New Insights into Hookipa's TheraT® Replicating Viral Vector Platform published in *Immunity*

- TheraT®-induced CD8+ T cells are resistant to select checkpoint inhibitors, unlike CD8+ T cells induced by other vectors such as recombinant Listeria
- TheraT®-induced CD8+ T cells are qualitatively differentiated from CD8+ T cells induced by other vector systems; they have a much higher capacity to kill target cells in tissues
- TheraT® unleashes the tissue-destructive capacity of CD8+ T cells by inducing the master transcription factor TOX, corresponding with the ability of TheraT®' to turn 'cold' tumors 'hot'

Vienna, Austria, 15 May 2018 - Hookipa Biotech AG ("Hookipa"), a clinical stage biotech company pioneering an innovative class of active immunization therapies for oncology and infectious diseases, today announces the publication of a new preclinical study of its TheraT® replicating viral platform in the May edition of the prestigious international peer-reviewed journal *Immunity*[1].

The study was led by Professor Doron Merkler, M.D., and his team at the Department of Pathology and Immunology at the University of Geneva, Switzerland. CD8+ cytotoxic T lymphocytes (CTLs) are important in the body's defense against infection and cancer and, in addition, contribute to the pathogenesis of several autoimmune diseases. In this study a mouse model of central nervous system autoimmune disease was used to investigate how priming by distinct microbes may enable CTLs to destroy self-tissues.

The study demonstrated that TheraT®-induced CD8+ T cells have a unique transcriptional profile, characterized by expression of the master transcription factor thymocyte selection-associated HMG-box protein (TOX). TOX expression unleashes the tissue-destructive potential of CD8+ T cells by repressing the immune checkpoint 2B4/CD244. Expression of TOX, which is selectively induced by TheraT®, enables CD8+ T cells to establish long-lasting interactions with their target cells inside solid tissues and kill them.

Professor Daniel D. Pinschewer, M.D., Hookipa's Chief Scientific Officer and a co-author of the paper, said, "These data are very encouraging. They show that TOX expression enables TheraT®-induced CD8+ T cells to attack and destroy "self" tissue. A limitation of other immunization approaches has been that cancer also being a "self" tissue avoids immune mediated destruction. This feature of TheraT®-induced CD8+ T cells is of paramount importance in the immune response against cancer, which in essence represents an autoimmune attack that is desired and beneficial to the patient as it is directed specifically to and effective against the cancer.

Joern Aldag, Hookipa's Chief Executive Officer added, "Eliciting a potent T cell response is vital to treating patients with some of the most aggressive types of cancer. These novel findings by the Merkler group build on previously published data on our TheraT® platform and provide additional mechanistic insights highlighting why TheraT® represents a uniquely potent approach, capable of turning 'cold tumors hot'[2]."

Hookipa is performing IND-enabling studies for HB-201/TheraT® to be tested in Human papillomavirus positive (HPV+) head and neck squamous cell carcinoma. A Phase 1 trial is scheduled to start in 2019 as a monotherapy. In 2020, HB-201 will be combined with a checkpoint

inhibitor and later with HB-202, a complementary TheraT®-based product in preclinical development.

References

1. The DNA-binding factor TOX expression promotes the encephalitogenic potential of microbe-induced autoreactive CD8+ T cells in *Immunity* by Doron Merkler et al., posted online on 15 May 2018.
2. Replicating viral vector platform exploits alarmin signals for potent CD8+ T cell-mediated tumour immunotherapy – published online in *Nature Communications* on 26 May 2017 http://www.nature.com/ncomms/

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About Hookipa Biotech

Hookipa Biotech is a clinical stage company developing next-generation immunotherapies for infectious diseases and cancer using novel proprietary arenavirus vector platforms.

Hookipa´s Vaxwave® technology presents a completely new replication-defective viral vector platform designed to overcome the limitations of current technologies. Vaxwave® is based on lymphocytic choriomeningitis virus (LCMV). In this vector the gene encoding the LCMV envelope protein, normally responsible for virus entry into target cells, has been deleted and replaced with an antigen of interest. The resulting vectors infect dendritic cells and stimulate very potent and long-lasting immune response, however they cannot replicate and are therefore non-pathogenic and inherently safe.

Hookipa's TheraT® platform is based on an attenuated replicating arenavirus and is capable of eliciting the most potent T cell responses - a crucial step in treating patients with aggressive cancers. Significant pre-clinical data demonstrates that TheraT® is a powerful modality capable of turning "cold tumors hot" which should result in an additional layer of efficacy in the fight against solid tumors. Specifically, TheraT® has proven to be safe in animals as well as capable of eliciting uniquely potent antigen-specific CD8+ cytotoxic T cell responses and strong tumor control in mice. The first clinical trial with HB-201 targeting human papilloma virus-induced head and neck cancer is currently being prepared. This immuno-oncology technology is further being leveraged to target tumor self-antigens or shared neoantigens.

Find out more about Hookipa online at http://hookipabiotech.com/.

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