세미나 초록

성명	백두산
소속	GLPG US Inc. (Galapagos)
발표 주제	Therapeutic Antibody Development
발표 내용	Antibody-based immunotherapies that precisely target tumor-associated antigens or immune checkpoints offer powerful strategies to treat otherwise intractable cancers. In the first part of this seminar, I will present the discovery and pre-clinical characterization of 1G9, a fully human monoclonal antibody directed against the carcinoembryonic antigen-related cell adhesion molecule 5 (CEACAM5), a surface marker highly enriched in neuroendocrine prostate cancer (NEPC), an aggressive and treatment-refractory subtype of castration-resistant prostate cancer. 1G9 recognizes the membrane-proximal A3/B3 domains of CEACAM5 with high affinity and exceptional specificity, showing no cross-reactivity to other CEACAM family members or a large human membrane protein panel. As an IgG1, 1G9 mediates potent CEACAM5-dependent ADCC in vitro and suppresses tumor growth in vivo, and 1G9-based CAR-T cells exhibit strong and selective antitumor activity in CEACAM5-positive tumor models, supporting its potential as a therapeutic for NEPC and other CEACAM5-expressing malignancies. In the second part, I will discuss our development of fully human antibodies targeting NKG2A, an inhibitory receptor upregulated on NK cells and $CD8^+$ T cells in the tumor microenvironment. Using phage and yeast display, we isolated antibodies that bind specifically to the human CD94/NKG2A heterodimer without recognizing the activating NKG2C receptor. Structure–function studies identified Ser170 of NKG2A as a key determinant of this selectivity. Functionally, NKG2A-blocking antibodies enhance NK-cell cytotoxicity and augment the ADCC activity of tumor-targeting antibodies in vitro. Together, these studies illustrate how fully human antibody platforms can be used both to directly target tumor cells (CEACAM5) and to relieve inhibitory immune checkpoints (NKG2A), providing complementary strategies for next-generation cancer immunotherapy.