

Sample prep

Integrated quality control processes for cell therapy workflows using modular benchtop instruments for automation

In this application note we show:

- The KingFisher Apex Purification System can automate key cell therapy development workflows from discovery to preclinical stages, enhancing efficiency and consistency.
- Cytokines and other biomarkers released during CAR T cell-targeted killing can be quantified with ProcartaPlex multiplex immunoassays using the KingFisher Apex Purification System by automating the plate preparation and pipetting steps of the assay.
- The MagMAX Sequential DNA/RNA Kit can be used for effective quality control of cultures post-transduction while streamlining automated workflows and preserving limited input samples.

**Introduction**

Most cell therapies utilize CAR T cells for treatment of B cell malignancies. To help ensure safety, efficacy, and stability, the FDA has developed industry guidelines to assure identity, quality, purity, and strength of the product. Cytokine secretion assays may be used to evaluate the potency of CAR T cell drugs during their development. Further evaluation of cytokine expression may be considered to identify safety and activity of a cell and gene therapy (CGT) product. Accurate preclinical and CAR T drug development testing is necessary to avoid certain risk factors, including cytokine-release syndrome (CSR), a major source of CAR T cell therapy toxicity [1].

The development and manufacturing of CGT products face multiple bottlenecks, especially in the characterization and quality control (QC) processes that are traditionally manual and time-consuming. An automated solution to streamline the workflow and minimize manual intervention is critical to improving

throughput and consistency. Figure 1 showcases a typical CAR T cell workflow from isolation to characterization, with techniques like flow cytometry, PCR, ELISA, and fluorometric assays utilized to drive applications and quality evaluations such as phenotyping and purity, transduction efficiency, cytokine release, endotoxin detection, and cytotoxicity.

Here we evaluate the effectiveness of automation in cell therapy workflows utilizing the Thermo Scientific™ KingFisher™ Apex Purification System to automate plate preparation for the Invitrogen™ ProcartaPlex™ immunoassay as well as to isolate DNA and RNA sequentially from a single sample to assess quality and performance of cell cultures with the Applied Biosystems™ MagMAX™ Sequential DNA/RNA Kit.

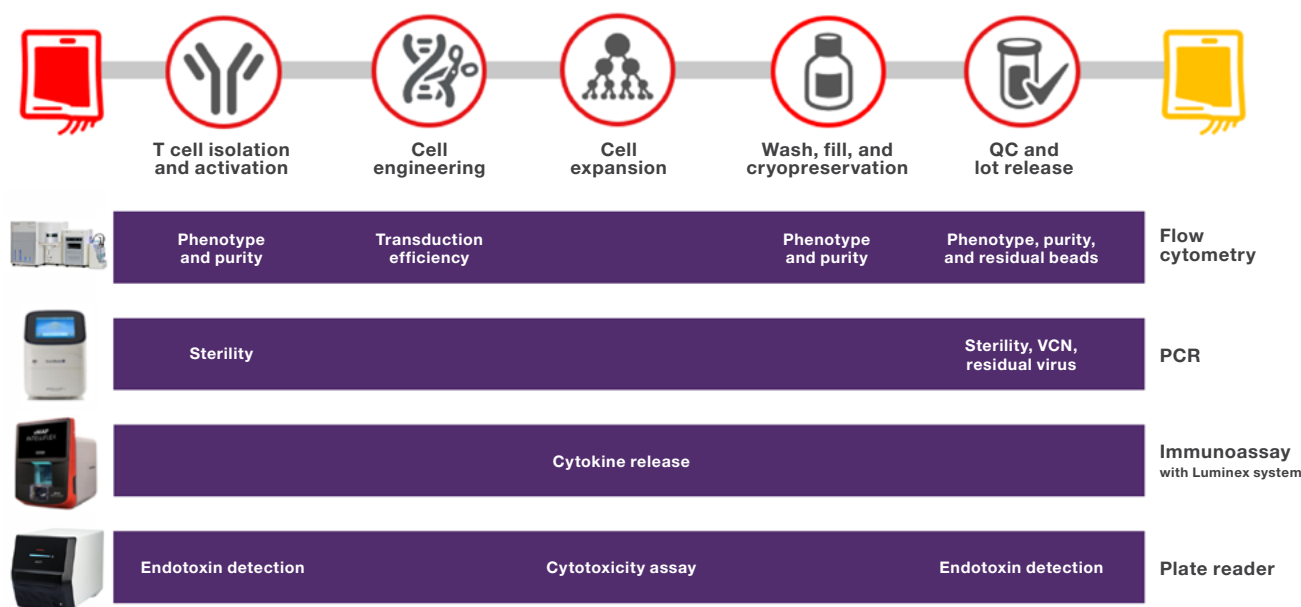


Figure 1. A typical CAR T cell workflow. Throughout each stage of CAR T cell drug development, various quality control (QC) methods may be deployed within development before the final lot release and subsequent implementation.

Background

The Invitrogen™ multiplex assays on the Luminex® platform enable simultaneous detection of multiple proteins in a single well, significantly reducing the bottleneck associated with traditional ELISA assays [2]. The implementation of the KingFisher Apex platform automates and streamlines the ProcartaPlex assay, enhancing productivity and consistency while significantly reducing hands-on time. Figure 2 highlights key features of the KingFisher Apex system, and Figure 3 compares manual and automated workflows of the ProcartaPlex immunoassay to measure the amount of cytokines secreted. Automation aims to increase efficiency and assay performance, reduce manual labor, and standardize procedures.

Although the MagMAX DNA/RNA Sequential Kit was originally developed for isolating genomic DNA from whole blood and bone marrow in genomics and oncology research, its application in CGT discovery and preclinical development workflows offers similar biological techniques with technical automation systems while leveraging the robustness and reproducibility of MagMAX chemistries. Figure 4 details the standardized MagMAX Sequential workflow for the sequential isolation of DNA and RNA from a single sample source, maximizing QC and characterization post-transduction capabilities by automating processes, improving productivity, and reducing sample waste when compared to manual workflows or multiple isolation methods.



Figure 2. KingFisher Apex Purification System features.

The benefits of the system include a touchscreen interface to modify protocols directly on the instrument, and a feature to have two magnetic heads installed at the same time.

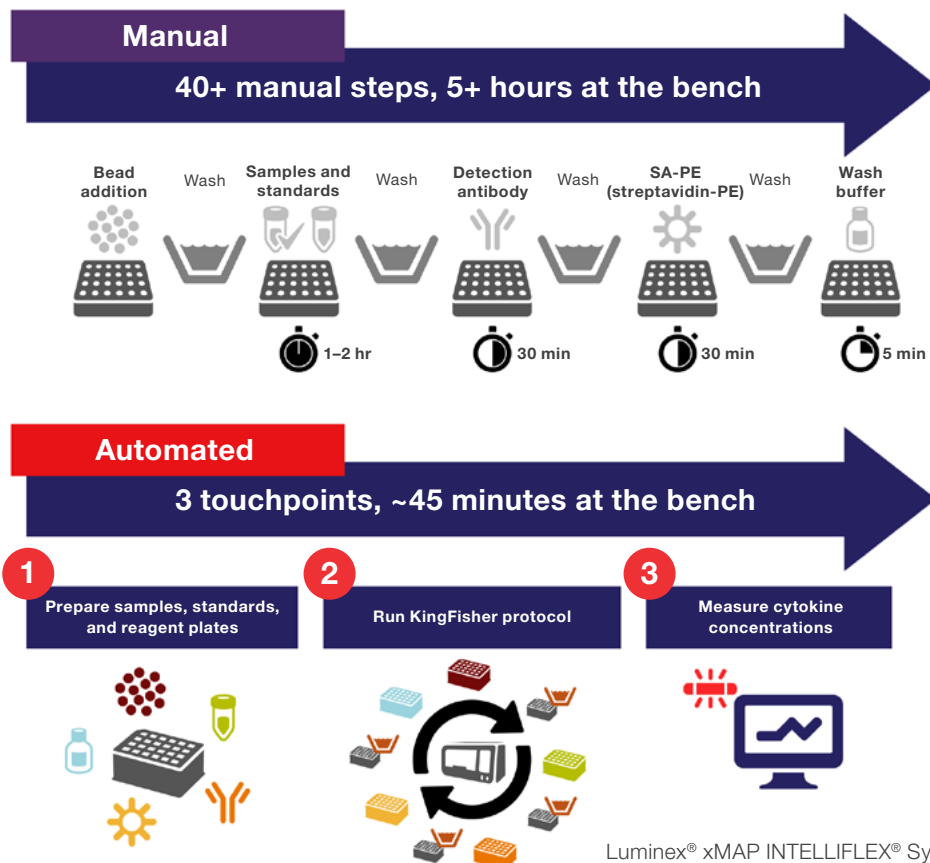


Figure 3. Manual vs. automated ProcartaPlex workflow. By minimizing touchpoints from over 40 to just 3, the automated process can save up to 80% of the hands-on time while standardizing workflows and reducing the risk of human error.

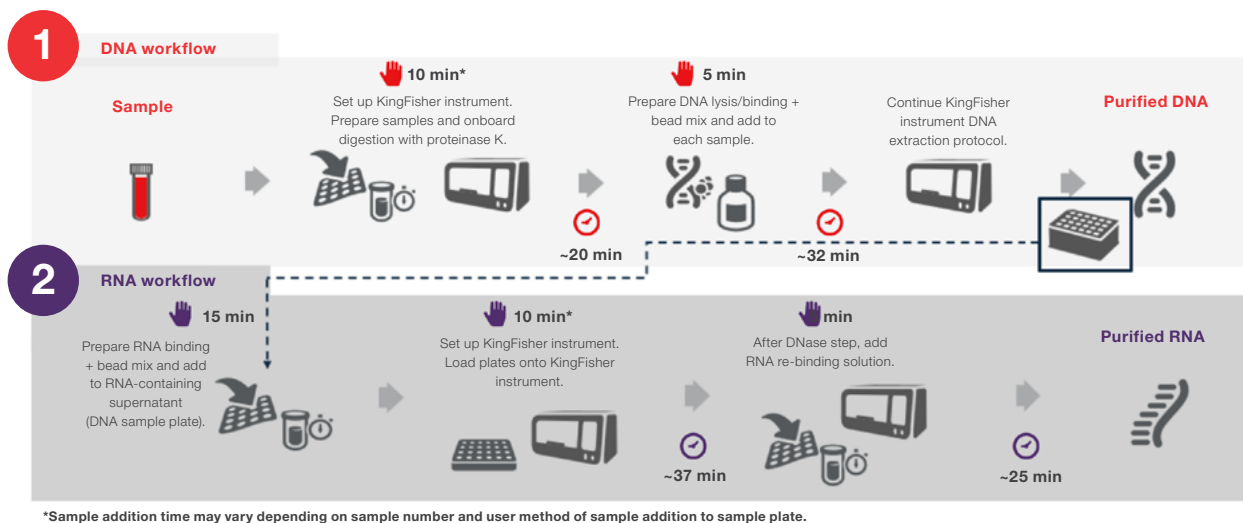


Figure 4. MagMAX Sequential DNA/RNA Kit workflow on the KingFisher Apex Purification System. The workflow has a total turnaround time of approximately 2.5 hours with minimal hands-on time. Both DNA and RNA can be isolated sequentially from a single sample without the need to return to the sample source. The same sample is carried through a single sample plate from DNA isolation into RNA isolation.

Methods

CAR T cell generation, transduction, and expansion

Frozen leukopaks were obtained from Charles River Laboratories. T cells were isolated using the Gibco™ CTS™ DynaCollect™ Magnetic Separation System along with Gibco™ Dynabeads™ Human T-Activator CD3/CD28 magnetic beads, which stimulate activation after isolation. Three days following isolation, cells were released from the beads utilizing Gibco™ CTS™ Detachable Dynabeads™ Release Buffer. Lentiviral vectors used for transduction were supplied by Patheon™ Pharma Services using the Gibco™ CTS LV-MAX™ Lentiviral Production System. T cell transduction was performed at a multiplicity of infection (MOI) of 2 approximately 3 days post-isolation. T cells were then cultured in Gibco™ CTS™ OpTmizer™ Pro SFM supplemented with 2.5% Gibco™ CTS™ Immune Cell SR, 2.3% Gibco™ CTS™ GlutaMAX™-I Supplement, 1% Gibco™ L-Glutamine (200 mM), 100 U/mL Gibco™ PeproTech™ Human IL-7 Recombinant Protein, and 100 U/mL Gibco™ PeproGMP™ Human IL-14 Recombinant Protein in a G-Rex™ 24 well plate, with a seeding density of 2.5 x 10⁶ cells/cm². Cells were split 1:2 on day 3 post-transduction and allowed to grow to confluency for 7 days.

Confirmation of transduction with flow cytometry

Flow cytometry was used to calculate transduction efficiency. Cell samples were collected 7 days post-isolation and centrifuged at 400 x g for 5 minutes at room temperature to remove the medium, then washed with 1 mL of Invitrogen™ eBioscience™ flow cytometry staining buffer. Following another centrifugation, samples were resuspended in a 20% solution of Invitrogen™ eBioscience™ Fc Receptor Binding Inhibitor Polyclonal Antibody (Fc block) diluted in flow cytometry staining buffer and plated into 96-well round-bottom plates at ~0.3 x 10⁶ cells per well in 100 µL of the diluted solution. Samples were divided into three groups: (a) stained, (b) unstained plus viability indicator dye, and (c) unstained controls. They were incubated in the dark with the Fc block solution for 15 minutes at 4°C, followed by incubation in the dark with an antibody cocktail containing anti-CD19 CAR T cells, for 15 minutes at 4°C. After centrifugation and washing with

200 µL flow cytometry staining buffer, the samples that were stained, or unstained but with viability indicator dye included, were resuspended in a 1:500 dilution of Invitrogen™ LIVE/DEAD™ Fixable Aqua Dead Cell Stain Kit, for 405 nm excitation viability dye, incubated for 30 minutes at room temperature, and protected from light. The unstained controls were resuspended in 200 µL flow cytometry staining buffer. The data were collected using the Invitrogen™ Attune™ CytPix™ Flow Cytometer using the Attune™ Cytometric Software v6.0.0, and data analysis was performed utilizing FlowLogic™ 8.6 software. GraphPad Prism v9.3.1 software was used for data visualization.

Cytotoxicity

Cytotoxicity of the CAR T cells was confirmed via luminescence-based assay. The CAR T cells were co-cultured with luciferase-expressing NALM6 cells for 5 hours. CAR T:target (E:T) cell ratios used in these studies ranged from 10:1 to 0.312:1. Cytotoxic activity of the CAR T cells was evaluated with an on-market luciferase assay according to the manufacturer’s instructions. Luciferase levels were measured using the Thermo Scientific™ Varioskan™ LUX Multimode Microplate Reader.

Transduction efficiency with immunoassays

Five hours after confirming the performance of the cytotoxicity assay, samples were prepared for immunoassay evaluation via automated and manual methods utilizing the Invitrogen™ ProcartaPlex™ Human Th1/Th2/Th9/Th17 Cytokine Panel, 18plex, and KingFisher Apex Purification System. The manual workflow used the control as mentioned in the ProcartaPlex user guide (Pub. No. MAN0028348). The KingFisher protocol was designed to mimic the workflow described in MAN0028348 [3]. The script “Luminex_gentle_Inc_w_combi_head.kfx” was loaded onto the KingFisher Apex Purification System. KingFisher 96-standard and 96 deep-well plates were prepared as detailed in Table 1 below, utilizing the same volumes and working reagents as the manual workflow (control). Plate 3 was prepared last, just before addition onto the KingFisher Apex Purification System.

Table 1. KingFisher Apex plate setup for automated ProcartaPlex assay on the KingFisher Apex Purification System.

Instrument	KingFisher Apex Purification Instrument			
Magnetic head	96 Combi Head			
Plate no.	Plate ID	KingFisher plate type	Plate contents	Volume (µL)
1	Bead plate	Standard	ProcartaPlex Simplex Beads	100
2	Bead wash plates (1 and 2)	Deep-well	ProcartaPlex Wash Buffer (1x)	300
3	Standards and samples	Standard	50 µL of sample or ProcartaPlex Standard	50
4	Detection antibody plate	Deep-well	ProcartaPlex Detection Antibody Mixture	25
5	Bead wash plates (3 and 4)	Deep-well	ProcartaPlex Wash Buffer (1x)	300
6	SA-PE plate	Standard	ProcartaPlex Streptavidin-PE (SA-PE) (1x)	50
7	Reading plate	Deep-well	ProcartaPlex Wash Buffer	165
8	Tip plate	Standard	96 Deep-Well Tip Comb	N/A

Samples collected from the cytotoxicity assay were thawed and added to the KingFisher sample plate (plate 3) that also contained the prepared standards according to MAN0028348 in designated wells. All plates were immediately loaded onto the KingFisher instrument, and the script “Luminex_gentle_inc_w_combi_head.kfx” was started. The KingFisher protocol was complete approximately 4 hours after starting, without any need to return to the instrument. After completion, ProcartaPlex sample plates were removed, and samples were transferred to the Mylar™ plate provided in the ProcartaPlex kit. They were placed on a shaker set to 600 rpm for 5–30 minutes, and analyzed on the Invitrogen™ Luminex® 200™ Instrument System running the Luminex® xPONENT® Software or 100 or 200 software. Data from both manual and automated workflows were collected on the same instrument and analyzed using the Invitrogen™ ProcartaPlex™ Analysis App available on the Thermo Fisher™ Connect Platform.

Nucleic acid isolation (DNA and RNA)

1.5 x 10⁶ CAR T cells were obtained as described earlier, and 100 µL aliquots of cell supernatants post-transduction were collected for DNA and RNA isolation. Non-transduced T cells were used as a negative control. Manual control workflows were performed and compared to automated sequential isolation on the KingFisher Apex Purification System from the cell supernatant using a 96 deep-well magnetic head. DNA was isolated manually from a cell pellet and from 100 µL of cellular supernatant with the Invitrogen™ PureLink™ Genomic DNA Mini Kit under sterile conditions as described by the user protocol [4]. DNA was eluted into 100 µL sterile DNase- and RNase-free 1.5 mL Invitrogen™ RNase-free microcentrifuge tubes and stored at –80°C until use.

The RNA was isolated manually from a cell pellet and from 100 µL cellular supernatant post-transduction with the Applied Biosystems™ PrepSEQ™ Nucleic Acid Sample Preparation Kit, eluted 80 µL into sterile DNase- and RNase-free 1.5 mL microcentrifuge tubes, set aside on ice, and utilized within one hour of sample purification according to MAN0026126 [5]. Sequential isolation was performed using the MagMAX Sequential DNA/RNA Kit and Reagents on a single cell pellet and 100 µL of cell supernatant post-transduction. The procedure followed user guide MAN0030308 for 50–150 µL for bone marrow or 100–150 µL for whole blood samples, utilizing KingFisher Apex protocol script “SEQ_DNA_Low_Apex.kfx” and “SEQ_RNA_Low_Apex.kfx” [6]. DNA and RNA sequentially isolated with the MagMAX kit on the KingFisher Apex system were eluted in 100 µL and 80 µL, respectively. Concentrations of DNA and RNA isolated from manual and automated workflows were quantified on the Thermo Scientific™ NanoDrop™ Eight UV-Vis Spectrophotometer.

Molecular quality control of DNA and RNA from T cell cultures

To evaluate mycoplasma contamination, sterility, viral copy number, and residual lentiviral vector titers the Applied Biosystems™ QuantStudio™ 12K Flex Real-Time PCR System was used. Table 2 lists assay kits utilized for quality control along with purpose, cellular input, and workflow referenced. Assays were prepared following similar guidelines as referenced in Ahmadi et al. [7].

Table 2. Quality control assays to evaluate extracted DNA and RNA from cell culture post-transduction.
User manuals and workflows were followed, with cell culture volume inputs listed within the table [5,8,9].

Purpose	Target analyte	Applied Biosystems™ assay	User manual reference	Volume of input to reaction (µL)
Evaluation of <i>Mycoplasma</i> species contamination	DNA	MycoSEQ Plus Mycoplasma Detection Kit	MAN0028695	3
Evaluation of microbial contamination (bacterial and fungal)	DNA	SteriSEQ Rapid Sterility Testing Kit	MAN0029388	3
Quantification of lentiviral DNA targets within transduced cells	DNA	ViralSEQ Lentivirus Proviral DNA Titer Kit	MAN0026126	5
Quantification of lentivirus physical particles present	RNA	ViralSEQ Lentivirus Physical Titer Kit	MAN0026126	5

Results and discussion

Confirmation of transduction efficiency was performed via flow cytometry 7 days post-transduction. A luciferase-based cytotoxicity assay was performed in which CAR T cells and non-transduced T cells were cocultured with NALM6 cells expressing CD19. The results suggested that non-transduced T cells do not exhibit cytotoxicity, while the transduced CAR T cells exhibited cytotoxicity against the NALM6 target cells. The results suggest a high likelihood of success with the ProcartaPlex immunoassay.

The KingFisher Apex Purification System is versatile and adaptable, making it easy to use as an open system. It offers flexibility in selecting instrument log options, installing regular security upgrades, processing various sample volumes (from low to high), and eluting into volumes as small as 10 µL. This system supports good laboratory practices and facilitates opportunities for sample and user tracking, meeting the needs of biopharma and cell therapy research labs. Furthermore, the ability to edit the ProcartaPlex protocol on the screen in real time adds to the efficiency and convenience of carrying out the immunoassays.

Transduction efficiency with immunoassays

With just 3 touchpoints and approximately 45 minutes of hands-on time, combining the automated KingFisher Apex system with ProcartaPlex assays significantly saved operator time compared to 4.5 hours of manual labor at the bench and over 40 manual steps. Using Luminex assay workflows and analysis tools, the number of cytokine-specific beads was counted post-collection

on the KingFisher Apex Purification System and compared to collection counts from the manual workflow. Figure 5 indicates that across all 18 cytokines, manual and automated KingFisher Apex methods were comparable and both methods met the minimum assay threshold of 50 beads per analyte. Using the ProcartaPlex Analysis App, standard curves were generated to calculate cytokine concentrations, which were compared across manual and automated KingFisher Apex methodologies for all 18 cytokine targets. High degrees of linearity were observed between the two workflows, with an average R² value showing an absolute difference of 0.0098 when plotting the linearity of log-measured concentration in pg/mL. The differences in R² values between the two workflows ranged from 0 to 0.0951, with all targets except IL-2, IL-5, and IL-17A having linear R² >0.98 (Table 3). Although targets IL-2, IL-5, and IL-17A did not have an R² value >0.98, they did still show a quality degree of linearity. None of the targets recovered had an R² value <0.90. Evaluation of cytokine concentration post-CAR T cell killing of targets was conducted across samples containing only target cells, only CAR T cells, and CAR T plus target cells. Results showed higher cytokine concentrations with the automated KingFisher Apex method compared to the manual method. Key cytokines, such as IFN-γ, indicated potential increased recovery with the automated procedure (Figure 6).

Table 3. Analysis of standard curves and linearity generated by plotting log-measured concentrations (pg/mL) against log-expected concentrations (pg/mL) across 18 cytokine targets.

Cytokine target	Manual R ²	Automated KingFisher instrument R ²	Absolute difference R ²
GM-CSF	0.9996	0.9933	0.0063
IFN-γ	0.9847	0.9994	0.0147
IL-1β	0.9991	0.9988	0.0003
IL-2	0.9710	0.9797	0.0087
IL-4	0.9992	0.9928	0.0064
IL-5	0.9878	0.9500	0.0378
IL-6	0.9922	0.9975	0.0053
IL-9	0.9999	0.9986	0.0013
IL-10	0.9999	0.9991	0.0008

Cytokine target	Manual R ²	Automated KingFisher instrument R ²	Absolute difference R ²
IL-12 p70	0.9929	0.9994	0.0065
IL-13	0.9999	0.9940	0.0059
IL-17A	0.9998	0.9047	0.0951
IL-18	0.9996	0.9996	0.0000
IL-21	0.9971	0.9949	0.0022
IL-22	0.9843	0.9765	0.0078
IL-23	0.9999	0.9997	0.0002
IL-27	0.9920	0.9968	0.0048
TNF-α	0.9992	0.9996	0.0004

Simplex bead count: manual vs. automated with KingFisher instrument

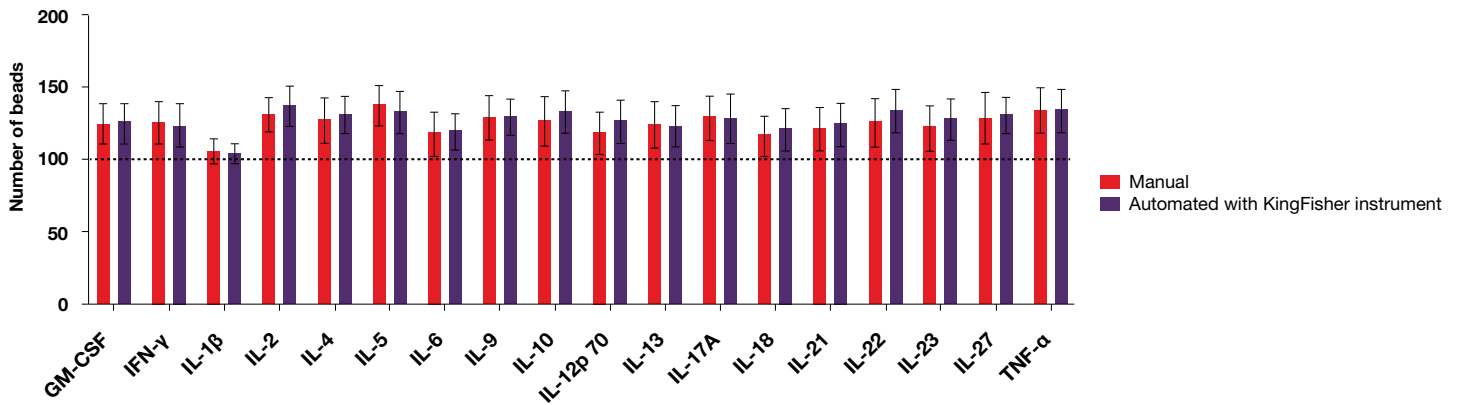


Figure 5. ProcartaPlex assay bead count across 18 cytokine targets for manual vs. automated methods on the KingFisher Apex system showed comparable performance, with no significant variation in the number of beads.

Cytokine concentration post-CAR T cell killing of target cells

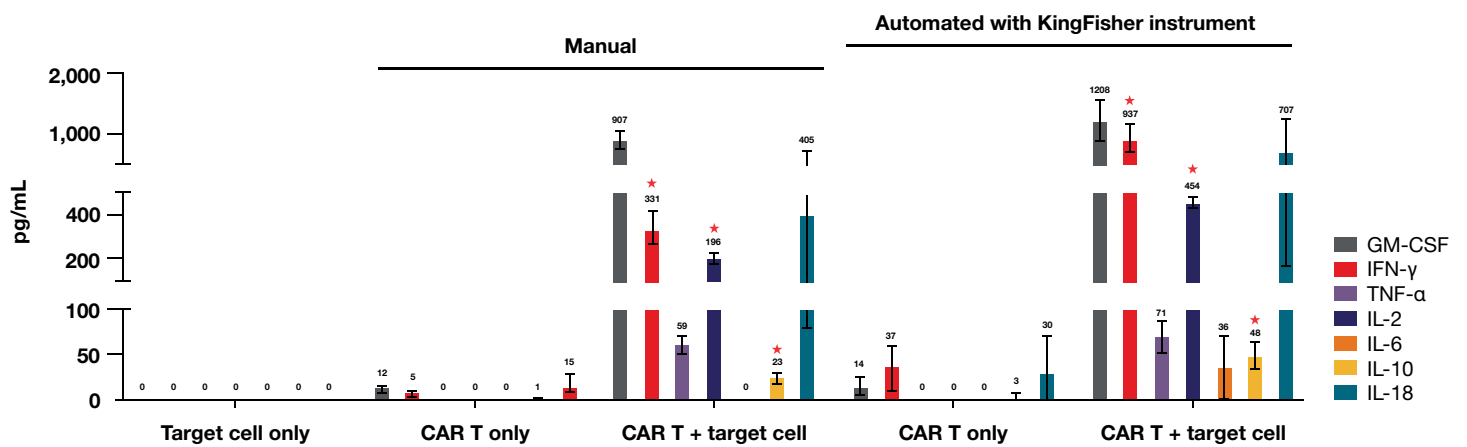


Figure 6. Comparison of cytokine concentration between the manual and automated KingFisher Apex system methods. ProcartaPlex assay workflows were used to analyze CAR T cells post-transduction across key cytokine targets: GM-CSF, IFN-γ, TNF-α, IL-2, IL-6, IL-10, and IL-18. Red stars indicate cytokines that had minor variations in linearity of $R^2 > 0.98$ when comparing expected vs. actual recovery of standards.

Molecular quality control of DNA and RNA from T cell cultures

Sequential isolation of nucleic acids from cells from a single source saved operator time at the bench compared to manual isolations of DNA and RNA independently. DNA extracted from both 1.5×10^6 cells and 100 μL of supernatant showed comparable or improved performance when using the automated MagMAX Sequential DNA/RNA extraction chemistries on the KingFisher Apex Purification System, compared to traditional manual extraction techniques. The MagMAX Sequential DNA/RNA Kit gave significantly higher DNA yields when automated on the KingFisher Apex system compared to the manual method using the Thermo Scientific™ PureLink™ Genomic Mini Kit (Figure 7A). Assessment of DNA purity indicates that the MagMAX sequential DNA/RNA isolation kit chemistry resulted in slightly improved purity with average A_{260}/A_{280} ratios of >1.9 (Figure 7B). Sterility performance with the Applied Biosystems™ MycoSEQ™ Mycoplasma Detection Kit and SteriSEQ™ Rapid Sterility Testing Kit indicated no false-positives across either manual or automated KingFisher Apex methods. Slight differences in C_t values between the manually prepared samples and those prepared with the KingFisher system were due to intrinsic background signal from the MagMAX kit chemistry explained by the NTC and NEC.

Figure 8A shows that the internal positive and negative controls for mycoplasma confirmation have C_t values between 25 and 30, while the isolated cells do not amplify until after at least 36 cycles. This indicates the absence of mycoplasmas in the isolated cells. The SteriSEQ assay confirmed that there were no bacteria or fungi present in any of the extracted cell samples or negative extraction controls (Figure 8B). The Applied Biosystems™ ViralSEQ™ Lentivirus Proviral DNA Titer assay demonstrated that the number of copies per cell, averaged across technical replicates, was similar between traditional manual isolations and automated DNA isolation using the MagMAX Sequential kit on the KingFisher Apex system (Figure 9). However, when comparing RNA from lentiviruses, there was a difference in viral particles/mL (VP/mL) between the two systems (Figure 10). This difference in viral titers could be due to the low volume of nucleic acid sample input, which is only 5 μL . Smaller inputs of nucleic acid into the assay can lead to larger variations between samples.

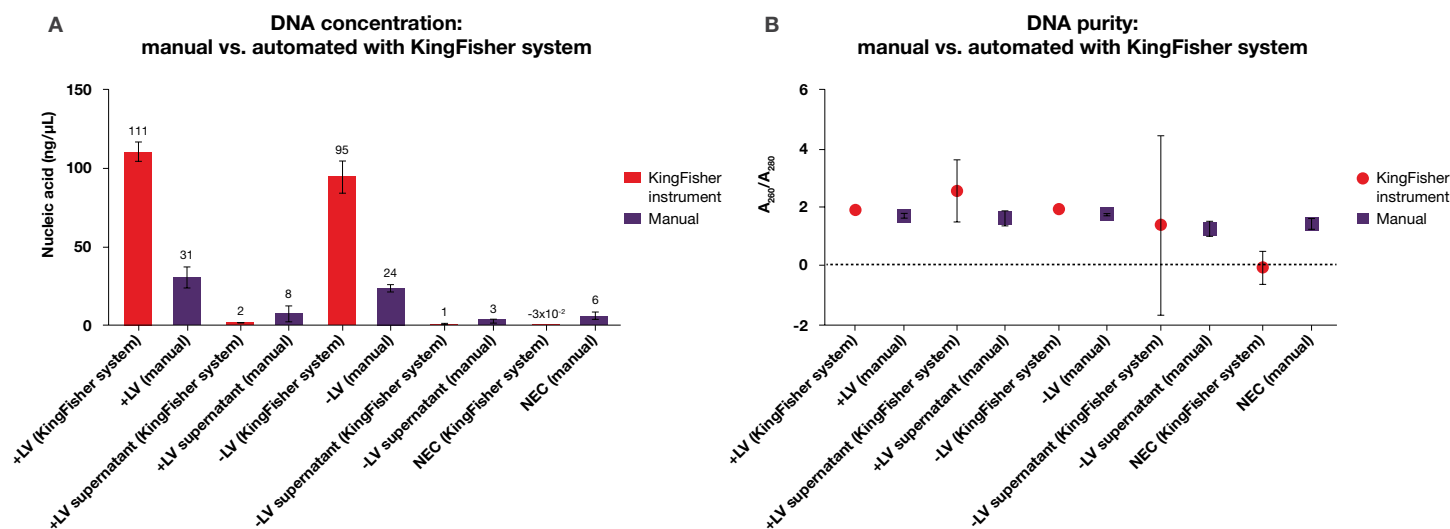


Figure 7. Concentration and quality analysis of nucleic acid. The Thermo Scientific™ NanoDrop™ Eight UV-Vis Spectrophotometer was used to measure (A) DNA concentration and (B) DNA purity absorbance ratio (A_{260}/A_{280}) and compare the samples isolated manually with those isolated sequentially using the MagMAX Sequential kit on the KingFisher Apex System.

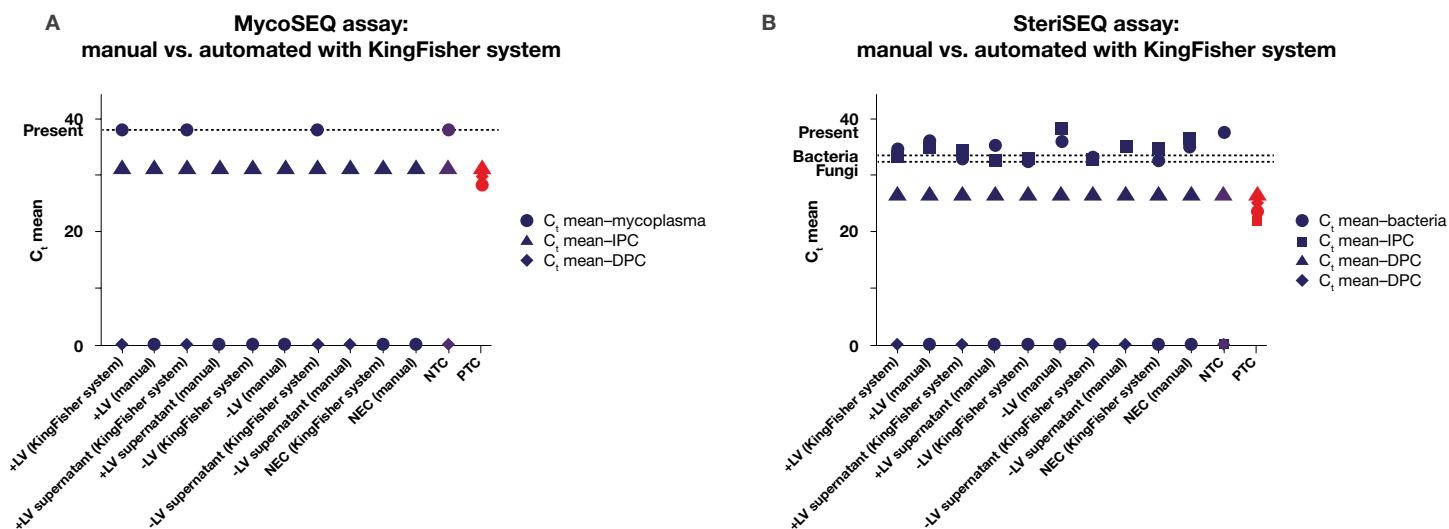


Figure 8. Sterility results obtained by PCR using nucleic acid isolated from manual and KingFisher workflows. The two assays—(A) MycoSEQ PCR assay to determine mycoplasma contamination and (B) SteriSEQ assay to determine microbial (fungal and bacterial) contamination—compare the effectiveness of the two isolation techniques: manual DNA isolation and automated sequential isolation of DNA and RNA using the MagMAX Sequential DNA/RNA Kit on the KingFisher Apex Purification System.

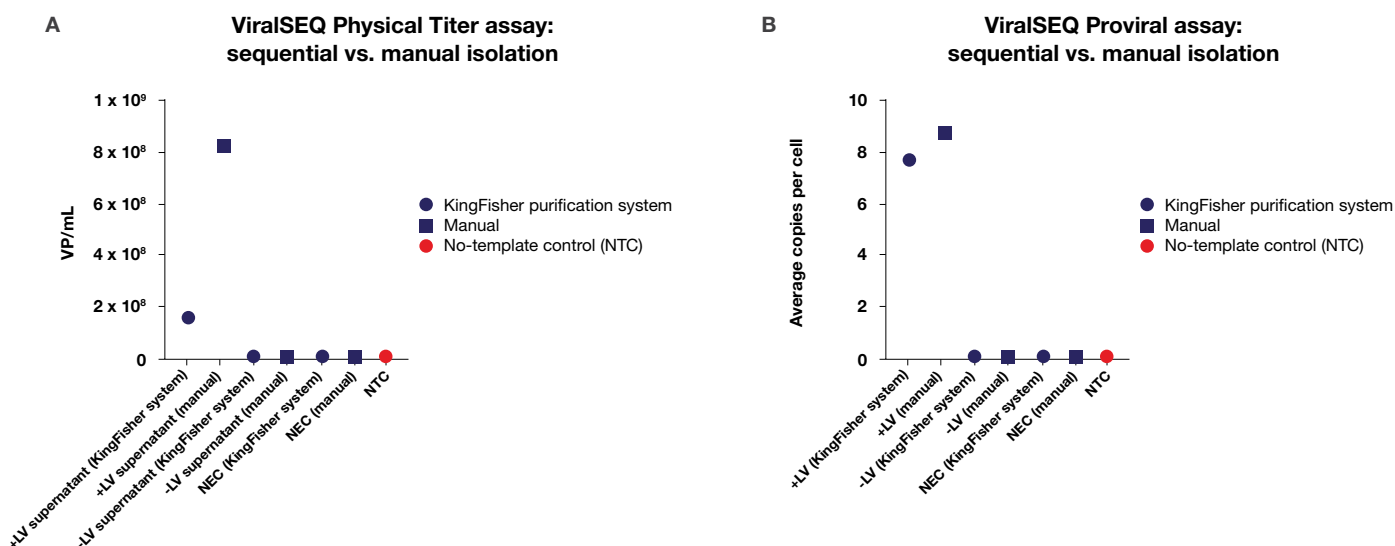


Figure 9. Quantification of physical viral particles per mL. RNA evaluation with the ViralSEQ Physical titer assay between nucleic acid from manual and automated isolations utilizing the MagMAX Sequential DNA/RNA Kit on the KingFisher Apex Purification System.

Figure 10. Quantification of DNA from the lentivirus. Evaluation with the ViralSEQ Proviral assay between nucleic acid from manual and automated isolations utilizing the MagMAX Sequential DNA/RNA Kit was carried out on the KingFisher Apex Purification System.

Conclusions

The study outlines the use of the KingFisher Apex Purification System to achieve significant time savings, potential increased productivity, and streamlined consistency in cell therapy translational research, from discovery to preclinical workflows. The KingFisher Apex system reduces touchpoints and can help automate QC testing workflows, including cytotoxicity assays, sterility and microbial contamination evaluation, and copy number counting of cell growth media post-transduction. This application note demonstrates that integration of a single-module benchtop KingFisher Apex Purification System can suit the needs of various workflows.

With the integration of KingFisher Apex software, further automation could be achievable with adoption of robotic arms and liquid handlers. Maintaining benchtop stand-alone instruments like the KingFisher Apex system, Attune CytPix Flow Cytometer, Varioskan LUX reader, Luminex platform, and QuantStudio 12K Flex Real-Time PCR System can facilitate consistency in productivity in a full workflow.

Authors

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Ordering information

Product	Cat. No.
CAR T cell generation, transduction, and expansion	
CTS DynaCelect Magnetic Separation System	A55867
CTS DynaCelect Cell Isolation Kit	A52300
Dynabeads Human T-Activator CD3/CD28 for T Cell Expansion and Activation	11161D
CTS Detachable Dynabeads Release Buffer	A5588303
CTS LV-MAX Production Medium, 1 L	A4124001
CTS Opti-MEM I Medium, 100 mL	A4124801
CTS LV-MAX Transfection Kit	A4132601
CTS OpTmizer Pro SFM	A4966101
CTS Immune Cell SR	A2596101
CTS GlutaMAX-I Supplement	A1286001
PeproGMP Human IL-15 Recombinant Protein	GMP200-15-50UG
LIVE/DEAD Fixable Aqua Dead Cell Stain Kit, for 405 nm excitation	L34966
Cytotoxicity	
Varioskan ALF Multimode Microplate Reader	VA000010C
Varioskan LUX Multimode Microplate Reader	VL0000D0
Confirmation of transduction with flow cytometry	
eBioscience Flow Cytometry Staining Buffer	00-4222-26
Fc Receptor Binding Inhibitor Polyclonal Antibody	14-9161-73
Attune CytPix Flow Cytometer	A51848
Transduction efficiency with immunoassays	
ProcartaPlex Human Th1/Th2/Th9/Th17 Cytokine Panel, 18plex	EPX180-12165-901
KingFisher Apex Purification System with 96 Combi Head	5400920
KingFisher Apex 96 DW Head	24079930
KingFisher Apex 96 Tip Comb	97002570
KingFisher Apex 96 Barcoded Tip Comb	97002534B
KingFisher Apex Barcoded 96-well Deep Well Plate	95040450B
KingFisher Apex 96 Microplate (200 µL), barcoded	97002540B
Luminex 200 Instrument System	APX10031
Luminex xMAP INTELLIFLEX System	APX2020
Nucleic acid isolation (DNA and RNA)	
RNase-Free Microcentrifuge Tubes, 1.5 mL Graduated	AM12400
MagMAX Sequential DNA/RNA Kit and Reagents	A65309
NanoDrop Eight and Laptop	NDEIGHT-LAPTOP

Product	Cat. No.
Molecular quality control of DNA and RNA from T cell cultures	
QuantStudio 12K Flex Real-Time PCR System, 384-well block, laptop	4471081
Mycoseq Plus Mycoplasma Detection Kit	A55124
SteriSeq Rapid Sterility Testing Kit	A57185
ViralSeq Lentivirus Proviral DNA Titer Kit	A53561
ViralSeq Lentivirus Physical Titer Kit	A52597

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9. Thermo Fisher Scientific (2021). [SteriSeq Rapid Sterility Testing Kit User Guide.](#)

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