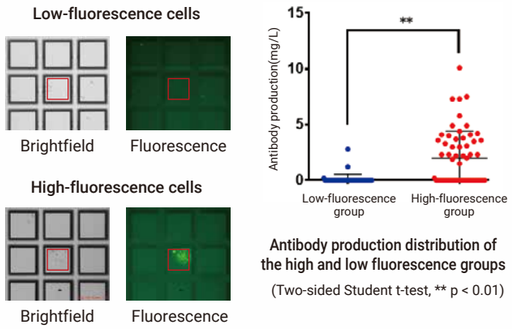
Results

Result-1: Fluorescence values correlate antibody-producing capacity of cells

We measured the antibody production of the high-fluorescence group (top 59) and the low-fluorescence group (bottom 43) selected by the CELL HANDLER™. More than half of the high-fluorescence group demonstrated antibody-producing capacity, compared to only 7% of the low-fluorescence group.

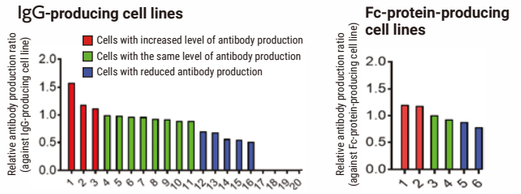


Antibody production distribution of the high and low fluorescence groups

(Two-sided Student t-test, ** p < 0.01)

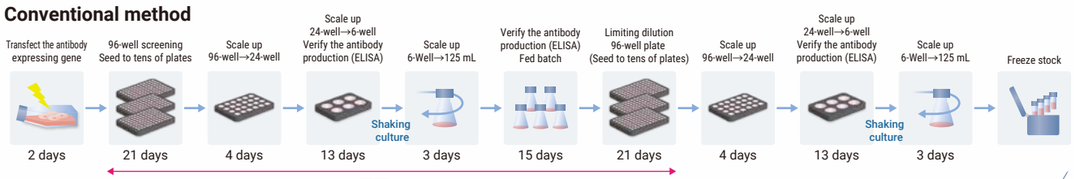
Result-2: The CELL HANDLER™ increases the efficiency of antibody-producing cell recloning

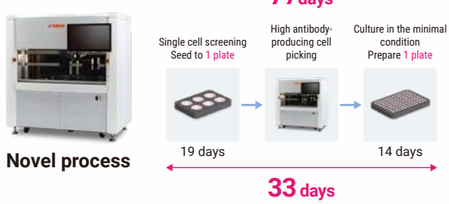
The IgG-producing cell line, which was established using a conventional method, was re-cloned, and cells in 20 grids were selected and transferred ("selected cells") using the CELL HANDLER™. After fed-batch culture, ELISA was employed to verify the antibody production. Based on the result, we were able to identify 8 out of 20 selected cells (#4-11) with the same level of antibody production as their parent cell, and 3 selected cells (#1-3) with antibody production 10% or higher than that of their parent cell. Similarly, we tested the antibody production of 6 Fc-protein-producing cell lines. The result showed a similar sorting efficiency as in the experiment with IgG-producing cell line: 2 (#3&4) out of 6 selected cells had the same level of antibody production as their parent's, and 2 selected cells (#1&2) had antibody production 10% or higher than their parent's.



Result-3: The new process was significantly simplified compared to conventional methods, increasing efficiency and saving time

The conventional method (single cell cloning using the limiting dilution analysis) took 77 days from screening to fed batch and required tens of plates. The novel process significantly reduced the screening-to-fed-batch time to only 33 days, with only 2 plates.





Conclusions

- The novel process easily isolates high-antibody producing cells in a short time while maintaining monoclonality.
- The novel process is significantly simpler than conventional methods, thereby reducing the time and cost of manufacturing antibody therapies. (Patent pending: Japanese Patent Application No. PY61173JP0, PY61174JP0)

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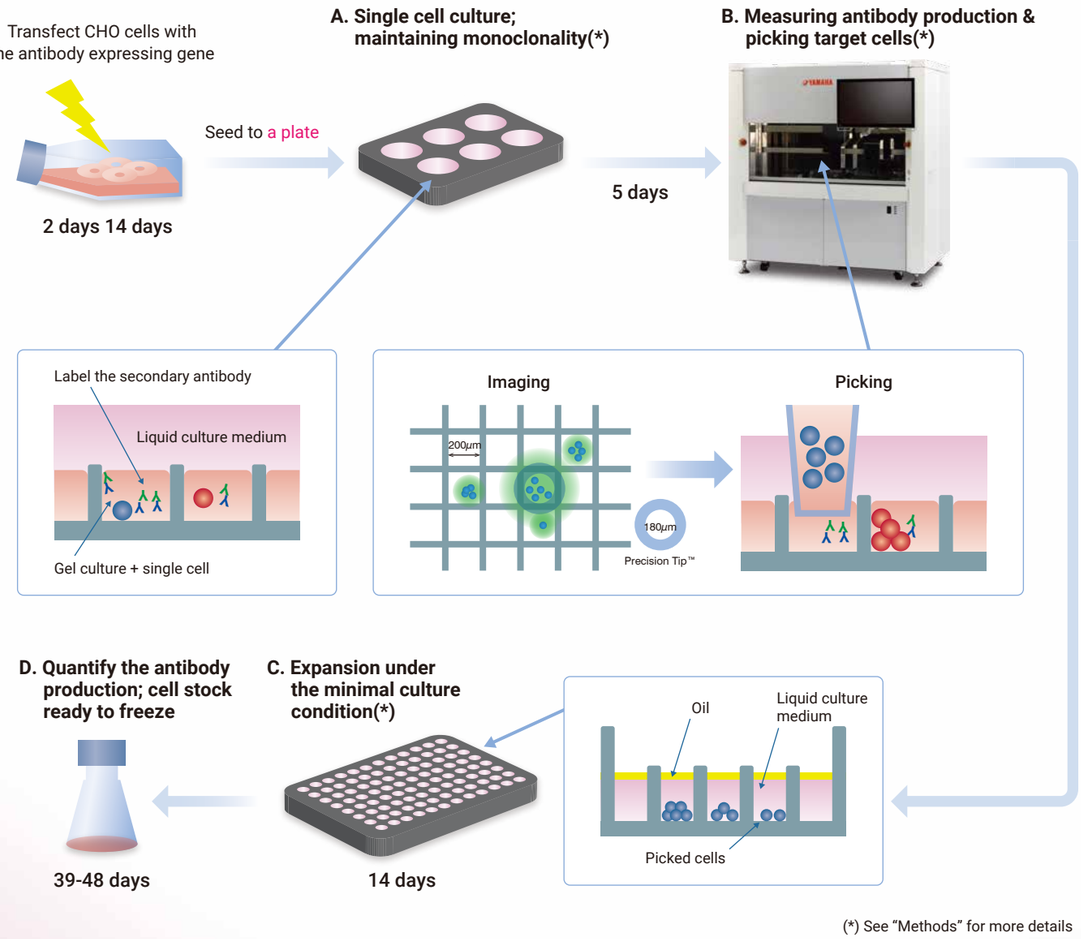
Overview

Process to sort high antibody-producing cells using the CELL HANDLER™

The fast-growing antibody therapy market is experiencing the rapid development of new technologies. The isolation of high antibody-producing cells is critical and yet challenging, and the market requires improved and more efficient processes. The YAMAHA CELL HANDLER™ cell picking & imaging system automates the detection, isolation, and transfer of single cells. This cell isolation technology was used to develop a new process that sorts high antibody-producing cells in a highly efficient and effective manner.

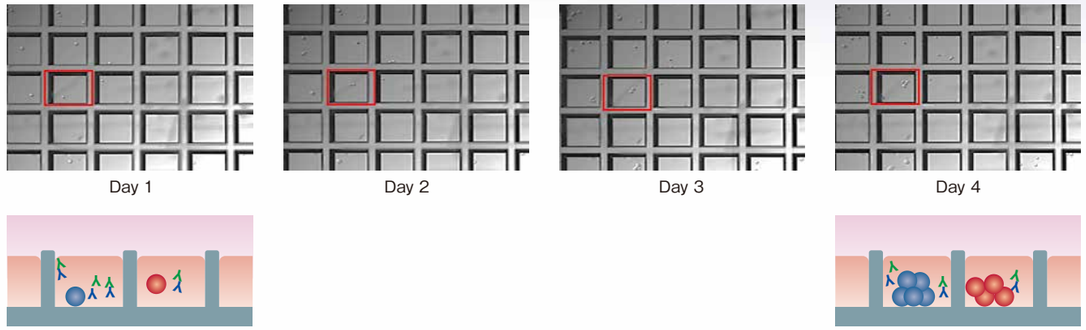


(*) See “Methods” for more details

Methods

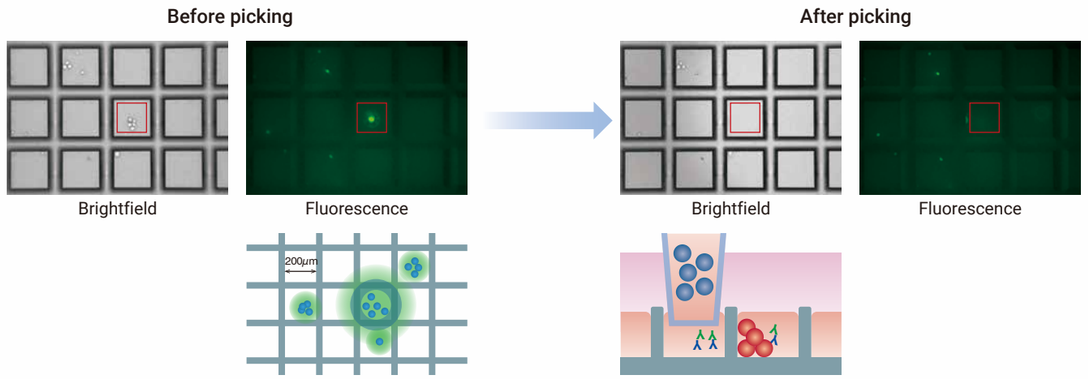
A. Single cell culture; maintaining monoclonality

By capturing the plate image daily with the CELL HANDLER™, the expansion and proliferation of single cells were verified, allowing the increase in cell numbers to be tracked.



B. Measuring antibody production & picking target cells

The CELL HANDLER™ can easily sort and transfer cells with high antibody producing capacity by capturing the plate image, measuring the fluorescence intensity of fluorescence-labeled antibodies, and identifying and picking target cells.



C. Expansion under the minimal culture condition

We also developed a cell expansion method that does not require growth activators, such as feeder cells, serum, or recombinant proteins exemplified by cytokine. The imaging function of the CELL HANDLER™ helps maintain the traceability by tracking the expansion process.