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Universal Rapid Clear® 24-Well Filter Plate: 15-Minute Lysate Clarification solution for intracellular proteins

Data provided by Pfizer, Genetech and Leash Bio

Abstract

Thomson's new method provides a fast, efficient approach for clarifying cell lysates prior to intracellular protein purification. The Thomson Universal Rapid Clear® 24-Well Filter Plate offers a fast, standardized solution for processing up to 24 samples (7mL each) in as little as 15 minutes. Using a non-binding depth-filter matrix, it removes debris while preserving protein integrity across diverse hosts including insect cells, *E. coli* and mammalian expression systems. Optimized protocols for insect cells and *E. coli* demonstrate up to 2 hours of time savings and improved reliability, establishing the Universal Rapid Clear® Plate as a robust, automation-friendly tool for accelerated protein screening and downstream process development.

Introduction

Traditional clarification approaches - centrifugation alone and sequential depth-filter steps - can be slow, variable, and difficult to automate at scale. The Universal Rapid Clear® 24-Well Filter Plate solves these issues with a standard ANSI/SLAS footprint that integrates into existing automation platforms and plate handlers. Its depth-filter design efficiently removes cells and debris while preserving protein integrity, making it well-suited to lysate clarification for intracellular proteins, protein-expression studies, and early downstream process development. As biopharma teams rely more heavily on robotic screening to shorten timelines, this format provides consistent, reproducible results across multiple samples with minimal method changes.

Product Features

- **Works with all intracellular lysates:** Insect cells (Sf9, *T. ni*), *E. coli*, CHO & HEK293
- **Filtered lysates are ready for purification**
- **Clarifies up to 7 mL each well:** Supporting screening without the bottleneck of manually processing samples
- **Depth-filtration technology:** Effectively removes cells and particulates - no sequential filter steps, no risk of clogging, and minimal protein loss due to non-binding filter matrix
- **Automation-friendly:** Standardized *(ANSI/SLAS format)* footprint

Materials

Intracellular Protein Methods

Centrifugation Method

1. Collect cells from expression system (*E. coli*, insect cells, etc.)
2. Evaluate cell density – transfer appropriate number of cells to centrifuge and pellet
3. Remove supernatant and gently resuspend pellet in appropriate amount of lysis buffer (reference Table 1)
4. Set centrifuge settings to RCF[1] and centrifuge lysate sample at 4,000 x g for 10 minutes to pre-clear
5. Place filter plate (PN 921547) on top of collection plate (PN 931569-G-1X)
6. Transfer up to 7 ml of pre-cleared cell culture supernatant to empty filter wells2
7. Set centrifuge settings to RCF and spin at 336 x g RCF (340RPM) for 5 minutes
8. Remove filter plate and collect clarified samples[3]
9. Measure protein concentration in clarified samples (Octet® (Sartorius), SDS-PAGE, HPLC/FPLC, etc.)
10. Purify via PhyTip® (Biotage), IMCStips® (IMCS) or other purification system
11. Assess biological activity, if applicable

Cell type	Culture Density	Lysis buffer resuspension volume (volume Lysis buffer: original culture volume)
E. coli	3 x 10^9 cells/ml (~OD600 ≤ 3)	1:10 to 1:20
Insect Cells (Sf9, *T.ni*, etc.)	1.5 – 2.5 x 10^6 cells/ml	1:6 to 1:8

Table 1 – Recommended general ratio of volume of lysate to culture to prevent clogging[4]

Case Study 1 : Pfizer

Pfizer

Intracellular protein lysate clearance method for *E. coli*

Materials

- Thomson 24-well Universal Rapid Clear® Filter Plate (PN 9251547)
- Thomson 24-well plate (PN 931568)
- Beckman Coulter Avanti J Series
- B-PER™ Bacterial Protein Extraction Reagent (Thermo Fisher PN 78243)
- PhyTip, IMCStips or similar purification systems

Procedure

1. Collect 35 ml of *E. coli* culture (OD_{600} ≤ 3.0) by centrifugation in conical centrifuge tube at 4000 x g RCF for 5 minutes
2. Completely remove supernatant and gently resuspend pellet in 2mL of B-PER reagent
3. Centrifuge lysate sample at 4,000 x g RCF for 10 minutes to pre-clear lysate
4. Place filter plate (PN 921547) on top of collection plate (PN 931569-G-1X)
5. Transfer 7mL of pre-cleared cell culture supernatant to empty filter wells
   A. For denser cultures of OD_{600} > 3.0 please transfer 6mL of pre-cleared supernatant
6. Set centrifuge settings to RCF and spin at 336 x g RCF for 5 minutes
7. Remove filter plate and collect clarified samples

8. Measure protein concentration in clarified samples (Octet, SDS-PAGE, HPLC/FPLC, etc.)
9. Purify via PhyTip, IMCStips or other purification system
10. Assess sample purification by SDS-PAGE

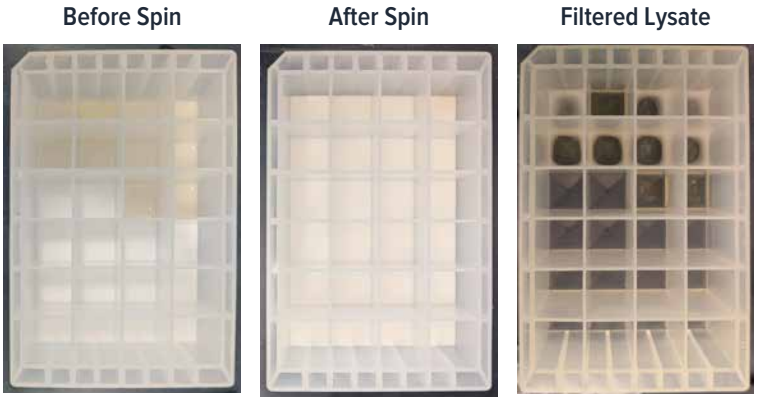


Figure 2 – Pre-clearance of intracellular protein from *E. coli* lysates ensures uniform filtration through the Universal Rapid Clear filter plates. Left: Lysate samples loaded on the Universal Rapid Clear filter plate; Middle – post-filtration Universal Rapid Clear® filter plates retain debris and not samples; Right – Filtered lysate cleared of cell debris.

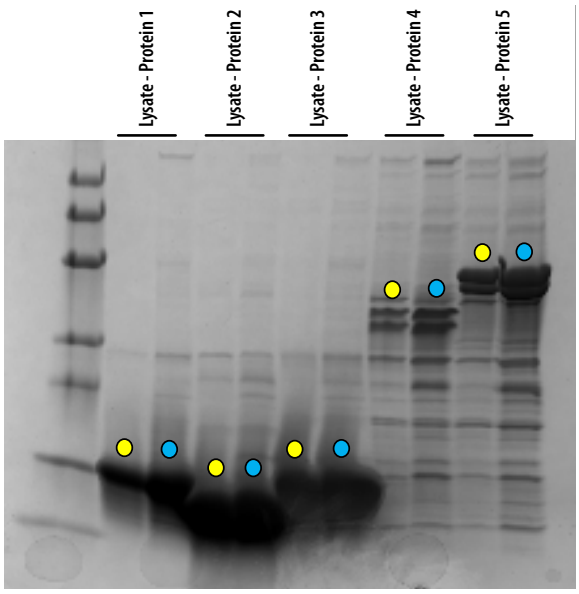


Figure 3 – Analysis of five different intracellular proteins expressed in *E. coli* and purified using the above procedure, then resolved by SDS-PAGE for either standard 2-hour protocol (yellow dot), or the Thomson protocol (Blue dot); Left lane: MW marker.

Summary Study 1

The Thomson Universal Rapid Clear® 24-well filter plates performed well to clarify lysates while shortening processing times. As observed in Figure 2, pre-clearance of intracellular protein lysates using a 10-minute centrifugation ensured uniform filtration through the Universal Rapid Clear filter plates. SDS-PAGE analysis (Figure 3) of five different intracellular proteins purified using PhyTips after the normal, 2-hour processing time procedure, versus the rapid 15-minute Thomson procedure, yields reliable and reproducible purified protein profiles. This demonstrates that the Thomson Universal Rapid Clear® 24-well filter plates reliably clarified debris prior to PhyTip, IMCStips or similar, preventing clogging and sample loss.

Case Study 2 : Pfizer

Intracellular protein lysate clearance method for Expression Systems or ATCC Sf9 cells

Materials

- Thomson 24-well Universal Rapid Clear® Filter Plate (PN 9251547)
- Thomson 24 well plate (PN 931568)
- Beckman Coulter Avanti J Series
- B-PER Bacterial Protein Extraction Reagent (Thermo Fisher PN 78243)
- PhyTip, IMCStips or similar purification systems

Procedure

1. Collect 35mL of Sf9 culture (2.5 x 10^6 cells/ml) by centrifugation in conical centrifuge tube at 400 x g RCF for 10 minutes
2. Completely remove supernatant and gently resuspend pellet in 2mL of B-PER reagent
3. Centrifuge lysate sample at 4,000 x g RCF for ten minutes to pre-clear lysate
4. Place filter plate (PN 921547) on top of collection plate (PN 931569-G-1X)
5. Transfer 4mL of pre-cleared cell culture supernatant to empty filter wells
6. Set centrifuge settings to RCF and spin at 336 x g RCF for 5 minutes
7. Remove filter plate and collect clarified samples
8. Measure protein concentration in clarified samples (Octet, SDS-PAGE, HPLC/FPLC, etc.)
9. Purify via PhyTip, IMCStips or other purification system
10. Assess sample purification by SDS-PAGE

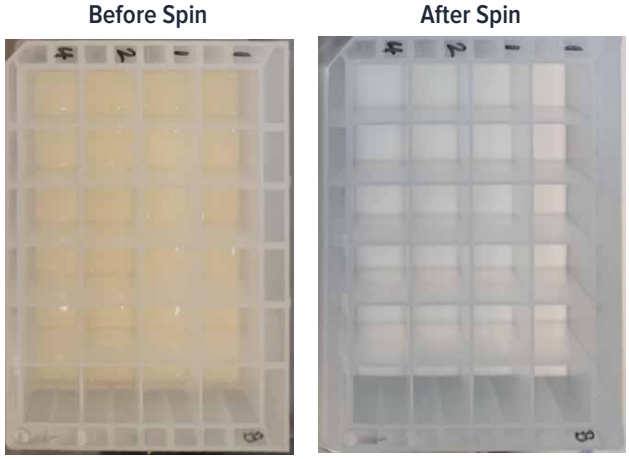


Figure 4 – Pre-clearance of intracellular protein from Sf9 lysates ensures uniform filtration through the Universal Rapid Clear® filter plates. Left: Before spin; Right – Filter after spin.

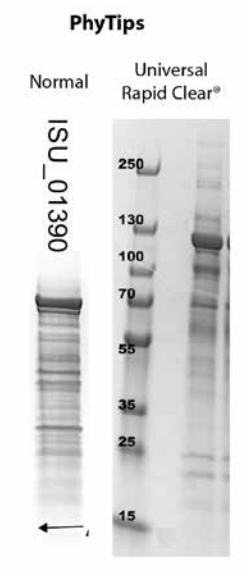


Figure 5 – Analysis of an intracellular protein expressed in Sf9 cells and purified using the above procedure, then resolved by SDS-PAGE for either standard 2-hour protocol (Normal) or the Thomson protocol (Universal Rapid Clear®). Molecular weight marker for reference.

Summary Study 2

As shown in Figure 4, pre-clearance of intracellular SF9 protein lysates ensured uniform filtration through the Universal Rapid Clear filter plates. SDS-PAGE analysis (Figure 5) demonstrates how the simple and quick Thomson procedure yields the same profile as purified proteins using the slower, 2-hour procedure.

Case Study 3 : Leash Bio

Leash

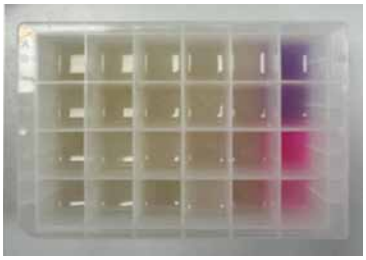
Intracellular protein lysate clearance method for Expression Systems or ATCC Sf9 cells

Materials

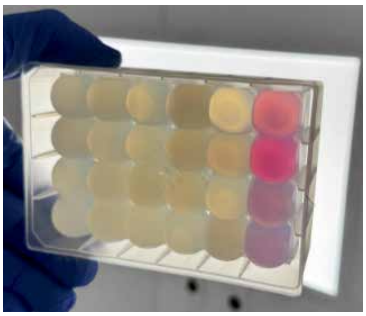
- Thomson 24-well Universal Rapid Clear® Filter Plate (PN 9251547)
- Thomson 24 well plate (PN 931568)
- Thomson Optimum Growth® 6-well plate (PN 931167)
- Beckman Coulter Avanti J Series

Procedure

1. 30mL cultures of *T.ni* cells (2 x 10^6 cells/mL at 98% viability; 30mL per well in Thomson Optimum Growth® 6-well plates; harvested 64-66 hrs. post-infection by ~2 VP/cell MOI) were pelleted and resuspended in 4mL of lysis buffer, transferred to Thomson 24-well collection plates and sonicated.
2. Plates were spun until large debris pelleted out at 4°C for 30 minutes at 4000 x g RCF in JS5.3 rotor using the Beckman Coulter Avanti® J Series.
3. Crude, clarified lysates were applied to the Thomson 24-well Universal Rapid Clear® Filter Plate and spun at 800 x g RCF for 5 minutes.
4. An optional initial enrichment was performed by applying Ni-NTA resin to the bottom of the 24-well collection plate.
5. Optical Clarity was successfully achieved after Universal Rapid Clear filtration of *T.ni* lysates.



30mL cell pellet lysed in 4mL of buffer



Clarified Lysate with NiNTA resin in bottom of wells

Figure 6 – Left – 4 ml of clarified lysates (from 30mL cultures) are observed filtration by the Universal Rapid Clear® 24-well Filter Plate. Right – Clarified lysates with Ni-NTA resin in the bottom of the wells.

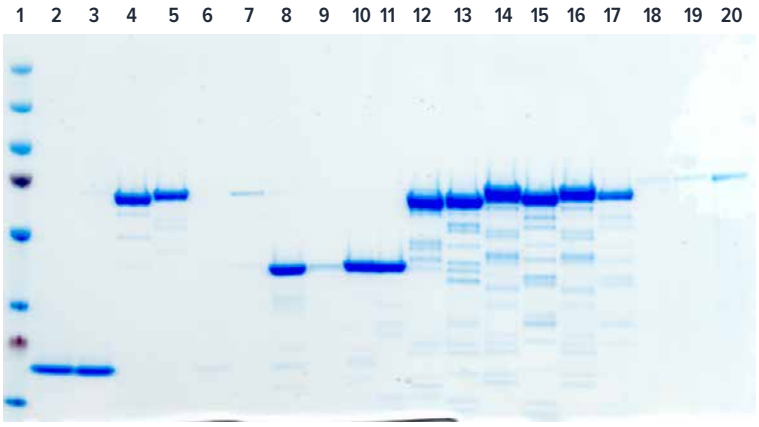


Figure 7 – Multiple intracellular proteins of different molecular weights were resolved by 4-14% SDS-PAGE (in 1x MOPS). Proteins were purified using Streptactin XT are represent 240µl of the eluted volume for each sample.

Summary Study 3

As shown in Figure 7 (gel image from Leash Bio) SDS-PAGE resolved proteins were abundant and all yields were as expected. Protein titer and yield benefited from Universal Rapid Clear® Clarification. This quick and reliable method was reproducible for multiple intracellular proteins, illustrating its universal benefits.

Discussion

Universal Rapid Clear® 24-well filter plates remove of cellular debris and particulates.

Complete clarification of lysates for multiple different intracellular proteins from *E. coli* or insect cells (Sf9 or *T.ni*) in only 15 minutes. This is a 2-hour savings over the standard processing time.

Non-binding depth filter matrix for 90-95% recovery.

Minimal variation between different lots of plates.

Seamless integration with liquid handling systems – able to be used on deck to be later manually transferred to a collection plate and centrifuged.

Conclusion

The Thomson Universal Rapid Clear® 24-Well Filter Plate provides a faster procedure (15 minutes spin) solution for high-throughput clarification of cell lysates for intracellular proteins expressed in *E. coli*, insect cells, and mammalian cells, commonly used in biopharmaceutical development environments.

The plate's proven compatibility with multiple intracellular proteins, as well as standard antibodies, bi-specifics, multispecifics, fusion proteins, and antigens enables seamless integration into existing workflows, significantly reducing processing time. The Thomson Universal Rapid Clear® system supports accelerated development timelines while ensuring protein integrity and maintaining the quality standards required for biopharmaceutical applications.

For laboratories seeking to optimize their clarification workflow by two hours, reduce processing time, and improve throughput capacity, the Thomson Universal Rapid Clear® 24-Well Filter Plate represents a valuable advancement in sample preparation technology.

Acknowledgements

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Notes

[1] **RCF:** RCF (relative centrifugal force) also known as g-force (x g) is the force applied in relation to the sample. The radius of the centrifuge will determine the force which is dependent on radial length from axis to sample.

RCF = 1.18×R×1000/RPM

RPM is the number of revolutions per minute. This application note focuses on RCF rather than RPM. Machine-to-Machine, RCF is a more accurate measurement of force.

[2] To avoid spilling it is recommended to apply a foil seal to the plates during centrifugation (Thomson PN 899405-1).

[3] Flow though of lysate may not be very clear, however this will not affect the downstream purification procedures.

[4] It is recommended to avoid clogging by testing optimal dilution and lysis conditions for your specific sample. Please contact your Thomson representative for any assistance (info@htslabs.com).

Thomson Part Numbers

Well Plate	Part Number
24-Well Universal Rapid Clear® Filter Plate	921547
24-Well Plate I Square Well Round Bottom	931565-G-1X
24-Well Plate I Square Well Round Bottom	931568
24-Well Plate I Square Well Pyramid Bottom	931569-G-1X
24-Well Plate I Square Well Pyramid Bottom	931571
Adhesive Foil Seal	899405-1

Appendix

Lane	Mw	Construct Name and Boundaries
1	-	PageRuler Plus Protein Ladder
2	20.05	SMARCA4_A1447-D1569_pBAC-1-N-tags
3	19.92	SMARCA4_A1447-D1569_pBAC-1-C-tags
4	62.70	SOS1_E564-T1049_pBAC-1-N-tags
5	62.57	SOS1_E564-T1049_pBAC-1-C-tags
6	30.86	PARP7_S445-I657_pBAC-1-N-tags
7	30.73	PARP7_S445-I657_pBAC-1-C-tags
8	40.28	PTPN1_E2-D298_pBAC-1-N-tags
9	40.14	PTPN1_E2-D298_pBAC-1-C-tags
10	40.77	PTPN2_P2-D302_pBAC-1-N-tags
11	40.64	PTPN2_P2-D302_pBAC-1-C-tags
12	65.44	PTPN6_V2-S528_pBAC-1-N-tags
13	65.31	PTPN6_V2-S528_pBAC-1-C-tags
14	66.44	PTPN11_T2-E530_pBAC-1-N-tags
15	66.31	PTPN11_T2-E530_pBAC-1-C-tags
16	66.44	PTPN11_T2-E530_E76K_pBAC-1-N-tags
17	66.31	PTPN11_T2-E530_E76K_pBAC-1-C-tags
18	66,463	BSA 100ng
19	66,463	BSA 250ng
20	66,463	BSA 500ng