In vivo mechanism of antibody-based immunotherapy

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Curriculum vitae

Heng Sheng Sow was born on 29th October 1986 in Kuala Lumpur, Malaysia. He received his bachelor's degree in Biotechnology in 2009 from UCSI University in Kuala Lumpur. In 2010, he started his master's degree in Cancer immunotherapy and biotechnology at the University of Nottingham, England where he started a research project on the humanization of novel anti-glycan antibody for human pancreatic cancer under the supervision of Dr Ian Spendlove. After obtaining his master's degree in 2011, he went to Australia for a 6-month internship at University of Queensland, Diamantina Institute to study the combination therapy of metronomic chemotherapy and γδ T cell vaccination in a B cell lymphoma mouse model. Heng Sheng started his PhD study in October 2019 in the department of Human Genetics (head professor Silvère van der Maarel) under the supervision of Associate professor Sjef Verbeek, Dr Marieke Fransen and Professor Ferry Ossendorp (Department of Immunohematology and Bloodtransfusion) of the Leiden University Medical Center, the Netherlands. His PhD project focused on different cancer immunotherapy approaches exploiting tumor targeting and immunostimulatory antibodies. The project was part of the EU funded Marie-Sklodowska-Curie Initial training Network (ITN) TIMCC (Tumor Infiltrating Myeloid Cell Compartment) initiated and coordinated by Sjef Verbeek. Heng Sheng also spent the last 6 months of his PhD in Prof Peter ten Dijke's lab to investigate the therapeutic efficacy of combined inhibition of TGF-β signalling and the PD-L1 immune checkpoint. From 2018 to 2020, he worked for Epsilogen therapeutics and Prof. Sophia Karagiannis at King's College London where he investigated the mechanism of action and therapeutic efficacy of tumor targeting IgE antibodies. Currently, he works at University of Southampton, under the supervision of Dr Sean Hua Lim.

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List of publication

1. Immunogenicity of rat-neu^{+} mouse mammary tumors determines the T cell-dependent therapeutic efficacy of anti-neu monoclonal antibody treatment. **Sow HS**., Benonisson H., Breukel C., Linssen MM., Camps M., Brouwers C., Claassens JWC., van Hall T., Ossendorp F., Verbeek JS. Sci Rep. 2020 Mar 10:3933.

2. FcγR interaction is not required for effective anti-PD-L1 immunotherapy but can add additional benefit depending on the tumor model. **Sow HS**., Benonisson H., Breukel C., Visser R., Verhagen OJHM., Bentlage AEH., Brouwers C., Claassens JWC., Linssen MM., Camps M., van Hall T., Ossendorp F., Fransen MF., Vidarsson G., Verbeek JS. Int J Cancer. 2019 Jan 15; 144 (2): 345 – 354.

3. Combined inhibition of TGF-β signalling and the PD-L1 immune checkpoint is differentially effective in tumor models. **Sow HS**., Ren, J., Camps M., Ossendorp F., Ten Dijke, P. Cells. 2019 Apr 5; 8 (4).

4. High FcγR expression on intratumoral macrophages enhances tumor-targeting antibody therapy. Benonisson H*., **Sow HS*.,** Breukel C., Claassens J., Brouwers C., Linssen MM., Fransen MF., Sluijter M., Ossendorp F., van Hall T., Verbeek JS. J. Immunol. 2018 Dec 15; 201 (12): 3741 – 3749. *equally contributed first author

5. FcγRI expression on macrophages is required for antibody-mediated tumor protection by cytomegalovirus-based vaccines. Benonisson H., **Sow HS.,** Breukel C., Claassens J., Brouwers C., Linssen MM., Redeker A., Fransen MF., Sluijter M., Ossendorp F., van Hall T., Arens R., Verbeek JS. Oncotarget. 2018 Jun 29;9(50): 29392 – 29402.

6. A restricted role for FcγR in the regulation of adaptive immunity. Fransen MF., Benonission H., van Maren WW., **Sow HS.,** Breukel C., Claassens J., Brouwers C., Linssen MM., van der Kaa J., Camps M., Kleinovink JW., Vonk KK., van Heiningen S., Klar N., van Beek L., van Harmelen V., Daxinger L., Nandakumar KS., Holmdahl R., Coward C., Lin QS., Hirose S., Salvatori D., van Hall T., van Kooten C., Mastroeni P., Ossendorp F., Verbeek JS. J. Immunol. 2018 Apr 15; 200 (8): 2615 – 2626.

7. *In vivo* safety profile of a CSPG4-directed IgE antibody in an immunocompetent rat model. Williams IP., Crescioli S., **Sow HS.,** Bax HJ., Hobbs C., Illieva KM., French E., Pellizzari G., Cox V., Josephs DH., Spicer JF., Karagiannis SN., Mele S. MAbs. 2020 Jan-Dec; 12(1): 1685349

8. AllergoOncology: Expression platform development and functional profiling of an anti-HER2 IgE antibody. Illieva KM., Fazekas-Singer J., Bax HS., Crescioli S., Montero-Morales L., Mele S., **Sow HS.,** Stavraka C., Josephs DH., Spicer JF., Steinkellner H., Jensen-Jarolim E., Tutt ANJ., Karagiannis SN. Allergy. 2019 Oct; 74(10): 1985 – 1989.