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Anna-Barbara Hachmann

Megan Pajak-Lee

David Klinkenberg

Andrew M. Campbell

Aneg L. Cortes

See next page for additional authors

Authors

Anna-Barbara Hachmann, Megan Pajak-Lee, David Klinkenberg, Andrew M. Campbell, Aneg L. Cortes, and Isabel M. Gimeno

THE NEXT GENERATION OF FIBROBLAST-BASED VACCINE DEVELOPMENT

Anna-Barbara Hachmann, Thermo Fisher Scientific, Grand Island, NY 14072
anna-barbara.hachmann@thermofisher.com
Megan Pajak-Lee, Thermo Fisher Scientific, Grand Island, NY 14072
David Klinkenberg, Thermo Fisher Scientific, DK- 4000 Roskilde
Andrew M. Campbell, Thermo Fisher Scientific, Grand Island, NY 14072
Aneg L. Cortes, North Carolina State University, Raleigh, NC 27695
Isabel M. Gimeno, North Carolina State University, Raleigh, NC 27695

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Chicken embryo fibroblasts (CEF) and diploid cells have a long history in vaccine production since their isolation in the 1960s at the Wistar Institute (WI-38 cells) as well as the Medical Research Council (MRC-5 cells). The cells quickly became adopted for a number of vaccines: varicella zoster (VZV), MMR, yellow fever, polio, hepatitis A, rotavirus, rabies, Marek's disease, and dengue virus. Most of these vaccine processes were developed with classical media supplemented with Fetal Bovine Serum (FBS). The Hayflick limit of diploid cells restricted their adaptation to a serum-free process. While some of the vaccines such as polio and rabies have been transitioned to Vero cells, several vaccines continue to be manufactured with CEF and human diploid cells. Currently, FBS from Australia and New Zealand are utilized for the highest level of patient safety for human vaccines. However, this supply of serum is challenged by two factors: growth of existing vaccines to improve global access and the development of new gene therapies that require FBS. In order to reduce dependency on serum, we initiated a medium development program. Using metabolite analysis and DOE, we have developed a serum-reduced growth medium and a serum-free virus production medium for MRC-5 and other fibroblast cells. With a serum reduction of 90-100%, the growth medium can support direct recovery from thaw and adaptation-free expansion, resulting in performance that is comparable to classical medium with 10% serum. We confirmed virus production with VZV and vesicular stomatitis virus in MRC-5 cells as well as Marek's disease virus in CEFs and demonstrate a higher specific productivity. By switching to a low serum process, vaccine manufacturers can reduce production and purification costs, and increase product consistency and safety.