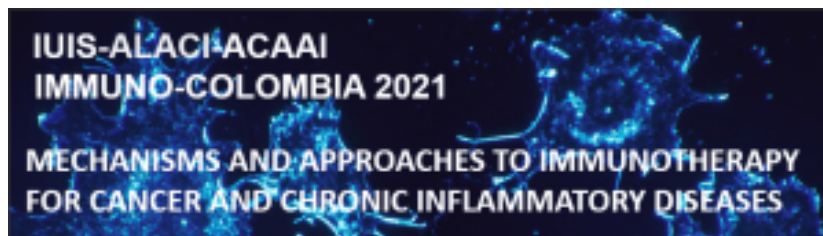
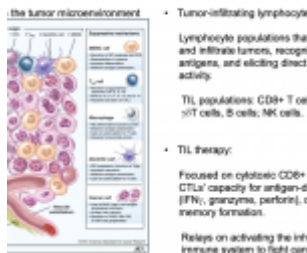


Immuno-Colombia: Tumour infiltrating lymphocyte therapy (Part 1)

Tumour infiltrating lymphocytes (TIL) therapy



[IUIS-ALACI-ACAAI](#)
[Immuno-Colombia 2021](#)
[course took place](#)
[remotely between 5th](#)
[to 16th April. The](#)

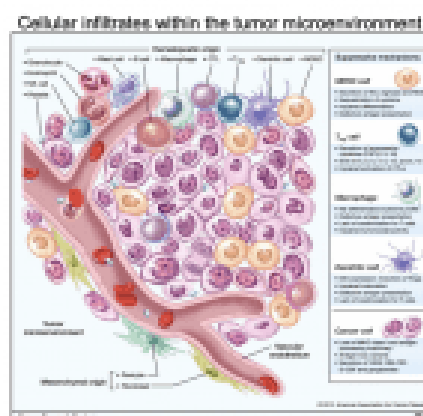
[theme of this meeting was “Mechanisms and Approaches to Immunotherapy for Cancer and Chronic Inflammatory Diseases”.](#)

This article highlights a talk by Professor Soraya Zorro which focused on Tumour Infiltrating Lymphocytes (TIL) therapy.

Professor Soraya Zorro began her lecture with an overview of TILs and TILs therapy. TILs are lymphocyte populations that migrate to and infiltrate the tumour. These

lymphocytes recognise specific antigens, elicit direct and indirect cytotoxic activity. The main populations that can be found infiltrating in the tumour microenvironment are CD8+ T cells, CD4+ T cells, $\gamma\delta$ T cells, B cells and NK cells. TIL therapy predominantly uses cytotoxic CD8+ T cells (CTLs) as

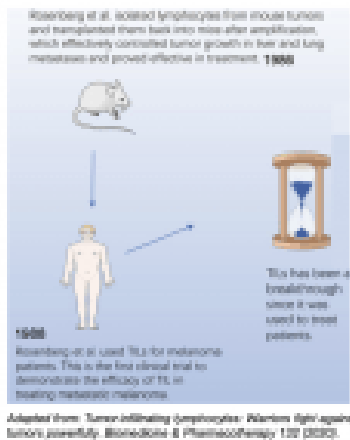
Tumour infiltrating lymphocytes (TIL) therapy



- Tumor-infiltrating lymphocytes (TIL):
Lymphocyte populations that have migrated to and infiltrate tumors, recognizing tumor specific antigens, and eliciting direct and indirect cytotoxic activity.
TIL populations: CD8+ T cells, CD4+ T cells, $\gamma\delta$ T cells, B cells; NK cells.
- TIL therapy:
Focused on cytotoxic CD8+ T cells (CTLs). CTLs' capacity for antigen-directed cytotoxicity (IFN γ , granzyme, perforin), clonal expansion and memory formation.
Relays on activating the inherent power of the immune system to fight cancer.

agents of immunotherapy, due to their antigen-specific cytotoxicity, clonal expansion, and memory formation.

The development of TIL therapy



- A type of adoptive cell therapy for cancer treatment (solid tumors). Developed at the U.S. National Cancer Institute by Dr. Steven A. Rosenberg.
- ACT requires prior lymphodepletion for optimal antitumor effect.
 - *Elimination of regulatory cells.
 - *Reduction of CK links, competitors for homeostatic CK8 (IL-7, IL-15; IL-21).
 - *Induction of tumor apoptosis/necrosis → release of tumor antigens → APC activation.
- IL-2 administration enhances *in vivo* ACT with T cells already expanded in IL-2.

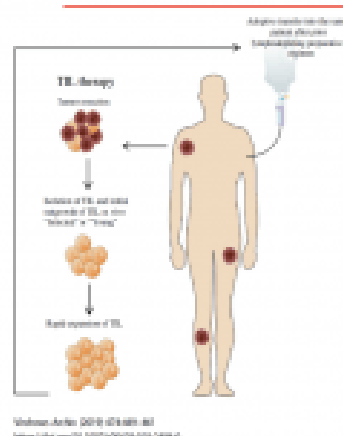
Next, she gave an overview of how Dr. Steven A. Rosenberg and colleagues developed the TIL therapy ([Lin B. et al., 2020](#)), using pre-clinical murine studies. During

his studies lymphocytes were isolated from mouse tumours and transplanted back into mice after amplification, effectively controlling tumour growth in liver and lung metastases. In 1988, the technique was used to treat melanoma patients enrolled in clinical trials. During the clinical trial, TIL therapy was made more effective by including prior lymphodepletion for optimal anti-tumour effect and IL-2 administration to enhance *in vivo* activation of T cells.

Prof Zorro then discussed immunotherapy is administered, specifically how anti-tumour T cells isolated from tumours are expanded *ex-vivo* and infused back into the same patient ([Rohaam M. W., Wilgenhof S., Haanen J. B. A. G., 2018](#)).

TILs represent a rich source of tumour-reactive clones, and high levels of CD8 TILs have been shown to correlate with a better clinical response. Currently, TIL therapy is only

TIL therapy



- Based on T cells isolated from tumors, expanded *ex-vivo* and infused back into the same patient.
- TILs represent a rich source of tumor-reactive clones (TAAs, CGAs and neoantigens).
- High CD8 TIL levels: associated with better prognosis and response to immunotherapy (melanoma, CRC); TIL products rich in CD8 T cells correlates with better clinical response.
- Metastatic melanoma patients treated with TIL: ~40%-50% clinical response (10-20% complete response).
- TIL therapy is an option for patients with solid metastatic tumors who have failed other therapies: clinical trials; seeking for FDA approval.

accessible to patients who have had unsuccessful cancer therapies and agree to enrol in clinical trials to access the cutting edge therapy. Another aspect that was raised during the lecture was the fact that TIL Therapy may not be an option for every type of cancer, to be a good candidate it is necessary to seek for tumours with a high mutational burden ([Martincorena I. and Campbell P.J., 2015](#)), and have a high proportion of TILs, and a diverse and reactive T cell repertoire.

In the next article, we shall discuss how cells for TIL therapy are produced, considerations for TIL therapy and utility of TIL therapy with other cancer immunotherapies.

- Interested in learning more about TILs: read advanced pre-course material on [Tumor-infiltrating Lymphocytes \(TIL\)](#)
- [Full lecture recording available at IUIS-ALACI-ACAAI Immuno-Colombia 2021 Lecture week 2](#)

Summary by Carla Sanzochi Fogolin