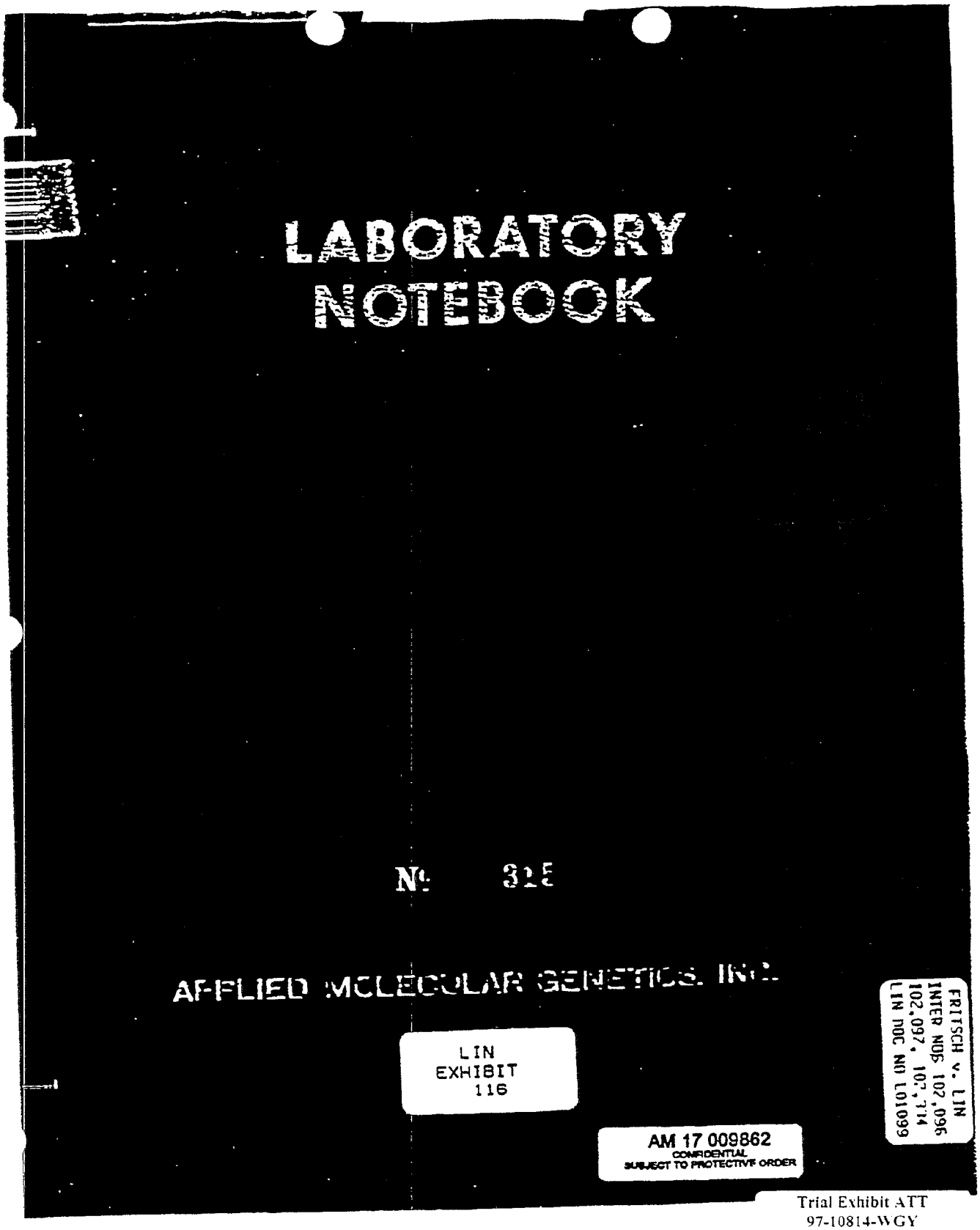
EXHIBIT 11



Trial Exhibit ATT
97-10814-WGY

Trial Exhibit 217
97-10814-WGY

NOTEBOOK NO. _____

ISSUED TO Jeri Hare

ON 2/11 1983

DEPARTMENT _____

RETURNED 10-10 1988

SCIENTIFIC NOTEBOOK CO.
5007 WEST DONNA DRIVE
STEVENSVILLE, MICHIGAN 49127

Project No.
2 Book No. TITLE Solution Competition - ① Jeffs human epo ② monkey sera ③ transfectifies ④ HUMRIG ⑤ Dubos

m Page No.

● 1/25/84

A variety of epo sources were tested for their ability to compete with standard epo in a solution phase against the anti-peptide Ab.

Procedure

1) Add 5λ trasylol / tube
2) Add sample to tubes along with an appropriate amt of PBS+ 1% BSA so the final volume is 300λ
3) Add 50λ of a 1:2500 dilution of 8C-180 #1 7.0.6 to each tube
4) Incubate at 37° for 1½ hrs.
5) Add 18λ I-125 epo to each tube 18λ = 14,117 cpm.
6) Incubate at 4° for ~20 hrs
7) Add STAPH-A (150λ / tube except monkey sera gets 600λ, 400λ, or 300λ depending on the size of the sample)
8) Process as usual

Results

Sample	EPO or species	EPO	PBS+.12%BSA	cpm	cpm - pre-immune	% inh.	calculated epo	EPO/ml
0	—		240	4883	4464			
0	—		240	5126				
5λ	D	1 mU	235	5068	4530	0		
10λ	D	2 mU	230	5176	4638	0		
5λ	C	10 mU	235	4248	3710	16.9		
10λ	C	20 mU	230	4305	3767	15.6		
2.5λ	B	50 mU	237	3446	2908	34.9		
5λ	B	100 mU	235	3018	2480	44.4		
10λ	B	200 mU	230	2142	1604	64.1		
15λ	B	300 mU	225	2075	1537	65.6		
5λ	A	1 U	235	1706	1162	74.0		
10λ	A	2 U	230	1231	693	84.5		
Pre-immune			240	441	538 - Pre-immune			
Pre-immune			240	635				
human	E7 60λ	15.1	180	5252	4714	0	0	
"	120λ	30.2	120	3995	3457	22.6	19 mU	22.3 mU/ml
human	M 60λ	0	180	6096	5558	0	0	
"	120λ	0	120	6050	5512	0	0	

To Page No.

FRITSCH v. LIN
INTER NOS 102,096
102,097, 102,334
LIN DOC NO 101101

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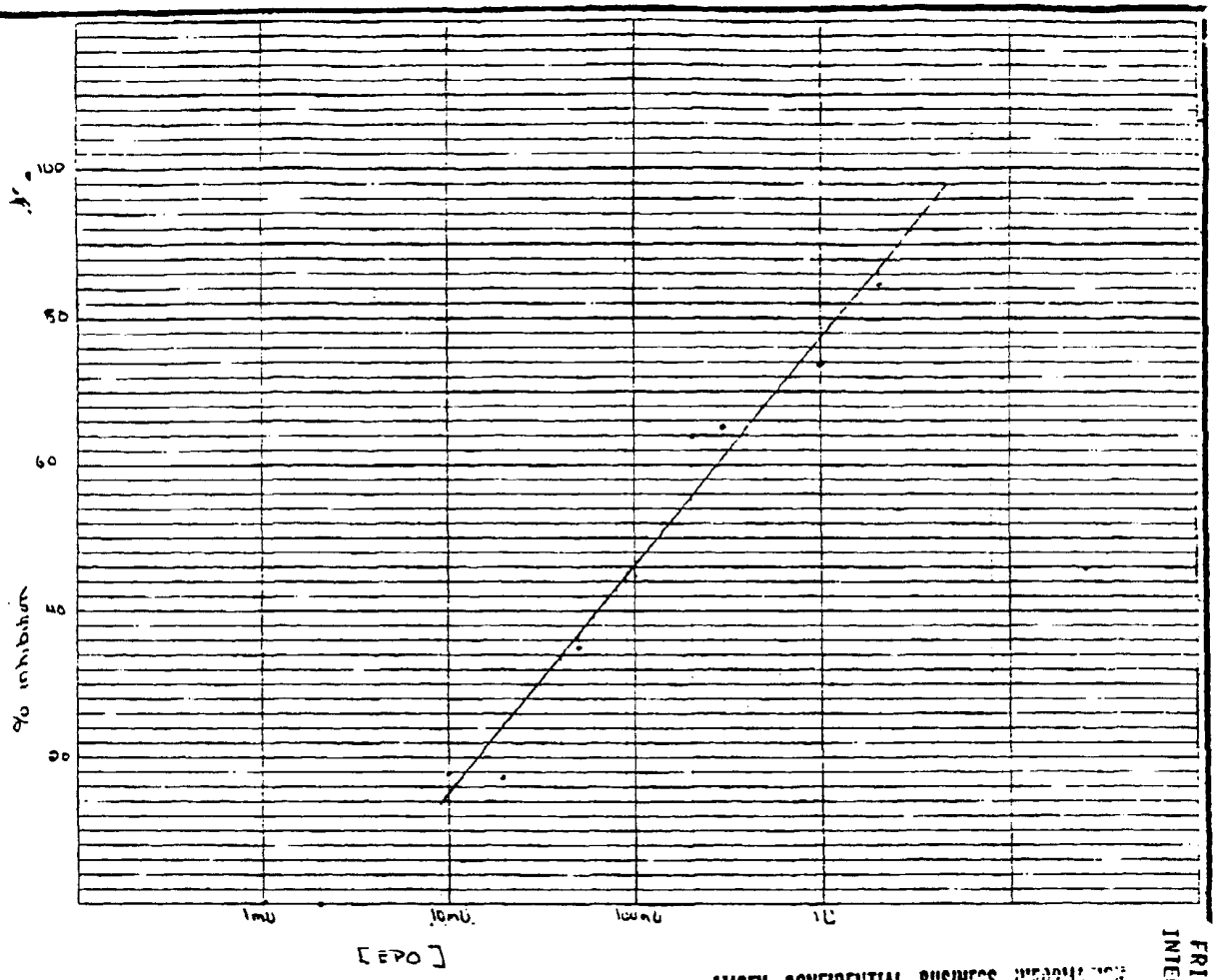
Project No.
Book No.
43



age 77) using α-crude Ab in a solid competition showed the titer of E7 to be 35.4 mU/ml (before concentration) The mock was negative This assay gives us 22.3 mU/ml for E7 and 0 for the mock

monkey EPO samples: monkey ③ is old monkey #3 which gives a titer 1.3U/ml in genes assay. monkey # 2 is from 1183 and gives a titer of 50 mU/ml using anti-crude Ab. Monkey control is monkey #1 1183 which give a titer of 50 mU/ml.

All monkey samples are negative w/ anti-peptide Ab

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TLE _____ Project No. _____ Book No. _____ 43

from Page No.	sample (EPO or expected EPO)	PBS+0.1%BSA	cpm	cpm-pre	% inh	calculated EPO	EPO/ml
9 monkey ②	50λ	190	5824	5286	0	0	
=0	25λ	215	5375	4837		0	
"	10λ	230	5650	5112		0	
=2 monkey ③	50λ	190	6794	6256		0	
=3 "	25λ	215	6270	5732		0	
=1	10λ	230	6614	6076		0	
=5 monkey-C	50λ	190	6092	5554		0	
=	25λ	215	7008	6470		0	
=7	10λ	230	6100	5562		0	
=α-therapeutics EPO							
=10λ	1 U	230	1365	827	81.5	1.3U	130 U/ml
20λ 1:10	200mU	220	1941	1403	68.6	510mU	25.5U/ml
=10λ 1:10	100mU	230	2597	2059	53.9	190mU	19.0 U/ml
5λ 1:10	50mU	235	2886	2348	42.4	110mU	22.0 U/ml
2λ 1:10	20mU	238	4040	3502	21.6	18 mU	9.0 U/ml
Hankins - 30U/ml							Avg = 17.7 U/ml
100λ 1:10	300mU	140	3829	2091	53.2	180 mU	18 U/ml
50λ 1:10	150 mU	190	3130	2592	41.9	72mU	14.4 U/ml
25λ 1:10	75mU	215	3451	2913	34.7	44mU	17.6 U/ml
Dukes 598 U/700λ							Avg = 16.7 U/ml
20λ 1:100	171 mU	220	5560	5022	0	0	
10λ 1:100	85mU	230	5782	5244	0	0	
5λ 1:100	42.7mU	235	6203	5665	0	0	

Human EPO samples - E7 = 293 cell transfected w/ a 6 Kb piece containing the sequence for human epo. M = mock transfection. Both samples were concentrated 7.1x before assaying. Previous results (book #340 - page 77) using α-crude Ab in a soln. competition showed the titer of E7 to be 35.4 mU/ml (before concentration). The mock was negative. This assay gives us 22.3 mU/ml for E7 and 0 for the mock.

Monkey EPO samples: monkey ③ is old monkey #3 which gives a titer of 1.3U/ml in genes assay. monkey #2 is from '83 and gives a titer of 500 mU/ml using anti-crude Ab. Monkey control is monkey #1 '83 which gave a titer of 50 mU/ml.

All monkey samples are negative w/ anti-peptide Ab.

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FRITSCH v. LIN INTER NOS 102,096 LIN DOC NO L01103 102,097, 102,334

Project No._____

4 Book No._____ TITLE _____

Num Page No.__

⇒ Therapeutics - Their titer is supposed to be 100 u/ml we get ~ 2x higher in the anti-crude assay and an avg of ~ 1.8x higher titer here using the anti-peptide.

⇒ Hankins material - a partially purified mouse erythroleukemia supernatant from 1483. The titer is 30 u/ml using the anti-crude. Its negative w/ the MCA in a plate binding. Our average value is 16.2 u/ml in the anti-peptide assay.

⇒ Dukes material - T-8-30 - fraction # 30 - peak from HA column ~ 50% pure. In vivo assay is 854 mu/ml. Anti-crude is ~ ½ that. Anti-peptide is negative.

FRITSCH v. LIN
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102,097, 102,334
LIN IDC NO L01104

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Project No. _____ Double Ab western - ① material from
68 Book No. _____ TITLE Lionel ② CHO cell material -

From Page No. _____

3/26/84 - We will be running two double Ab westerns. The first will be examining cell culture material from which we have a new preparation of his Hu-32 line as well as a new line called 201no 7.10-7/26/83 which is supposed to exhibit similar activity to the Hu32 line. The second western will be examining material from CHO cells (monkey ops

Immunoprecipitation
1) Add 75λ trasylol per tube
2) Add sample, Ab- and I-125 epoC for ~ calculation of recovery (20λ = 31,504 cpm)
3) Incubate overnight at 4°
4) Precipitate with 75λ of 1:5 protein-A sepharose. Wash as usual
5) Count
6) Add 55λ/tube of 3x HSB. Boil ~5 min Pellet Remove supernatant
Calculate recovery
7) Add dye & ficoll Prepare the remaining samples for the gel.
Boil ~5 min
8) Electrophorese overnight at ~30V on a 12.5% polyacrylamide gel
9) Transfer to nitrocellulose at 60V for 6 hrs
10) Block w/ 10% horse serum add RT for ~ 1½ hrs
11) Add mCA (protein A-sepharose #8) at 10 ug/ml in PBS⁻ + 5% horse serum w/ azide, trasylol and PMSF per usual. Incubate overnight
12) Wash 3x w/ PBS⁻ pH 7.6
13) Add biotinylated horse anti mouse (1 drop/10 mls)
Incubate at RT ~45 minutes
14) Wash 3x w/ PBS⁻ pH 7.6
15) Add ABC (2 drops/10 mls).
Incubate 60 minutes at RT
16) Wash 3x w/ PBS⁻
17) Add color development reagent

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To Page No. _____

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TITLE ______ Project No. ____ Book No. ____ 69

From Page No. __

Results

Immunoprecipitation: ↙ from RIA done in book # 569 p. ___ 3/13-3/14/84

sample	vol	[EPO]	Ab[(2)]	I-125 epo	cpm in pellet	% ppt (1)	cpm in LSB sup	cpm in LSB pellet	% recovery in extraction	ng loaded on gel
2 IW-32-5x conc as usual - 1/2 the act. as usual through line 1	3x1ml	233ng total	3λ/tube (9λ total)	30λ in 2 of the 3 tubes	8290	13.2 (37.6)	6150	1735	74.2	6.5 ng
3 201ng - newline 2 ~20ms 1ux conc	1ml	300ng	9λ	30λ	5285	16.8 (47.9)	4575	750	56.6	12.4 ng
4 IW-32 old batch 10x	1ml	15.4ng	PI-9λ	30λ	90	–	—	—	—	—
5 201-IW-32-10x	1.5ml	0	9λ	30λ	3570	12.3 (35)	3105	545	80.2	?
6 genes crude epo	17λd 1:10	300ng	9λ	30λ	8055	25.6 (72.9)	6365	1100	79.0	23.0 ng
7 genes crude epo	5.5λd 1:10	200ng	9λ	30λ	10525	33.4 (95.2)	8450	1255	80.6	15.3 ng
8 genes crude epo	5.5λd 1:10	200ng	PI 9λ	30λ	45	0	—	—	—	—
2 CHO-line 3 - ~20 u/ml	0.1ml	25ng	6λ	30λ	11045	35.1 (100%)	8745	1790	79.2	22.2ng
3 CHO-line 3 - ~20u/ml	0.3ml	54ng	8λ	30λ	9715	30.8 (87.8)	8190	1635	54.3	62.1
4 CHO-line 3 ~20 u/ml	0.7ml	186ng	10λ	30λ	6370	20.2 (57.6)	5720	950	89.8	101.3
5 control CHO	0.7ml	0	8λ	—	—	—	—	—	—	—
6 CHO-line 3	0.3ml	84ng	8λ PI	—	—	—	—	—	—	—

(1) The first # here is the % precipitation based on the 30,000 cpm in the starting material. The second number in parenthesis is the % precipitation using the 35.1% of the total in the first CHO sample as 100%. This number approximates the maximum precipitability of the system and is used to calculate the final recovery (i.e. ng loaded onto gel = % recovery in extraction X the % precipitation possible (if 35.1% of the total = 100%) x starting [epo]

(2) Ab: SC-204 #3089 t.b #3 - used undiluted in the amts mentioned

Comments - the % immunoprecipitability of the IW 32 lines is lower than usual - in fact the background is almost as high as the 'positives'. Genes crude epo precipitated as usual - as did the lower amts of the CHO material - the larger amts of CHO material didn't compete and lower the % precipitability of the I-125 epo as well as usual - however this has happened before.

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FRITSCH v. LIN
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102,097, 102,334
LIN DOC NO L01106

Project No.
70 Book No. TITLE

om Page No.

12.5% PAGE

Gel 1

1 low mw prestained marker 15 λ
2 1w32 - line 1 new material 6.5ng
3 201nn: new line 2 12.4ng
4 1w32 - old material + PI sera 0
5 201: 1w32 + Immune sera 0
6 gene crude epo 33
7 " 15.3
8 + PI sera 0
9 gene crude epo 17λ 1:10 No Ab 40ng
10 " 8.5λ 1:10 No Ab 20ng

Gel 2

2 low mw prestained marker 15λ
3 CHO line 3 222ng
4 CHO line 3 60.1ng
5 CHO line 3 101.3ng
6 control CHO 0
7 CHO line 3 + PI sera 0
8 Gene crude epo 1:10 No Ab 20ng

FRITSCH v. LIN
INTER NOS 102,096
102,097, 102,334
LIN DOC NO L01107

Results-

Gel #1 - can see material which co-migrates with authentic epo in lanes 2 and 3 - although fainter than was hoped however based on the amts that were theoretically loaded on the gel - the intensity of the bands is close

Gel #2 - Can see material in lanes 2-4 - none in the control lanes 5 & 6. This specific material is a very broad band which seems to have its average migration distance slightly less than authentic epo indicating an average mw above the control epo.

From some rough mw determinations it appears that the range of the CHO cell material is 30,000 - 35,000 - with the mode of intensity at about 34,000 d

To Page No.

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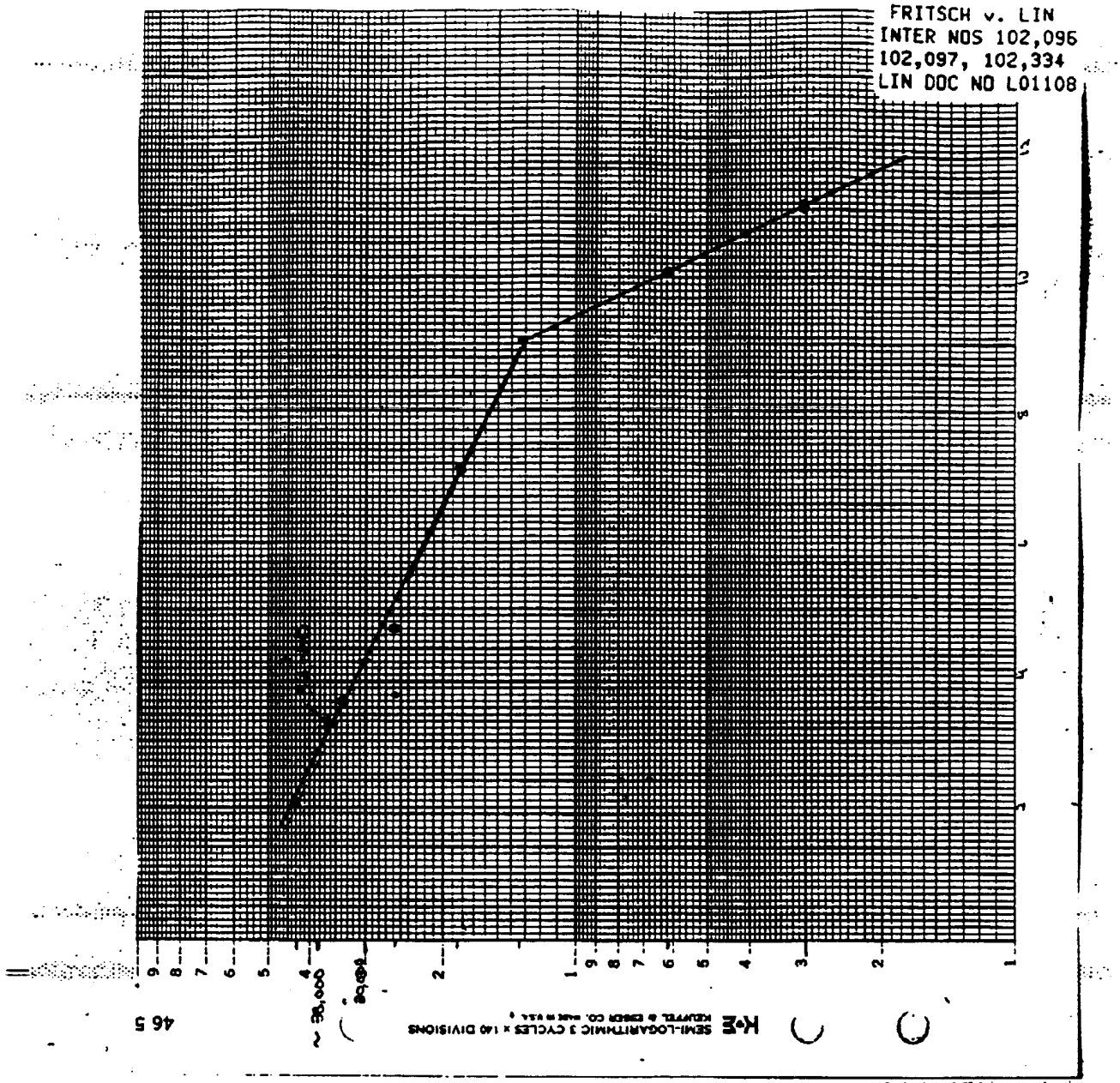

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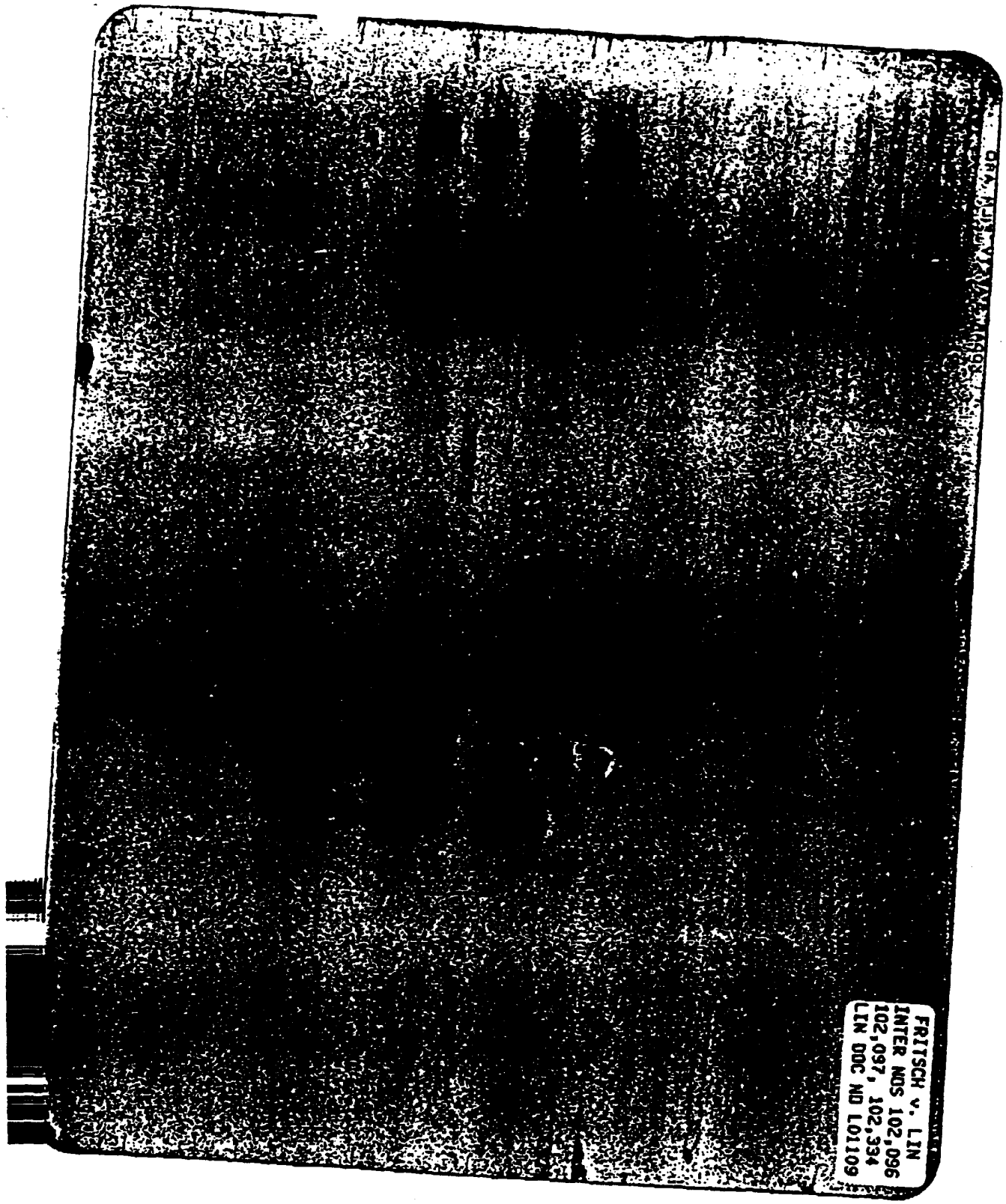

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102,097, 102,334
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AM 17 009873
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TITLE Project No. Book No. 71

From Page No.

migration = mw markers = 2.1cm, 4.7cm, 7.1cm, 9.05cm, 10.1cm and 11-11.1cm Authentic epo migrates with mode intensity at 3.6cm - The CHO cell material ranges from 2.5-4.2cm with the mode intensity at 3.2cm

Conclusion -

gel #1 - we are picking up material which co-migrates with authentic epo from variety cell lines. Although the intensity of the band isn't optimal - we will photograph this western since it shows reaction with positives - no reaction w/ negatives

gel #2 - we are visualizing a broad specific band from the CHO cell material This band is epo related since the Ab reaction is specific above background. The broad band ranges in mw from ~30,000 to ~38,000 with the mode of intensity at ~ 36,000 The band is quite continuous - no distinct bands within. In regard to the heterogeneity there are two possible explanations a) carbohydrate heterogeneity - or B) protein heterogeneity - probably at the C-terminus - since the visualization is done with mCA. Why the size includes material bigger than epo is also known - but the same 2 possibilities - may apply in conjugation - protein heterogeneity (maybe in processing protein and carbohydrate will need to test this hypothesis.

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