer *T cells* in bladder tumors that attack the underlying muscle as compared to non-muscle invasive tumors and control non-malignant bladder tissue. This suggests that blockade of these molecules could be more useful in muscle-invasive bladder cancer. Finally, further investigation of genes shown to be active in *T cells* in acute myeloid leukemia and bladder cancer patients may provide insight into the additional immunoregulatory mechanisms in these cancers, contributing to improved therapeutic interventions that can restore the impaired function of T cells.