Project number 1

The role of IL-17A-IL-17RA signaling in chronic lung allograft dysfunction

[1] Research group

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Expenditure report of research funds: Consumables 130,000YEN

[2] Research setup

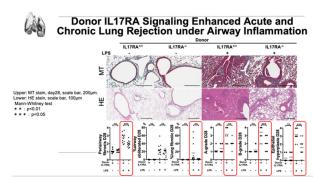
Chronic lung allograft dysfunction (CLAD) limits long term survival after lung transplantation. The purpose of this research is to investigate the mechanism of CLAD with mouse model of lung transplantation.

We had online meetings every 2 weeks. We have published a paper in JCI insight. Also, we will present another project at the International Society for Heart and Lung transplantation annual meeting 2024 at Prague.

[3] Research outcomes

(3-1) Results

This year, we have published a paper about IL-17A/IL17RA signaling in mouse CLAD model. We are analyzing RNA samples from two distinct mouse CLAD model. This work will provide profound understanding of mythical mechanism of CLAD. Also, we are discussing how we can connect mouse data and human CLAD lung data.



Donor I L-17RA signaling Enhances acute and chronic rejection

Summary Repeated Airway Inflammation TLR activation Air Space Airway Obliteration Airway Fibrosis Adaptive Immune Response Augmentation IL17RA on donor cells Epithelial Damage Repair Dysregulation

Summary of the paper

(3-2) Future perspectives

After publishment of previous works, we will work on followings;

- Further characterize innate immunity dependent mechanisms of CLAD by using mouse lung transplantation model.
- 2) Analyze our data by using RNAseq.
- 3) Link our findings generated with mouse model with the data obtained from human CLAD lung samples at Toronto General Hospital.

[4] List of research achievements

- (1) <u>Watanabe T</u>, Juvet SC, Berra G, Havlin J, Zhong W, Boonstra K, Daigneault T, Horie M, Konoeda C, Teskey G, Guan Z, Hwang DM, Liu M, Keshavjee S, <u>Martinu T</u>. Donor IL-17 receptor A regulates LPS-potentiated acute and chronic murine lung allograft rejection. JCI Insight. 2023 Nov 8;8(21):e158002.
- (2) <u>Watanabe T</u>, Lam C, Oliver J, Oishi H, Teskey G, Beber S, Boonstra K, Mauricio Umaña J, Buhari H, Joe B, Guan Z, Horie M, Keshavjee S, <u>Martinu T</u>, Juvet SC. Donor Batf3 inhibits murine lung allograft rejection and airway fibrosis. Mucosal Immunol. 2023 Apr;16(2):104-120.