

# A statistical approach to improve compound screening in cell culture media

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The Chinese hamster ovary (CHO) cell line is widely used for the production of recombinant proteins due to its high growing capacity and productivity, as well as other cell lines derived later than CHO. Adapting cell culture media for each specific cell line is a key to exploit these features for cost effective and fast product generation. Media supplementation is generally addressed by means of one-factor-at-a-time or classical design of experiments approaches but these techniques may not be efficient enough in preliminary screening phases. In this study, a novel strategy consisting in folding over the Plackett–Burman design was used to increase cell growth and trastuzumab production of different CHO cell lines through supplementation with nonanimal recombinant compounds. Synergies between compounds could be detected with a reduced number of experiments by using this methodology in comparison to more conventional fractional factorial designs. In the particular case reported here, the sequential use of this modified Plackett–Burman in combination with a Box-Behnken design led to a 1.5-fold increase in cell growth ( $10 \times 10^6$  cells/mL) and a two-fold in trastuzumab titer (122 mg/L) in suspension batch culture.

## 2.8 Trastuzumab quantification

Trastuzumab concentration was determined by the commercial solid-phase enzyme-linked immunosorbent assay **SHIKARI® Q-TRAS** (Matriks Biotechnology, Ankara, Turkey) according to manufacturer instructions.