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Development of a reporter assay to determine the bioactivity of anti-IL6/IL6R and anti-EGFR based monoclonal antibodies

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Background & Aim: Biopharmaceuticals will comprise around 27% of the global pharmaceutical market in the near future and monoclonal Antibodies (mAbs) are predicted to take the major share due to their favorable drug properties such as specificity, high efficacy and fewer side-effects. Hence, testing mAbs for their efficacy and stability before batch release is an important aspect of the mAb development and manufacturing program. Here, we aim to design and validate an *in vitro* reporter gene-based assay for the evaluation of anti-IL6/IL6R and anti-EGFR mAbs with immense therapeutic potential and to make the stability testing procedure more robust, precise and rapid in comparison to existing assays.

Method: The HEK293 cell line was first engineered to express the IL6 or EGF receptors and later transfected with the pGL4.21 reporter vector containing the Sis-Inducible Element (SIE) or the Serum Response Element (SRE), respectively. The anti-IL6R mAb, Tocilizumab and the anti-EGFR mAb, Cetuximab were tested for their ability to inhibit IL6 and EGF-dependent reporter gene expression, respectively in these cell lines. The assay was validated according to ICH Q2 (R1) guidelines and was used to test the stability of mAbs manufactured in-house in comparison to available market standards.

Result: Tocilizumab and Cetuximab were found to inhibit IL6 and EGF-dependent reporter gene expression, respectively, in the developed assay. The assay was successfully validated for robustness, specificity, precision, accuracy and in-house and market standards were tested for stability in this assay.

Conclusion: A robust, specific and rapid *in vitro* reporter gene assay for the evaluation of anti-IL6/IL6R and anti-EGFR mAbs was developed. This assay can effectively serve as a surrogate assay in the development and batch release of mAbs/drugs directed to target the IL6 and EGF signaling pathways. In a similar way, cell lines can be engineered to co-express multiple receptors and response elements so that mAbs with two different targets, such as bispecific antibodies or those used in combination therapeutics, can be effectively screened together.

Biography

Kriti Ray is currently pursuing her PhD at Deakin India Research Initiative program initiated between Reliance Institute of Life Sciences, India and Deakin University, Australia. Her study focuses on developing reporter assays for antibody-based therapeutics. She has also worked with siRNA-based therapeutics against cancer and dengue.

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