

## Mapping Cell Line Development Workflows with LabKey Biologics

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BioTherapeutics Development | Janssen Research & Development, LLC 2019 LabKey User Conference & Workshop | Seattle, WA











#### Introduction

Cell & Developability Sciences Cell line selection process

#### **Mapping CLD Process**

Molecule Registry Lineage tracking

#### Challenges

Unique ID Automation Project-centric

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## Introduction

1

#### Large Molecule Early Development



Drive candidate selection and development of the manufacturing cell line



#### **Off-Platform Programs Present New Challenges**

>50% of the Early Pipeline are not mAb

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#### More Molecules and Reduced Timeline



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## Typical Cell Line Development Timelines





#### New Cell Line / New Process



- Eliminated subcloning reduced timeline by 1.5 months (VIPS Technology)
- Site directed integration. Titers are more predictable, screen fewer clones.
- 'Early Look Material' produced from transfection pool (not clonal): Start Development Sooner.

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### Solutions in Cell line development

#### Timeline improvements with new CLD process:



First three CLD programs in new host and process



#### **Information Management** (3-4 hours/scientist/week 6,240 FTE hours per year)



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#### Reduced CLD Timeline (7 months -> 5months)

#### Information silos within ELN



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## **Mapping CLD Process**

2

## LabKey Biologics

Rev Biologics		
Q		
Registry	Assays	Samples
Media	Workflow	Experiments



## LabKey Biologics

C LabKey Biologics		a -
Q		
Registry	Assays	Samples
Media	Workflow	Experiments





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### Registry – Molecule Information Import

Main Proteins.   <u>Prote</u>	Targets	Polype Protein Inventor	eptide/Library <u>y Requests</u>   <u>Pr</u>	otein Scale	Constructs	Clones	-up Jobs	Plasmid Di	NA	Signal <u>Cell Line F</u>	Peptides tequests   1	Vi	ruses <u>n Plates</u>	Prot <u>Assay Pl</u>	teins lates   Pr	JNJ#	C-Codes	tic Moleo	ITS	Assa Assay Su	ays A <u>mmary   Help</u>	ssemblies	CBI	S Support	
Proteins   Isotyp	e Control Prote	ins   AA Prote	ins.										I	Logout I	BoZhai O	9/23/2019 4:1	)7:09 PM								
A Proteins	oine																								
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Select	Sort by	Columns	page size	25	<   >	>	page 1	(	of 1 ( 1 rec	ord )															
elect <u>mAb AA</u>	<u>Heavy Chain</u> CDS ID	Light Chain CDS ID	Heavy Chain CE	S	Light Chain CDS		ain CDS	Light Chain CDS ID 2	Heavy Chain CDS 2	Light Chain CDS 2	Assay Summaries	Chain Multiplier	Mol Wt	<u>Total</u> Length	<u>ug/pMole</u>	Extinction Coefficient	Theoretical Absorptivity Factor	<u>pi</u>	Charge at pH7	Protein Type	Biophysical Property Calc Date	Biophysical Property Calc By	Comments	Registered by	Registrat Date
0047 PT1B296	CDS000023144	CDS000023158	AA Sequence QVQL/ESGGG (448)	Peptide ID	AA Sequence	Peptide D							147952.8	1322	0.14795	2.1272E+05	1.4378	8.03	14.2	mAb	02/14/2018	Peter Buckley	,	Rebecca Custers- Allen	06/09/20
<   >	>																					1			-
													Pyt	:hc	on	Sci	ript	(9	Sus	sa	n)				
🍣 Lab	<b>Key</b> B	iologia	IS Se	arch	Registry	Sar	nples	Ass	says	Med	ia   V	/orkflov	w   1	Experii	ments										
Registry	Molecule S	ets Mol	ecules M	olecula	r Species	Protein	Seque	nces I	Nucleo	tide Sec	uences	Expre	ession §	System	ns C	onstruct	s Vecto	rs	Cell Li	nes					

 Select...

 Name 

 Alias 

 Description

 Mass 

 PI 

 </t



### Registry - Molecule

🤗 La	abKey	Biolo	giCS Search   Registry   Samples   Assays   Media   Workflow   Experimen	ts				
< Registry	Molec	ule Sets	Molecules Molecular Species Protein Sequences Nucleotide Sequences Expression Systems	Constructs Vect	ors Cell Lines			
🎢 In	isert New	-	Select					
N	ame 💿	Alias C	Description	JNJNumber ©	Components 💿	Avg. Mass 💿	pl 💿	۵ 3
	675	E	411 on hulgG4 PAA	65403117	CDS000049515, CDS000049696	143563.31	7.720	195000
	570	E	396 on hulgG4 PAA	66564069	CDS000048217, CDS000048239	145499.25	7.690	210000
	)04	3	04 PTM variant	66610479	CDS000054252, CDS000054268	146085.93	6.850	226000
	782	3	PTM variant	66563081	CDS000048396, CDS000046945	142818.28	7.330	231000
	878		GeneArt construct. Anti-PD1 agonist lead molecule 878 in Lonza vector. Both 405 and 169 utilize the MARKS signal	67484703	CDS000045130, CDS000055476	146250.72	7.460	221000
	849		GeneArt construct. Anti-PD1 agonist lead molecule         849 in Lonza vector. Both         403 and           170 utilize the MARKS signal         849 in Lonza vector. Both         403 and	65724243	CDS000045131, CDS000054038	145397.66	8.190	227000

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#### **Typical Cell Line Development Process**



#### Typical Cell Line Development Process - Data



#### Samples – Parental Cloning



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#### Sample – Subcloning



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#### Assays

😪 LabKey Biologics	Search	Registry	Samples	Assays	Media   Wo	orkflow   Exp	eriments	Reports					
Assays													Create - Manage -
Capture analytical data about samples													
	Oct	Nov	Dec	Jan	Feb	Mar	Apr	Mav	Jun	Jul	Aug	Sep	12 month total runs
CIEF													4
cSDS-NonReduced													1
cSDS-Reduced													1
Non-Reduced GXII													4
PeptideMap-PTM													4
Reduced GXII													4
SEC													4
Titer-aProA													9
Titer-Octet													20
Vi-CELL													26



#### Assay - RMA Glycosylation Profile Results

M	A Results											
Imp	port Data				Select							1 - 16 of 16
	Project 💿	JNJ #	C-Code	% Glycation	٢	% Agly ©	% Man5 💿	% G0 💿	% G0F-GlcNac 💿	% G0F 💿	% G1F 💿	% G2F
	(C):)	67484703	C3267B		3.1	C	0	3.6	0	89.3	7.1	
	(101)	67484703	C3268B		4	C	0	0	0	88.2	11.8	
	(10)	67484703	C3268C		3.6	0	0	0	0	80.6	19.4	
		67484703	C3268D		4	0	0	0	0	78.6	21.4	
	(101)	67484703	C3269B		4	C	0	1.8	0	90.6	7.6	
	(TD:)	67484703	C3270B		4.7	C	0	0	0	93.2	6.8	
	([]]	67484703	C3271B		4.7	0	0	0	0	91.5	8.5	
	(D):	67484703	C3272B		4.1	0	0	2.2	0	88.1	9.7	
	()	65724243	C3262B		0.9	0	3.7	7	4.2	72.6	12.5	
	([]]]	65724243	C3263B		0.9	0	3.9	7	4.1	72.7	12.1	
	(10:10)	65724243	C3264B		1	C	3.5	8.9	3.9	71	12.6	
	ED:	65724243	C3264C		1.1	C	4.2	8.5	4.4	68.9	14.1	
		65724243	C3265B		1.1	C	4.8	7.6	4.1	75.3	8.2	
		65724243	C3265C		1	0	0	8.2	2.1	77.7	12	
	E21	65724243	C3265D		1	0	3.5	5.9	4.4	81.3	4.9	

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#### Assay- RMA Glycosylation Profile Report



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#### Experiments – Included Samples

Expe	eriments	Overview	Assays Files													
0		I API N	/ledia Evaluation											' Star ₽	t Date: 201 End Date: N Modified	Delete 9-04-09 14:1 None specifie 5 months ag
Incl	luded San	ples														
N	lanage <del>-</del>	Charts	•				Select							1 - 10 of 10	<b>≵</b> G	rid Views <del>-</del>
S	Samples H	I T A (10)	Samples M S	(10)												
	AD # 💿	Project	Name	NJ # 💿	Clone C-Code	Sample D	escription ©	Comments ©	Group 💿	ELN Reference O	Concentration (	mg/ml) 💿	Buffer/Sample Matrix	⊙ Test ⊙	Scope (	Storage Te
	AD800		67	7957591		Level 2 Va Harvest	ariable Feed, 18d		API	Pre-NME- Dual Agonist-n001- 00027		18.84	86mM Bis Tris, 91mM Acetate, pH 6.0	API AMBR Module Package	API AMBR Module	-80°C
	AD800	(010000)	67	7957591		Level 2 Fi Harvest B	xed Feed, 18d		API	Pre-NME- Dual Agonist-n001- 00027		18.28	86mM Bis Tris, 91mM Acetate, pH 6.0	API AMBR Module Package	API AMBR Module	-80°C
	AD800	(01.777.7)	67	7957591		Level 2 Fi Harvest A	xed Feed, 18d		API	Pre-NME- Dual Agonist-n001- 00027		19.02	86mM Bis Tris, 91mM Acetate, pH 6.0	API AMBR Module Package	API AMBR Module	-80°C
	AD800	(JLI I I I)	67	7957591		Level 1 Va Harvest	ariable Feed, 18d		API	Pre-NME- Dual Agonist-n001- 00027		19.13	86mM Bis Tris, 91mM Acetate, pH 6.0	API AMBR Module Package	API AMBR Module	-80°C
	AD800	()	67	7957591		Level 1 Fi Harvest B	xed Feed, 18d		API	Pre-NME-Carlos Pre-NME-CAPCPA Pre-NME-CARLos Pre-NM		19.53	86mM Bis Tris, 91mM Acetate, pH 6.0	API AMBR Module Package	API AMBR Module	-80°C

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## Experiments – Assay

< Ex	perin	ments	Overview	Assays Files	3										
ţ				Nedia Evaluatio	'n									Start Date: 2019-04-09 End Date: None sp Modified 5 mont	Delete 9 14:11 pecified ths ago
A	ssay	/ Results	5												
	Cha	arts 👻					S	Select					1 - 10	of 10 🛃 Grid View	WS 🔻
	CIE	EF (10)	cSDS-N	onReduced (10	)) cSDS-	Reduced (10)	Non-Reduced	d GXII (10	)) Reduced GXI	I (10) SEC (10)					
0		AD # 💿	Project	Name	JNJ # 💿	Barcode ©	predicted pl	0	measured pl	pl Peak Area 🛛 🛇	Acidic Variants Peak Ar	ea 📀	Basic Variants Peak Area	% C-terminal Lysine	0
(	- 4	AD800	CL::	CL	67957591	NA0009935836			5.471	32.4		58.2	9.4		
1	- /	AD800	CL	CL	67957591	NA0009936901			5.472	34.4		58.3	7.3		
ĺ		AD800	CL::	C	67957591	NA0009998148			5.472	31.5		61.7	6.8		
1		AD800	CL	CL	67957591	NA0009998459			5.473	30.8		61.7	7.5		
(		AD800	CLERY	(01.7772.)	67957591	NA0009939313			5.47	29.8		56	14.2		
6		AD800	CL /	C	67957591	NA0009999549			5.472	28.3		57.1	14.6		
(		AD800	CLC CYM	()	67957591	NA0009998168			5.471	27.2		60.1	12.7		
(		AD800	CLERTY	(CL)	67957591	NA0009937693			5.468	28		60.4	11.6		
(		AD800	CL /	C	67957591	NA0009999314			5.47	25.7		62.1	12.2		
(		AD800	CL /	GLI 1104	67957591	NA0009998778			5.467	25.8		61.1	13		
					1	1				1					

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# Challenges

3

#### Sample ID and Lineage



- Where to get Parent/Children information from assay data file?
- Linking existing IDs with autogenerated IDs or barcodes
- Change management



#### Automation – exported data

NA0009269461 CDS000067080

1					[rupAlios	NA0009270898-	NA0009257530-	NA0009255595-	NA0009269461-	NA0009258176-	
2	Sequence\n(unformatted)	Mod.\nAA	Var. Pos.	Var. Pos.	Mod.\nNames	r C3426A	C3430A	C3431A	C3434A	3423A	
3	CTTTTT R	M	4	253	Oxidation/15.9949	6.47	7.64	5.9	7.09	10.5	
4	K	М	12	429	Oxidation/15.9949	2.68	3.79	2.5	3.54	5.3	
5	C	N	19	390	Deamidated/0.9840	0.787	0.777	0.466	0.885	0.78	
6		E	1	1	Glu-pyro-Glu/-18.0	lí 1.67	2.41	2.1	2.5	1.66	
7	CLOLOR C )			447		98.67	98.78	98.55	98.08	98.98	
8	CLOLOR GIV			448		1.33	1.22	1.45	1.92	1.02	
9	622777777777777777777777777777777777777	С	9	95	Cys->Tyr/3.0327	0.192			0.193		
10		С	7	368	Cys->Tyr/3.0327	0.0514	0.0491				
11	CTODOTAALOOLVK I	C	11	145	Cys->Tyr/3.0327	0.0521					
Results						Trans	form Sc	ripts (H	lannah)		
Import [	Charts -			Select					1 - 20 of 81	< > ±	G
Import [	Project ◎ Name ◎ JNJ # ◎ C-	Code 💿	Barcode	Select	uence O Chain O F	eptide	Mod Names	Mod AAs	1 - 20 of 81 Var Pos Protein	Condition	G
AD #	Project     Name     JNJ #     C-       6     Control     PT1B844     73292440     Ca	<b>Code</b> ③ 3428A	Barcode NA00092708	Select Prot Seq 98 CDS0000	uence O Chain F 267080 HC	eptide R	<ul> <li>Mod Names</li> <li>Cys-&gt;Tyr/3.032</li> </ul>	Mod AAs O 7 C	1 - 20 of 81 Var Pos Protein	Condition O 1	Perc
Import 0           AD #           AD81           AD81	Project         Name         JNJ #         C-           6         CD11000         PT1B844         73292440         C3           6         CD11000         PT1B844         73292440         C3	Code © 3428A 3430A	Barcode NA00092708 NA00092575	Select  Prot Seq Prot Seq Solution S	uence Chain F 067080 HC 2 067080 HC 2	eptide R R	Mod Names           Cys->Tyr/3.032           Cys->Tyr/3.032	Mod AAs O 27 C 27 C	1 - 20 of 81 Var Pos Protein	Condition O P5 RP P5 RP	G Perc

HC

Cys->Tyr/3.0327

С

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PT1B844 73292440 C3434A

AD816

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0.193

95 RP

#### Automation - instruments



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#### **Typical Cell Line Development Process**



#### Projects



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#### Business intelligence in the CLD process

#### **Efficient CLD process**

- Cell line development tracking
- Analytical data integration
- Automated report generation

#### **Informed Decision Making**

- Data Integrity
- Intelligence





#### Acknowledgement



Hirsh Nanda

Aapjeet Fnu



Hannah Brakke Kevin Krouse Susan Hert Ryan Luce





## Thank you

