Tumor growth suppression by releasing cancer immune suppression using an anti-CD25 antibody-immobilized material

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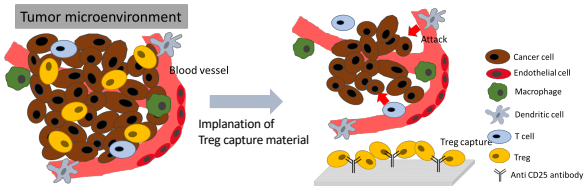
Introduction

T Regulatory T cell (Tregs) expressing CD4, CD25 and the transcription factor forkhead box P3 is one of immunosuppressive cells and roles on the regulation of immune reaction. Tregs play important roles in maintaining immunological self-tolerance and in suppressing excessive immune responses. For cancer, it is recently revealed that Treg cells suppress the activation of tumor-antigen–specific T cells. To evoke antitumor immunity, they can be one of the target cells, and reducing the number of Treg cells from cancer patients is an important treatment. Thus, the number of Treg cells should be selectively reduced from a cancer patient's body, e.g., peripheral blood, while retaining functional cells. Previously, we reported that an antibody-immobilized film could capture target cells effectively and selectively [1-3].

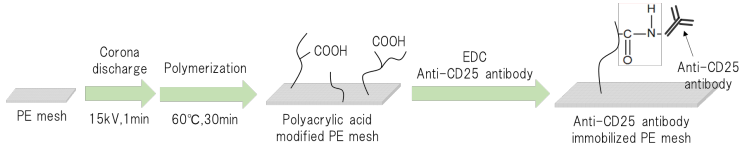
In this study, we proposed a removal of Tregs by implantation of anti-CD25 antibody-immobilized mesh. For this method, the anti-CD25 antibody-immobilized mesh was implanted around tumor of cancer-bearing mouse and the Treg accumulation on the mesh and tumor size was evaluated.

1. Kimura T. et al., Sens. Mater. 2016; 28(12): 1255-1264.
2. Kimura T. et al., J. Biomater. Sci. Polym. Ed. 2017; 28(10-12): 1172-1182.
3. Kimura T. et al., Sci. Tech. Adv. Mater. 2021; 22(1): 607-615.



Releasing of immune suppressive envirornment

Preparation of anti-CD25 antibody immobilized PE mesh



Acrylic acid conc. (%)	Methylene blue staining	Anti-CD25 antibody concentration[μg/mL]			
		0	0.5	5	50
0					
2					
5					

Fig.1 .Methylene blur staining of PAAc modified PE mesh and DAB staining of anti-CD25 antibody-immobilized PE mesh

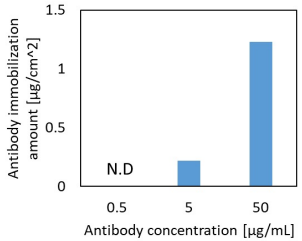


Fig.2 .Amount of anti-CD25 antibody on PE mesh.

➢ The anti-CD25 antibody-immobilized PE mesh (CD25-PE mech) was obtained.

In vitro Treg capture of the anti-CD25 antibody-immobilized PE mesh

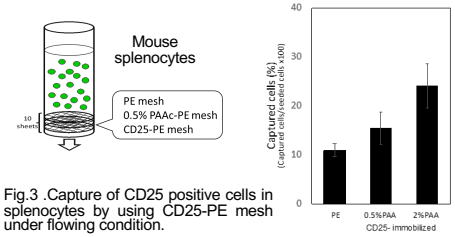


Fig.3 .Capture of CD25 positive cells in splenocytes by using CD25-PE mesh under flowing condition.

➢ CD25-PE mech could capture Tregs effectively under flow condition
➢ The capturing activity was increased with increasing amount of immobilized antibody.

Treg capture of the anti-CD25 antibody-immobilized PE mesh

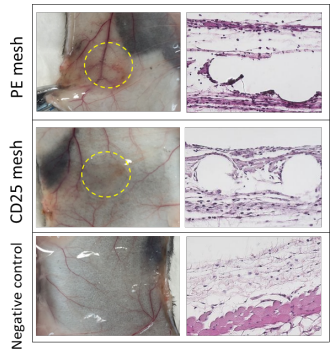


Fig. 4. Inflammatory response. HE staining of mouse subcutaneous PE mesh implantation

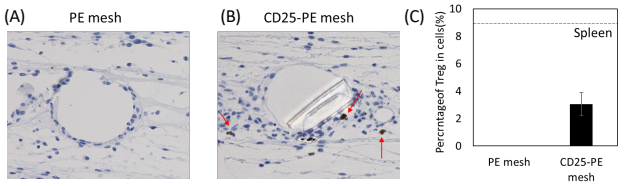
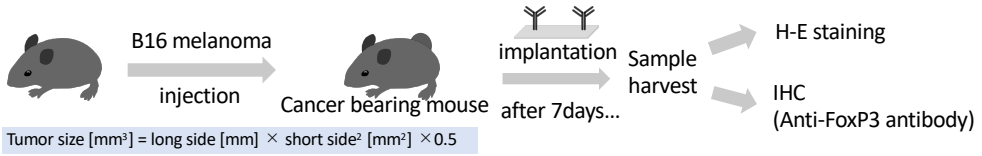


Fig. 5. (A), (B) FoxP3 immunostaining of mouse subcutaneously implanted PE mesh. (C) Number of Treg aroud the fibers of the implanted meshes (n=5).

➢ CD25-PE mesh showed anti-inflammation property
➢ Tregs accumulated around CD25-PE mesh in vivo

Tumor growth suppression using the anti-CD25 antibody-immobilized PE mesh



Tumor size [mm³] = long side [mm] × short side² [mm²] ×0.5

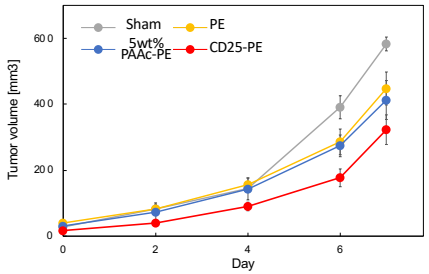


Fig. 6. Tumor growth following implantation of anti-CD25-PE meshes (n=3).

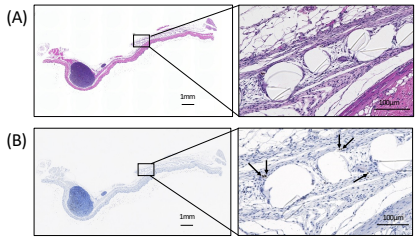


Fig.7. (A) H-E staining and (B) FoxP3 immunostaining of the CD25-PE meshes at 7 days after subcutaneous implantation into tumor-bearing mice.

➢ Tumor growth was decreased in the cases of implantation of various PE meshs compared with negative control (sham)
➢ Especially, the CD25-PE mesh induced dcrease in tumor growth effectively.

Conclusion

We synthesized a anti-CD25 antibody immobilized PE mesh. CD25-PE could capture Tregs effectively in vitro and in vivo. Also, the implanted CD25-PE around tumor prevented tumor growth, suggesting that the immune suppression in tumor microenvironment would be disordered. The antibody-immobilized material woud be applicable as a implantable immunomodulatory material.

Acknowledgements

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