



Cell culture media

Xuri™ Growth Factors

Growth factors stimulate cellular proliferation and are widely used for the expansion of T lymphocytes in cell therapy and research applications. Xuri Growth Factors are produced under GMP conditions and enable the rapid development of stable and reproducible cell expansion protocols.

Rapid process development

Each lot of Xuri Growth Factor includes clear information on biological activity to improve your control over cultivation variability. This information enables you to standardize your process and deliver reproducible cell expansion without the need for revalidation of each new lot.

High quality

Xuri Growth Factors are produced under a certified GMP license that is regularly qualified by the licensing authorities. The manufacturing process is in accordance to International Conference on Harmonization (ICH) guidelines and the release procedure is executed under a quality management system following ISO13485. With an endotoxin level of < 25 EU/mg, the safety of the cells used for treating the patients are the declared focus of Xuri Growth Factors.

USP <1043> compliance

A smooth regulatory submission process is key when dealing with cell therapy requirements. To help users assess and document their production processes, a comprehensive documentation support file that follows USP <1043> requirements on ancillary material for cell, gene and tissue-engineered products is provided (1).

Xuri IL-2

Xuri IL-2 is a reliable solution for the expansion of T lymphocytes (Fig 2). Xuri IL-2 includes information on biological activity, which improves reproducibility and removes the need for IL-2 revalidation.



Fig 1. Xuri IL-2 and IL-2 provide reliable activation of T lymphocytes for efficient cell expansion.

Xuri IL-2 offers:

- Minimized process development time
- Improved scale-out capacity
- Reproducible performance without revalidation of each lot
- Established protocol in Xuri Cell Expansion System
- Dedicated cell therapy ancillary product following USP <1043> for *ex vivo* cultivation

Xuri IL-2 supports compliance with USP<1043>(1). A comprehensive product documentation support file is available to facilitate risk assessment and validation for use in cell therapy manufacturing.

To further accelerate development of the cell expansion process, a detailed, straight-forward protocol for the expansion of T cells using Xuri IL-2 and the Xuri Cell Expansion System W5 is provided. This protocol delivers reproducible cell proliferation results in static and perfusion cultures (Fig 2). Even after 14 d of culture, the majority of cells were in the early/intermediate stages of differentiation based on CD27 and CD28 expression patterns (Fig 3) without detectable senescence of the cells.

¹ Xuri Growth Factor products meet USP <1043> "ancillary materials for cell, gene, and tissue-engineered products", within the responsibilities applicable to a supplier. Other aspects of USP <1043> will be the responsibility of the end-user to assess. GE Healthcare cannot fulfil USP <1043> in regards to application and therapy specific aspects (e.g., use in finished therapeutic, assessment of removal from a finished therapeutic and possibly biocompatibility, cytotoxicity or adventitious agent testing).

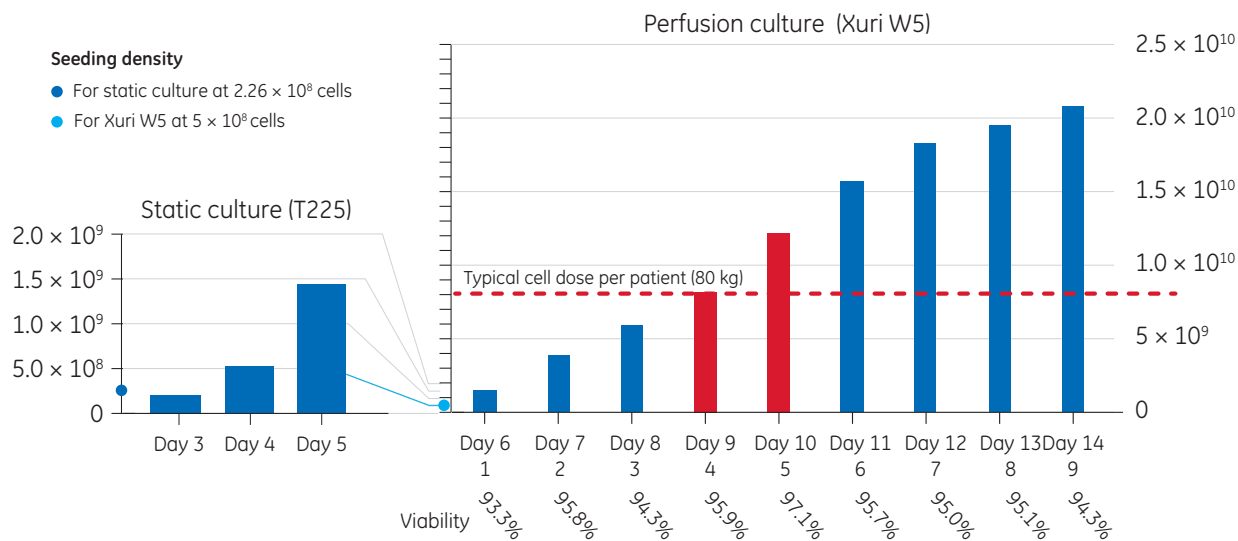


Fig 2. T lymphocytes isolated from peripheral blood were initially cultivated in static cell culture (T225 flasks) with 5% human serum plus 200 IU/ml Xuri IL-2 (left graph). Cells were activated using antibody coated beads. Cells were counted from day three onwards, and expanded until they passed the number needed for seeding in a 2 l Cellbag™ bioreactor (5×10^8). Cells were transferred and cultivated on a Xuri Cell Expansion System W5 for an additional 9 d under perfusion. Media composition and Xuri IL-2 concentrations were kept as in static culture (see application note 28-9650-52 available at www.gelifesciences.com/xuri). Cell count and viability analysis were performed each day.

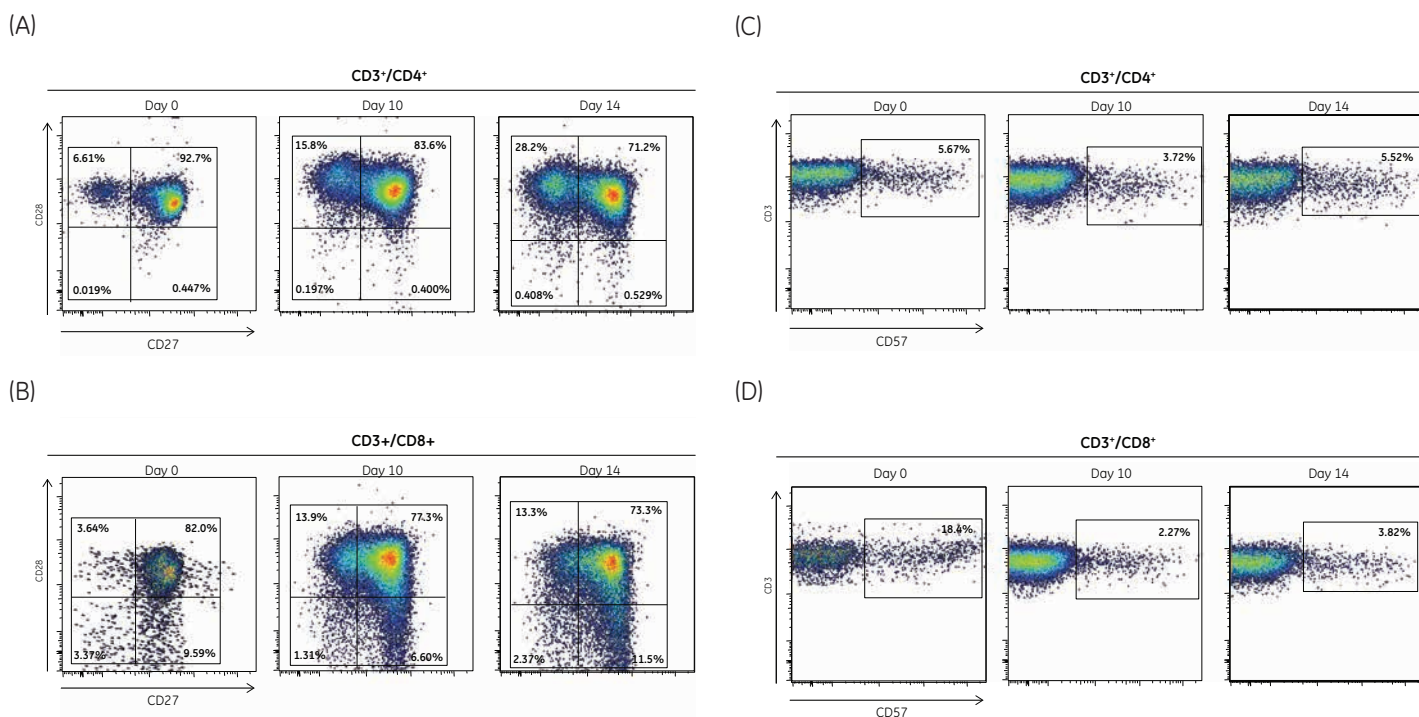


Fig 3. Expression of co-stimulatory molecules CD28 and CD27 as well as CD57 in CD3⁺/CD4⁺ T (helper) cells and CD3⁺/CD8⁺ (cytotoxic) T cells in Xuri Cell Expansion System W5 at day 0, day 10 and day 14 of culture (lymphocytes were gated based on their forward- and side-scatter profile). (A) Percentage CD28⁺ and CD27⁺ within CD3⁺/CD4⁺ T cells; (B) Percentage CD28⁺ and CD27⁺ within CD3⁺/CD8⁺ T cells. (C) Percentage CD57⁺ within CD3⁺/CD4⁺ T cells; (D) Percentage CD57⁺ within CD3⁺/CD8⁺ T cells. The expression patterns of the cell surface markers CD27 and CD28 give an indication of the differentiation state of T cells. Naïve or early differentiated T cells are CD27⁺/CD28⁺, effector T cells are CD27⁺/CD28⁻ or CD27⁻/CD28⁺ and late effectors or 'aged' T cells are CD27⁻/CD28⁻. Expression was high and after 14 d of culture the majority of cells were in the early/intermediate stages of differentiation. CD57 expression represents senescence of cells. Flow cytometric analysis showed no accumulation of CD57⁺ T cells.

Xuri IL-15

Interleukin 15 (IL-15) is known to regulate activation and proliferation of human blood lymphocytes. In cultivation procedures it is commonly used to stimulate natural killer (NK) cell growth.

Xuri IL-15 includes information on biological activity in reference to the international standard to allow consistent performance over different batches and experiments.

- Minimized process development time
- Improved scale-out capacity
- Reproducible performance without revalidation of each lot
- Dedicated cell therapy ancillary product following USP<1043> for *ex vivo* cultivation

Xuri IL-15 supports compliance with USP<1043> (1). A comprehensive product documentation support file is available to facilitate risk assessment and validation for use in cell therapy manufacturing.

Xuri IL-21

Interleukin 21 (IL-21) is recognized as being of significant importance in the human immune system. Its role to regulate NK cells and cytotoxic T cells renders it a key player in the destruction of cancerous and virally infected cells.

Xuri IL-21 includes information on biological activity developed in a functional assay against an internal standard. The clear information on the activity allows batch-to-batch consistency without time-consuming testing and revalidation.

- Minimized process development time
- Improved scale-out capacity
- Reproducible performance without revalidation of each lot
- Dedicated cell therapy ancillary product following USP<1043> for *ex vivo* cultivation

Xuri IL-21 supports compliance with USP<1043> (1). A comprehensive product documentation support file is available to facilitate risk assessment and validation for use in cell therapy manufacturing.

Growth factors for research

IL-2

IL-2 enables cost-efficient expansion of T lymphocytes in preclinical proof-of-principle experiments. Each lot of IL-2 includes information on biological activity to improve inter batch reproducibility and save time on revalidation. The close equivalence in production quality between IL-2 and Xuri IL-2 supports the transition of applications to clinical trial and process development for cell therapy manufacturing with minimal regulatory risk. The protocol provided with IL-2 was specifically developed to support the expansion of T cells in Xuri Cell Expansion Systems.

IL-2 offers:

- Reproducible performance without revalidation of each lot
- Accelerated setup time and reduced cost for transition from research to the preclinical stage
- Quicker move to clinical stage through solid results

Further growth factors for research use are available upon request.

Ordering information

Product	Pack size	Product code
Xuri IL-2 (USP<1043> for further manufacturing only)	10 µg	29062789
Xuri IL-2 (USP<1043> for further manufacturing only)	1 mg	29062790
Xuri IL-15 (USP<1043> for further manufacturing only)	40 µg	29112116
Xuri IL-21 (USP<1043> for further manufacturing only)	40 µg	29112119
IL-2 (For research use only)	10 µg	29062787
IL-2 (For research use only)	1 mg	29062788

www.gelifesciences.com/xuri

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