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Developing the host for Targeted Integration cell line development

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Unlike the conventional random integration (RI) cell line development (CLD), the targeted integration (TI) CLD introduces the transgene at a predetermined “hot-spot” in the CHO genome with a defined copy number (1-2 copies). Given the low copy number and the pretested integration site, TI cell lines likely exhibit better stability compared to RI cell lines. In this study, we performed a genome wide screening using transposon based cassette integration and established a TI host (255-3) that has a single landing cassette inserted in its genome. Host 255-3 was able to support the CLD for three test molecules with product titers similar to those of the corresponding RI cell lines. For two regular antibody test cases, the top four TI cell lines achieved ~4-5g/L. For a proven difficult to express antibody, the top four TI lines achieved ~1-1.2g/L. The product titer for this hard to express molecule was increased 3-fold with additional vector improvement. Moreover, the timeline for CLD was shortened by ~2 weeks and resources required per cell line were substantially reduced using the TI method. Together these data indicate that the TI host we developed can be a suitable host to support our clinical / commercial CLD.