

IMPROVING VACCINE PRODUCTION WITH A SERUM-FREE MEDIUM FOR MRC-5 CELLS

Anna-Barbara Hachmann, Thermo Fisher Scientific, Grand Island, NY 14072
anna-barbara.hachmann@thermofisher.com
Jennifer Donato, Thermo Fisher Scientific, Grand Island, NY 14072
Nicole DiNardo, Thermo Fisher Scientific, Grand Island, NY 14072
Andrew M. Campbell, Thermo Fisher Scientific, Grand Island, NY 14072

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MRC-5 cells are used for vaccine production, including varicella zoster virus, MMR, polio, rotavirus, rabies, hepatitis A, and dengue virus. As human diploid fibroblast cells, MRC-5 can be passaged for about 42-48 population doublings before they become senescent. Vaccine manufacturers generally culture diploid cells in classical medium with 10% serum. Due to the limited population doublings, there is a short window for adaptation to serum-free medium and successful scale-up for vaccine production. Here, we report the development of a serum-free medium for MRC-5 cells that allows for direct adaptation and reaches comparable doubling times and virus titers as serum-containing medium. Using metabolite analysis and a design of experiment rationale, we developed a serum-free medium for growth of MRC-5 cells that can support direct recovery from thaw and adaptation-free expansion, while resulting in performance that is comparable to serum-containing medium. Since requirements for production of viruses are different from cell growth, we optimized the production medium separately. With the animal-origin-free production medium, manufacturers can produce vaccines without concern about the bovine serum albumin limit of 50ng/dose as set by the WHO. We confirmed virus production with varicella zoster virus and vesicular stomatitis virus (as an analog to rabies virus) and demonstrate titers that are up to one log higher than classical medium control. Taken together, we have developed a serum-free medium for MRC-5 cells that supports growth and virus production. By switching to a serum-free process, vaccine manufacturers can reduce dependency on serum, production and purification costs, and increase product consistency and safety.