

# BK21 Plus Seminar

## “Application of Infectious Libraries of Protein Regulators for Extracellular Targets-From Basic to Applied Science”

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I am interested in studying cellular communication and developing therapeutics by infectious libraries of protein regulators for extracellular targets, including human combinatorial antibody libraries and cytokine libraries etc. Recently, we selected antibodies and cytokines that affect intriguing biological processes using infectious protein libraries. Firstly, we have developed an anti-Tspan12 antibody to reduce vaso-proliferative retinopathy using human combinatorial antibody libraries. Anti-angiogenic biologicals represent an important concept for the treatment of vaso-proliferative diseases. However, the need for continued treatment, the presence of non-responders and the risk of long-term side-effects limits the success of existing therapeutic agents. In this study, we found that Tspan12/ $\beta$ -catenin signaling is critical for the progression of vaso-proliferative disease. The newly developed anti-Tspan12 antibody has therapeutic effects in vaso-proliferative retinopathy enhancing the potency of existing anti-VEGF agents. Secondly, we reported on an agonist antibody against thrombopoietin receptor that induces malignant acute myeloid leukemia cells into the differentiation of potent cytotoxic killer cells. In this study, we suggested the possibility of agonist antibodies to change the differentiation state of cancer cells into those that attack and kill other members of the malignant clone from their origination. The cell that does the killing is also quite novel in that it has both natural killer cell and dendritic cell markers. It may, in fact, be a chimeric cell suggesting that antibodies such as these could open a whole new frontier in cancer therapy. Thirdly, by using an infectious cytokine library, we found that Interferon  $\gamma$  is a master checkpoint regulator of cytokine-induced differentiation. It operates partially by activating STAT1 signaling. However, more importantly is the mechanism that allows it to assume master regulator status, by inducing internalization of gp130, a common component of many heterodimeric cytokine receptors. Targeting of a receptor subunit that is common to all members of an otherwise diverse family solves the problem of how a master regulator can control so many diverse receptors.

- **Date: 11:00AM/Aug 9(Wed.)/2017**
- **Place: Conference room(#179), Postech Biotech Center**
- **Inquiry: Prof. Sung Ho Ryu (279-2292)**

\* This seminar will be given in English.

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