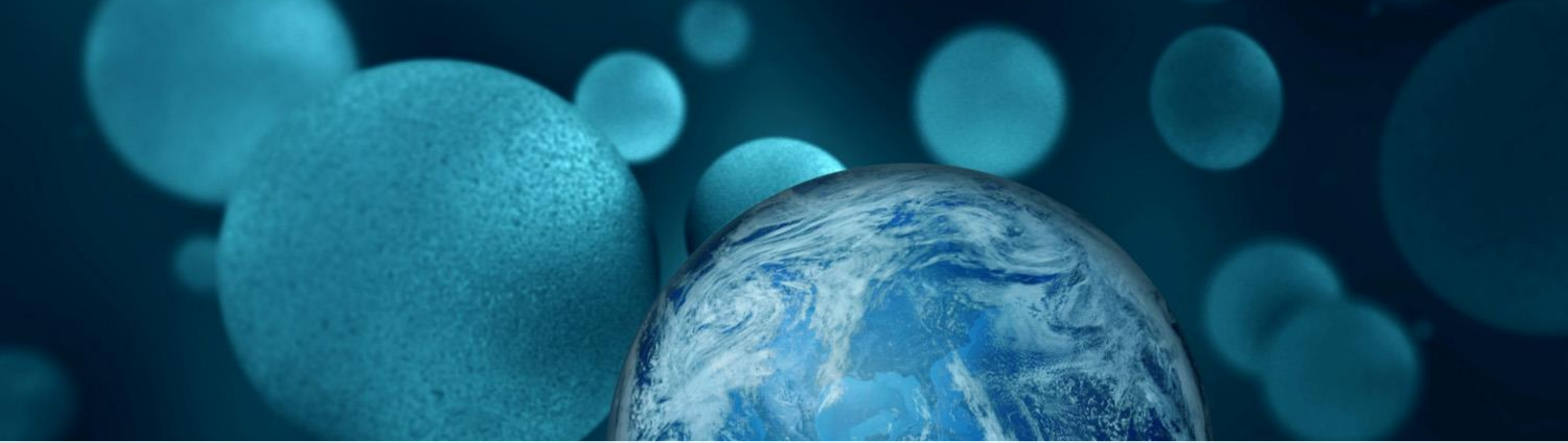

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From Synthetic Gene to Protein Purification: Confidence with Gene Synthesis services to accelerate protein drug development

Dr. Jay Yang
Market Development Manager, Synthetic Biology and Licensing and Commercial Supplies
2020-06-10

We Take Pride in Our Mission

We enable our customers to make the world healthier, cleaner, and safer

Agenda

1. GeneArt Services overview
2. Key applications of synthetic genes
3. Gene synthesis and synthetic genes
4. Protein expression services overview
5. Customer examples
6. Why partner with Thermo Fisher Scientific

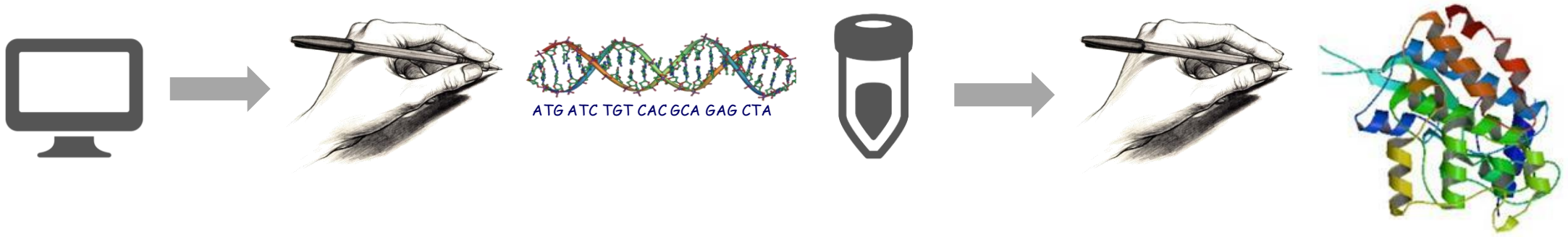
GeneArt and Downstream Services

Generation of DNA constructs delivered in vector of choice

Mutagenesis projects

Mammalian and insect cell protein expression projects

Project design | **Gene optimization** | **Gene synthesis** | **Gene variants** | **Gene libraries** | **Subcloning** | **Plasmid production** | **Cell lines** | **Proteins**



GeneArt Services support outsourcing of the full customer wet lab workflow from gene to protein

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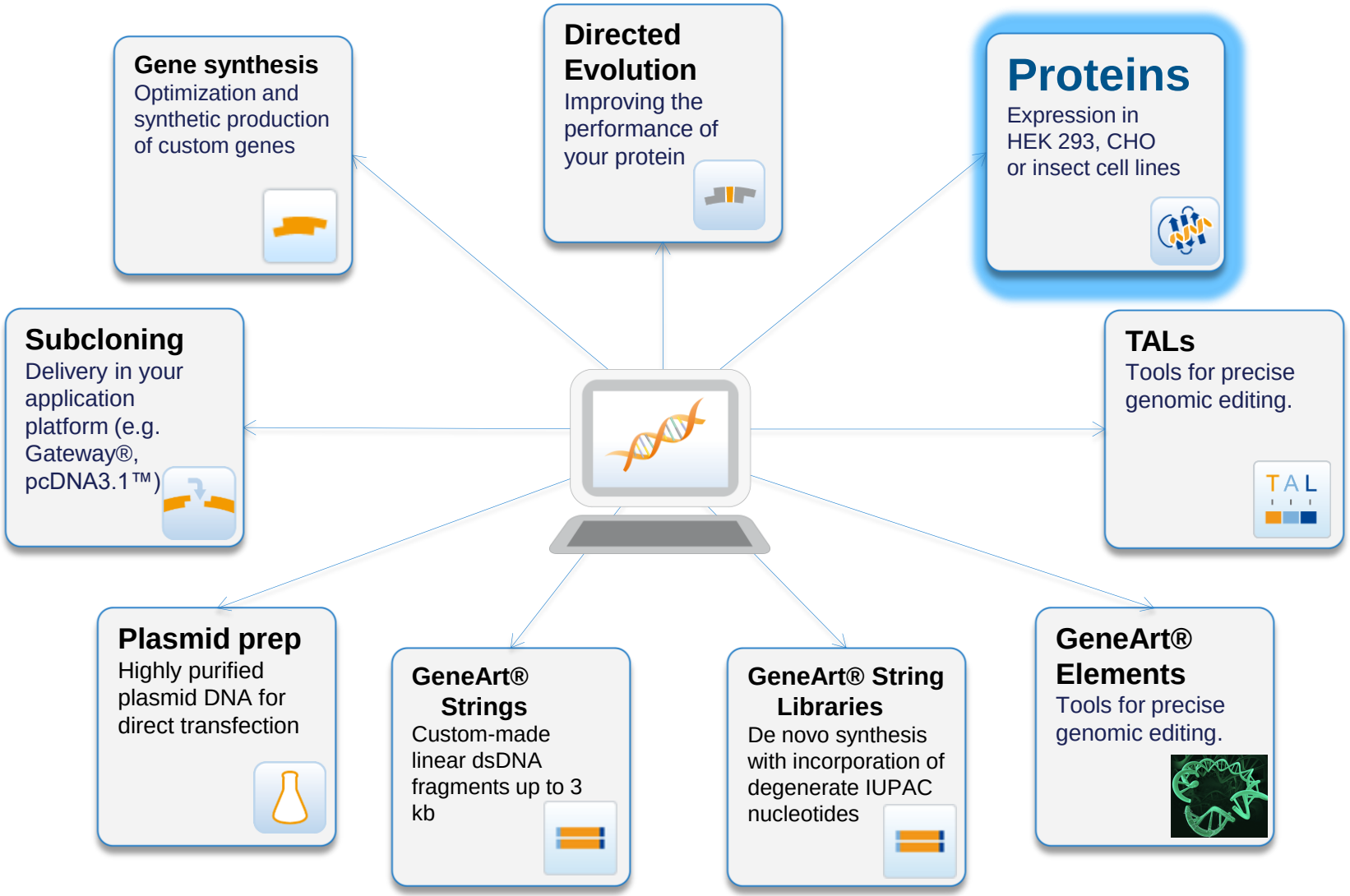
Comprehensive product and service portfolio



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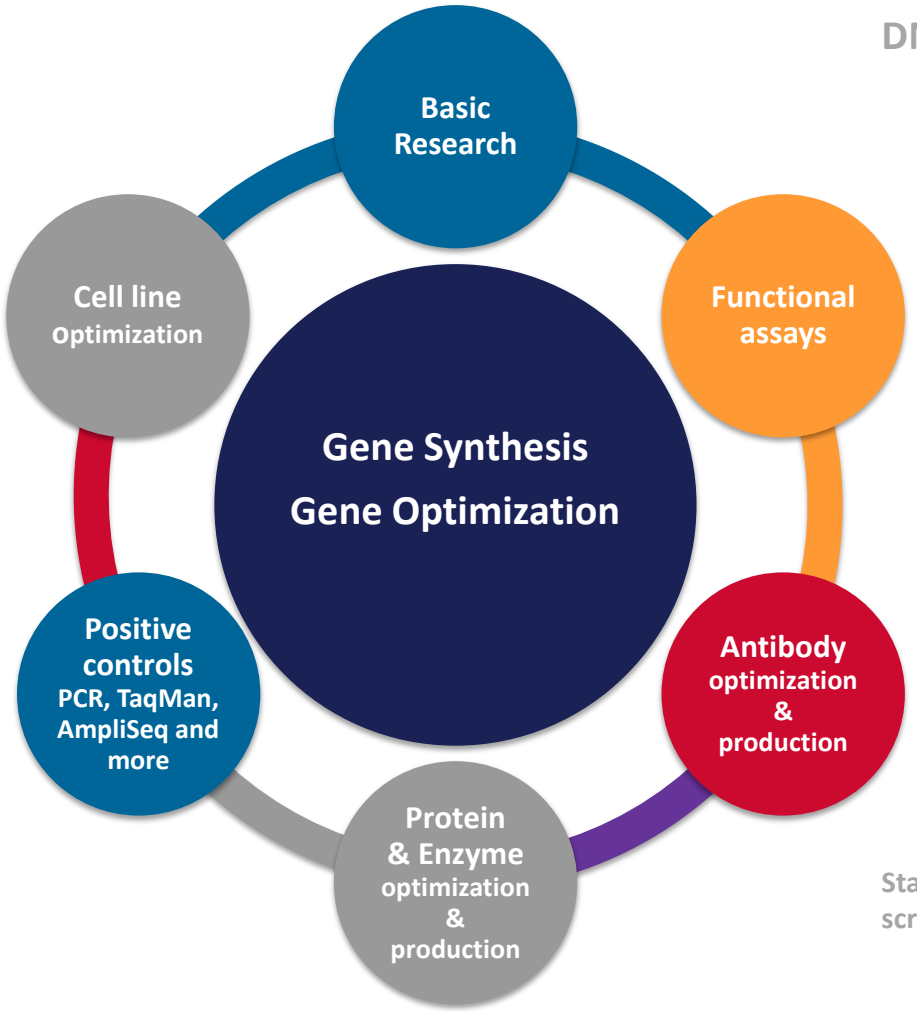
Examples of Applications for Synthetic Genes and Proteins



DNA engineering

Genetic engineering

Interaction studies

Transient expression

Protein engineering

Antibody optimization

Crystallization and structure analyis

Immunogene optimization for DNA- and RNA vaccines

Gene therapy

Rescue of siRNA mediated knock-out

Host engineering

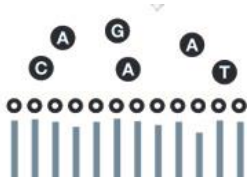
Cell line development

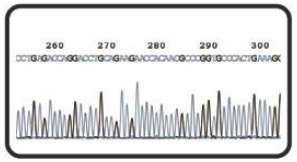
Stable protein expression for novel cellular screening assays

Drug and target validation

Gene synthesis to protein expression

Next-Generation Gene Synthesis





Bioinformatics | Oligo synthesis | Gene assembly | Cloning | Sequencing | Final documentation

Gene optimization

Multiparameter algorithm

Miniaturization and automation

Reduction of volumes down to nanoliters with acoustic liquid handling

Very high throughput

Capacity >30K oligos/day

NGS

Very high throughput

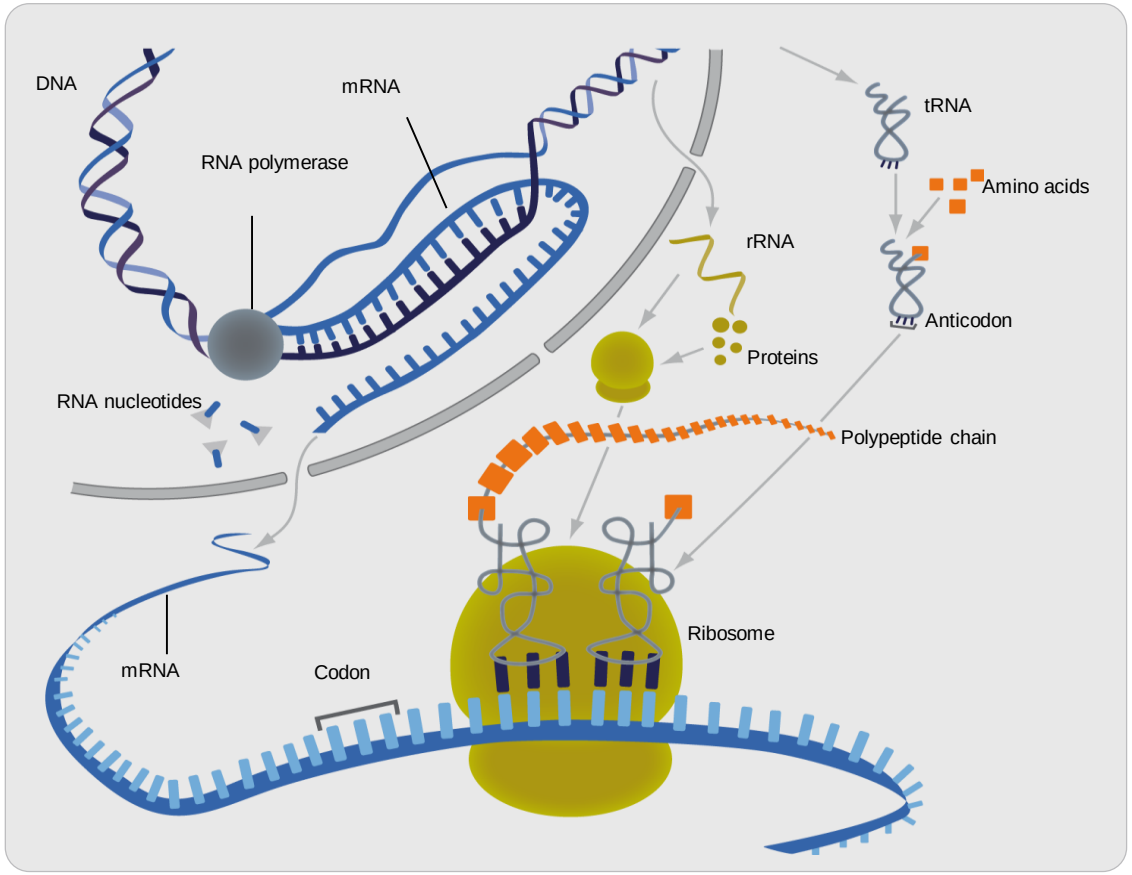
Increased reliability

Shorter TAT

GeneOptimizer Process

Invitrogen™ GeneOptimizer™ technology takes into account up 20 parameters to optimize the mammalian coding region, including:

- Codon usage
- GC content
- Cryptic splice sites
- Instability sequences
- RNA secondary structures
- Direct repeats



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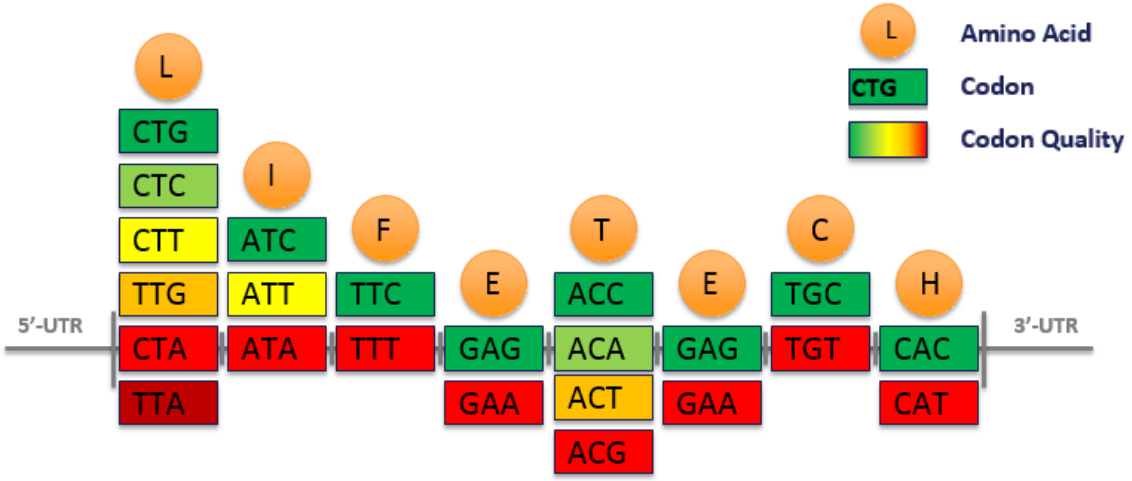
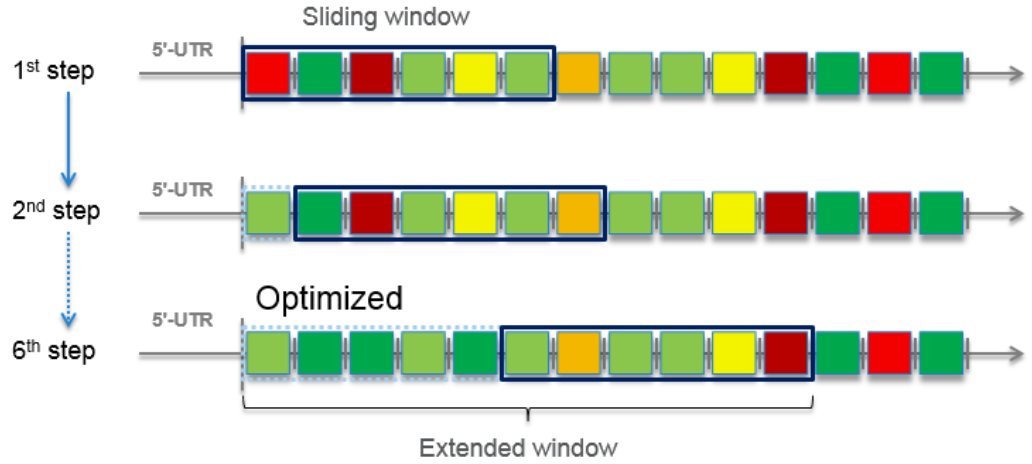
GeneOptimizer Process

GeneOptimizer technology takes into account up 20 parameters to optimize the mammalian coding region, including:

Gene expression is influenced by many factors



- Wild type not optimal for expression
- Best codon back-translation not optimal with respect to unwanted motifs/repetitions/secondary structures
- **Goal:** find a tradeoff



- The **sliding window** moves from 5'-UTR to 3'-UTR, one codon per step
- "All possible" codon combinations (with CAI higher than a threshold) are tested
- The **extended window** is considered for evaluating the codon combination
- Only the first codon of the **best** combination is fixed and the window slides one further
- Up to three phases with more and more relaxed thresholds

Human Recombinant Protein Production

Benefits of *E. coli*

- Fast growth
- Easy handling
- Cheap
- Well-studied genetics

Obstacles of *E. coli*

- Lack of posttranslational modifications
- No suitable membrane environment for membrane proteins
- Misfolding and aggregation
- Restrictions on large size and oligomeric proteins
- No authentic human glycoproteins possible

Mammalian and *E. coli* hosts are by far the most prominent expression systems

Expression of human recombinant proteins is an indispensable process in modern biotechnology and biomedicine

Accordingly, >70% of recombinant protein **pharmaceuticals** and most proteins used for **vaccination, human therapy,** or **diagnostics** are currently produced in mammalian cells

Benefits of mammalian

- Circumvents the obstacles of *E. coli* expression

Why is optimization still required for an autologous host?

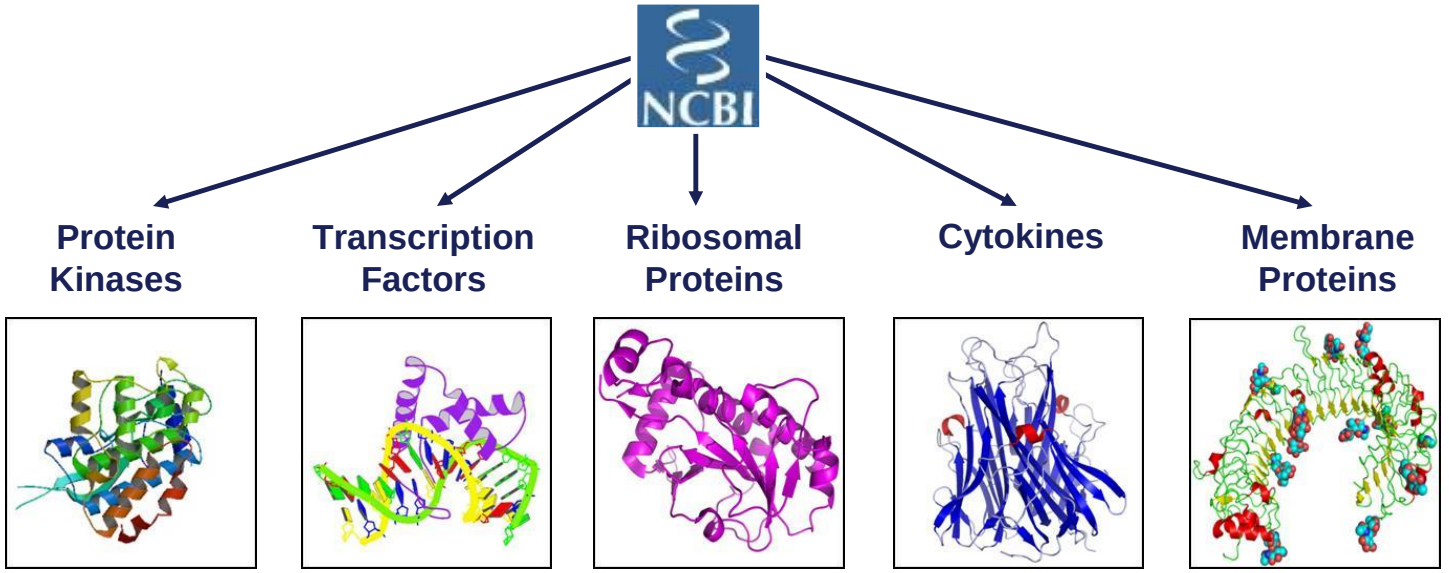
Obstacles of mammalian

- Transcriptional silencing
- mRNA destabilization
- Alternative splicing
- Premature polyadenylation
- Inefficient translation

Multigene Study in Mammalian Cells

Gene optimization as a general strategy to improve autologous expression of human genes

50 standard human genes representing the most interesting protein classes were selected from the NCBI data bank



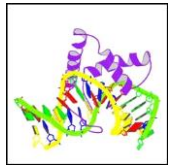
First large-scale study addressing the influence of multiparameter optimization on autologous human protein expression

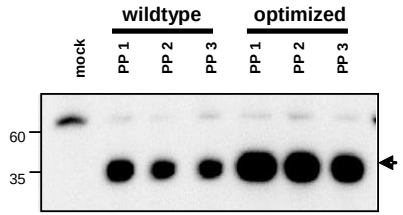
Fath S, et al. (2011) Multiparameter RNA and Codon Optimization: A Standardized Tool to Assess and Enhance Autologous Mammalian Gene Expression. PLoS ONE 6(3): e17596.

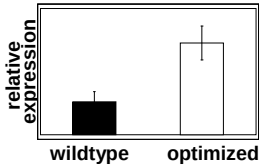
Mammalian Expression

Selected examples

Transcription Factors





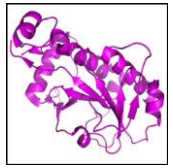


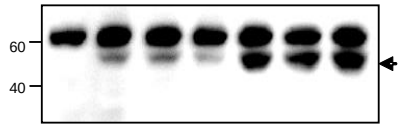
CREB1

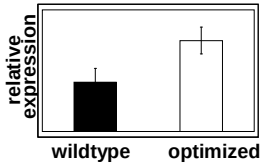
x 2.8

opt > wt	opt = wt	opt < wt	only opt
4	none	none	none

Ribosomal & other Proteins





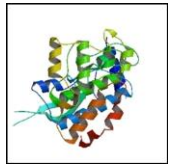


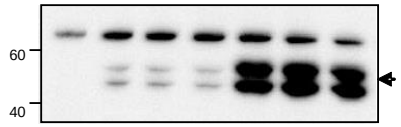
SMARCD1

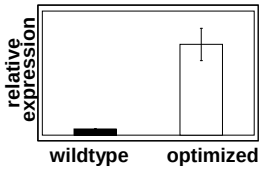
x 1.8

opt > wt	opt = wt	opt < wt	only opt
4	none	none	none

Protein Kinases





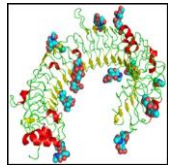


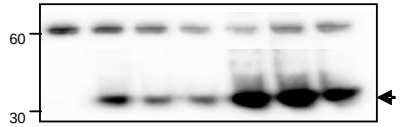
JNK3

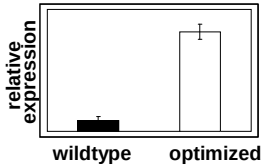
x 14

opt > wt	opt = wt	opt < wt	only opt
13	3	none	none

Membrane Proteins





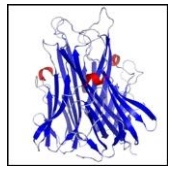


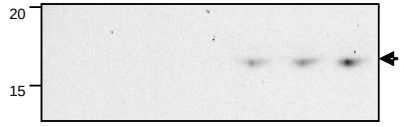
AQP5

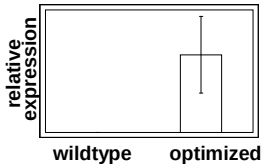
x 9

opt > wt	opt = wt	opt < wt	only opt
15	1	2	4

Cytokines







IL-2

only opt

opt > wt	opt = wt	opt < wt	only opt
6	2	none	2

Average variations of ≤10% are considered as equal (opt = wt)

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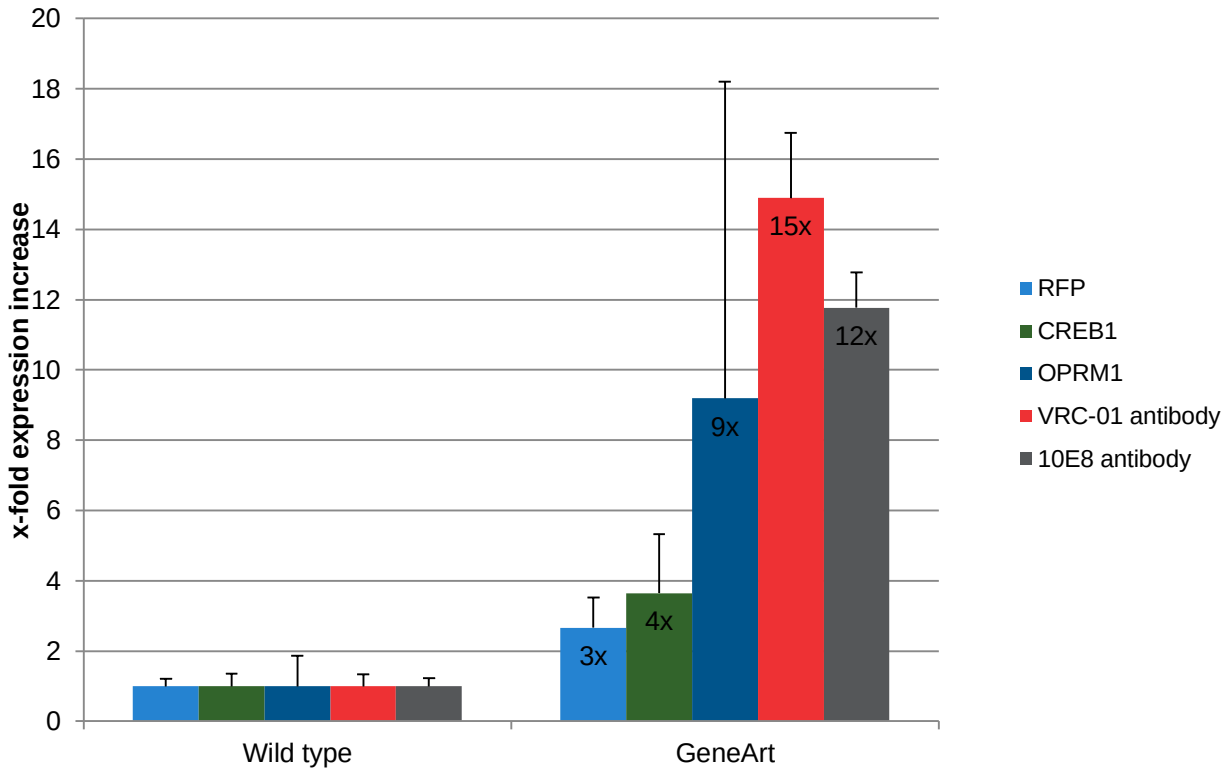
Comparison of WT vs. Optimized Sequences by GeneOptimizer Software

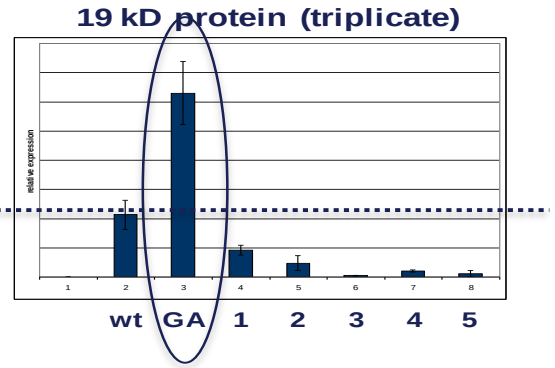


Open reading frames (ORFs) of three intracellular proteins and two antibodies were optimized with GeneOptimizer algorithm for expression in *H. sapiens*, and protein expression was compared to the respective wild type sequences. Wild type expression was normalized to 1.

All GeneOptimizer optimized sequences express better than wild type

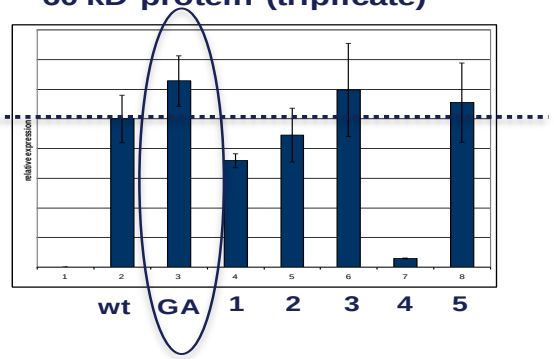
GeneOptimizer Technology: World-Class Performance

A)



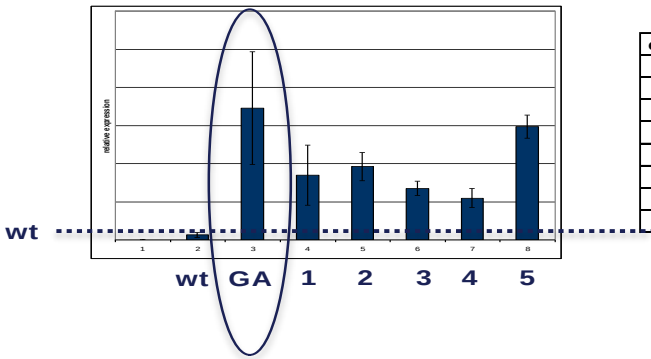
construct		opt / wt	
1	pcDNA3.1		
2	wildtype	1.00	
3	GeneArt	2.95	▲
4	competitor 1	0.43	▼
5	competitor 2	0.22	▼
6	competitor 3	0.02	▼
7	competitor 4	0.10	▼
8	competitor 5	0.06	▼

B)



construct		opt / wt	
1	pcDNA3.1		
2	wildtype	1.00	
3	GeneArt	1.25	▲
4	competitor 1	0.72	▼
5	competitor 2	0.89	▼
6	competitor 3	1.19	▲
7	competitor 4	0.06	▼
8	competitor 5	1.11	▲

C)



construct		opt / wt	
1	pcDNA3.1		
2	wildtype	1.00	
3	GeneArt	27.15	▲
4	competitor 1	13.37	▲
5	competitor 2	15.11	▲
6	competitor 3	10.61	▲
7	competitor 4	8.61	▲
8	competitor 5	23.32	▲

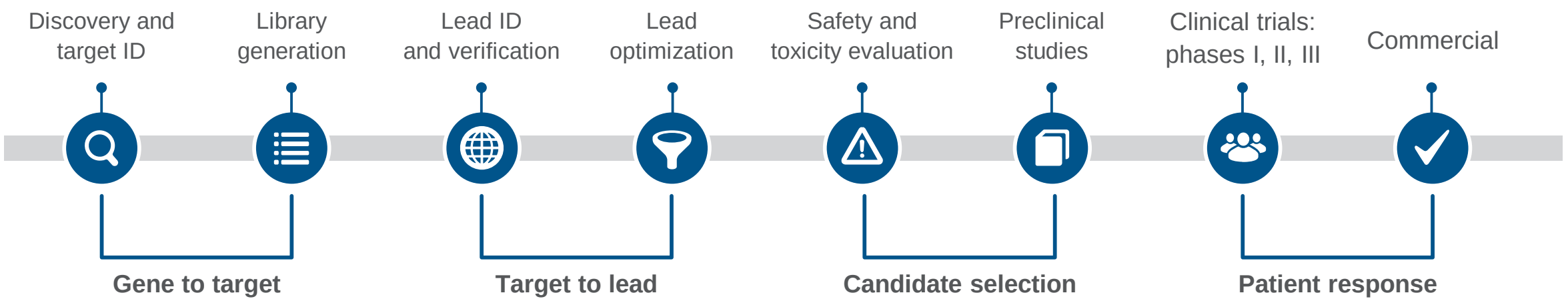
Expression comparison for optimized mammalian proteins from different suppliers

Mammalian expression comparison study for kinase proteins

- GeneOptimizer software **consistently** provided higher expression levels compared to wild type (200%, 25%, 27x)
- Demonstrating **high reliability** and **performance**
- Gene Optimizer technology provided the best results of those tested
- No competitor gene optimization algorithm tested in this study showed consistent results

GeneOptimizer software outperforms all other algorithms

Streamlining Biologics Development with the Expi Systems



mAbs Therapeutic proteins

Gibco Expi293 Expression System

Gibco ExpiCHO Expression System

Gibco ExpiCHO **Stable** Expression

Vaccines

Gibco ExpiSf Expression System

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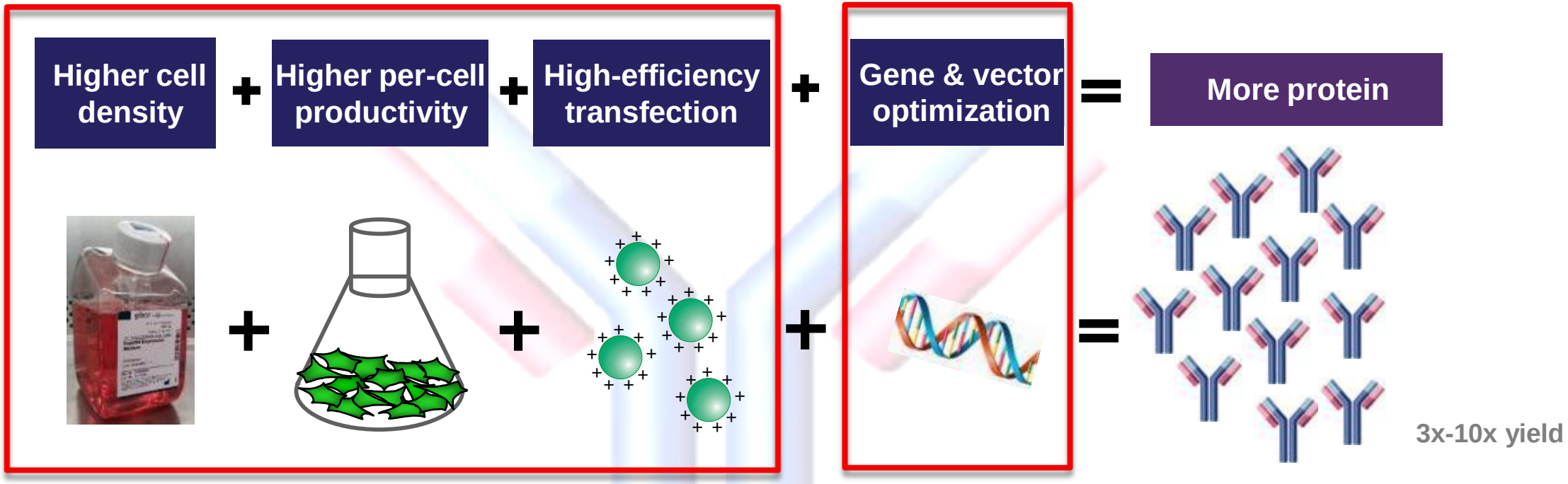
Strategy to Increase Transient Protein Yields



Advantages of Expi System:

- Culture medium that achieves 3-fold higher cell density
- Cells that express more protein per cell
- Transfection reagent that effectively delivers DNA into high-cell density cultures
- Protocol plugs directly into user's current 5–7-day workflow

Advantages of gene and vector optimization:

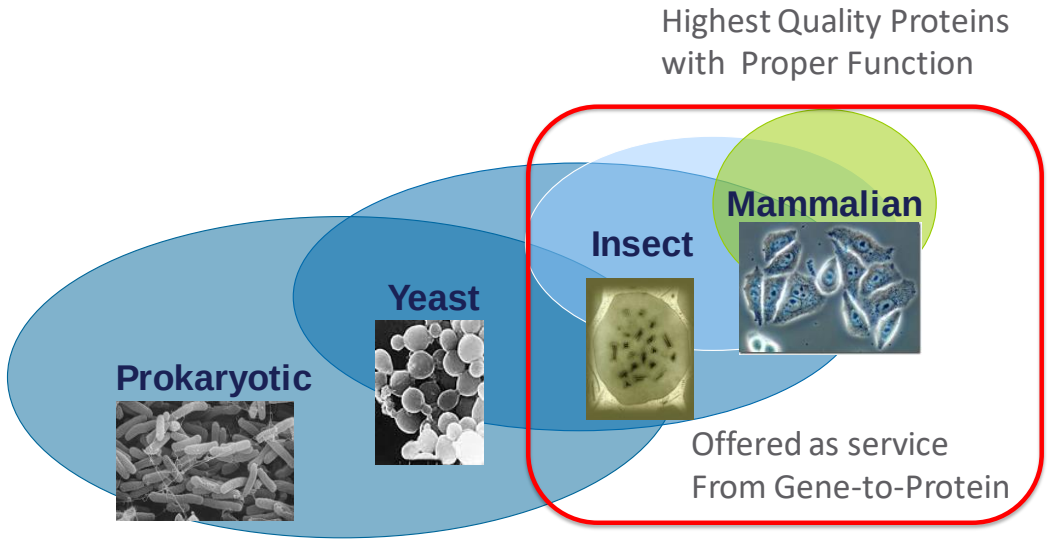
- Consistently provided higher expression levels compared to wild type
- More reliable and higher yield than other vendors

Combine highly advanced expression systems with expression-optimized genes

Protein Expression Service

Mammalian protein expression and purification using Expi293 or ExpiCHO Expression Systems

as well as Sf9 insect cells (Gibco™ Bac-to-Bac™ system)



all reagents commercially available
Gibco™

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BioProduction—Driving Performance Through Collaboration

Expression plasmid

- GeneOptimizer algorithm increase yield
- Full design flexibility
- Invitrogen™ vector suite
- High-quality plasmid preparation
- Gene-to-Protein all in-house process provides full control

Expression

- Flexible expression scales
- Parallel workflows for high throughput
- Gibco™ Expi™ (and FreeStyle™) expression systems
- Bac-to-Bac Sf9 (and Sf21, HiFive™)

Purification

- Multiple parallel purifications (ÄKTA)
- Crossflow filtration system
- Fast pre-purification titer detection system
- Capacity of >5,000 Ab purifications/year
- >500 non-Ab purifications/year

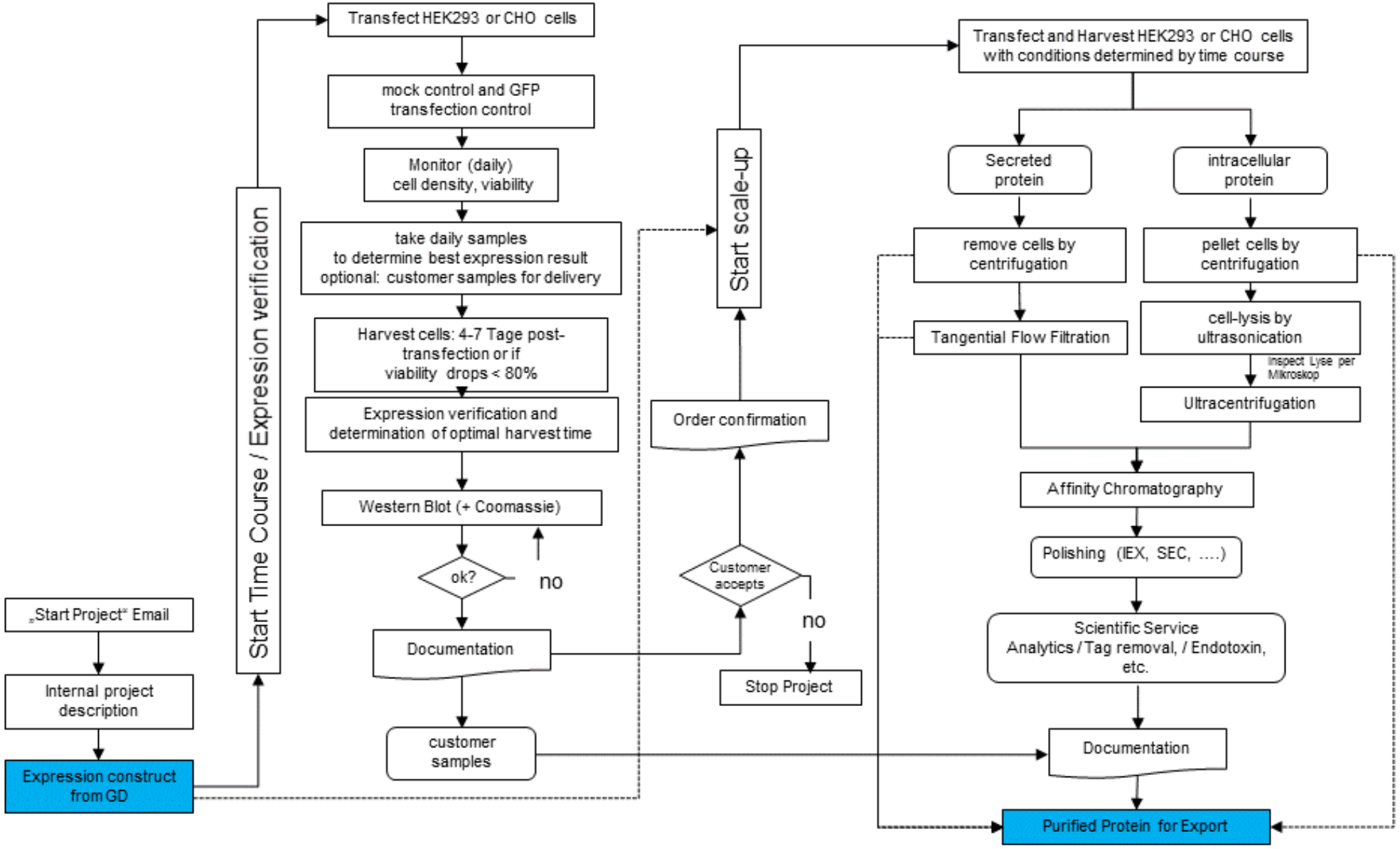
Analysis

Standard:

- SDS-PAGE/western blot
- A_{280} (NanoDrop)
- cGE (LabChip CX2, Caliper)
- Analytical SEC (HPLC)
- endotoxin detection (PTS cartridge or MW)

Project Management Team | **Manufacturing Team** | **Local Sales Support**

Example Workflow for Mammalian Cells (HEK293 or CHO)



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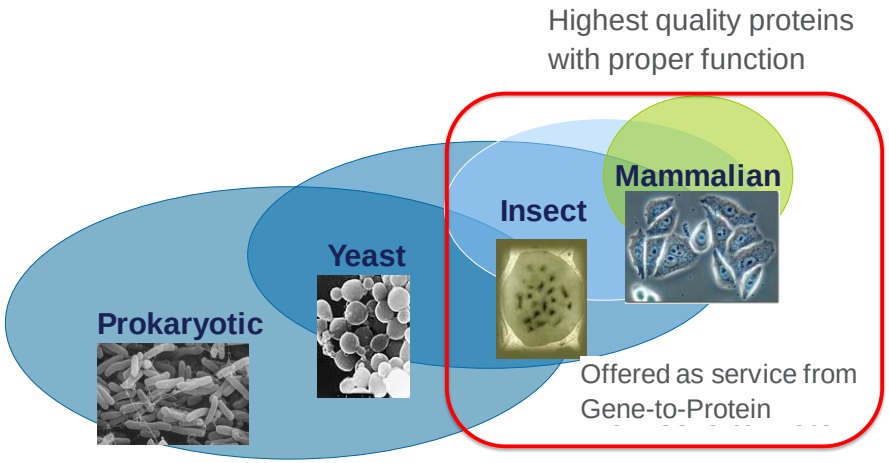
Gene-to-Protein Services Overview

Expression scales

- Highly flexible and extensible
- 30 mL to >25 L production scales
- Multiple shaker and WAVE bioreactor devices
- Current capacity >300 L of suspension culture/week
- Capacity for 100 L of WAVE Bioreactor culture/week
- Small-scale/24–96 multiwell expression

Mammalian and insect expression systems



Mammalian and insect protein expression & purification

- Expi293F and FreeStyle 293-F expression systems
- ExpiCHO-S and FreeStyle CHO-S expression systems
- Sf9 cells and ExpiSf9 (planned 2020)
- Bac-to-Bac Baculovirus Expression System

Reagents commercially available so can you also replicate work in house

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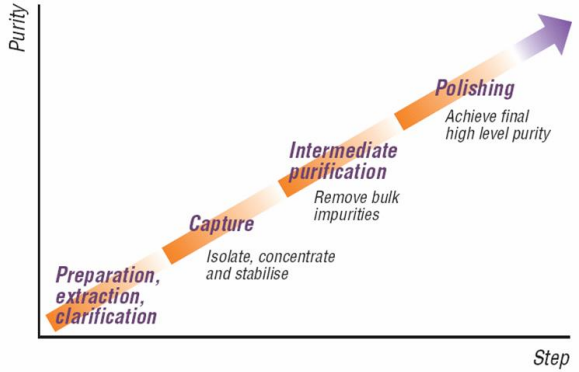
Gene-to-Protein Services Overview

Purification methods



- Highly flexible – capacity dependent on product mix
- >5,000 protein productions/year (various scales)
- Multiple ÄKTA Pure, Purifier, and Xpress devices
  - Up to ≥300 antibody purifications/week <250 mL scale possible
  - Up to ≥60 antibody purifications/week at 1 L scale possible
  - Up to ≥10 antibody purifications/month at 25 L scale possible
- ÄKTA Flux system for diafiltration
- Multiple tangential flow filtration devices

Service project phase	Standard specifications
Purification methods	• Affinity chromatography • Size exclusion chromatography (SEC) • Ion exchange chromatography (IEX)
Affinity tags	• His-Tag • Fc-Tag (Protein A/G/L) • Strep-Tag • FLAG-Tag • C-tag • HSA-tag • Others, upon request (Fabs, fusion proteins, bispecifics, …)
Additional options	• Polishing (additional column purifications) • Epitope tag removal by protease cleavage • Customized protocols, resins, buffers, reports • Aliquoting service • Protein concentration adjustment • Other, upon request

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Gene-to-Protein Services Overview

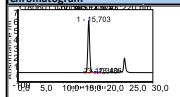
Analytical capabilities

Chromatogram and Results

Injection Details

Injection Name:	**No FT**	*Run Time (min):*	**30,00**
Vial Number:	**BG9**	*Injection Volume:*	**20,00**
Injection Type:	**Unknown**	*Channel:*	**UV_VIS_2**
Calibration Level:		*Wavelength:*	**280,0**
Instrument Method:	**Tosoh_isokratisch_Chugai_0.5ml_min_30min_22**	*Bandwidth:*	**n.a.**
Processing Method:	**160625 Chugai SEC**	*Dilution Factor:*	**1,0000**
Injection Date/Time:	**01.Jun.18 11:09**	*Sample Weight:*	**1,0000**

Chromatogram



Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		15,703	283,188	572,279	99,59	99,60	n.a.
2		17,340	0,575	1,194	0,20	0,21	n.a.
3		18,136	0,604	1,104	0,21	0,19	n.a.
Total:			**284,367**	**574,577**	**100,00**	**100,00**	

Quality control specifications	comment / equipment	Documentation
SDS-PAGE, visualization of protein	by Coomassie blue staining	**Included** in standard QC
Western Blot, visualization of protein	epitope-tag-specific antibody and/or target specific antibodies	**Included** in standard QC
protein concentration	NanoDrop One^{C} or VarioScan spectrophotometric determination of absorption at 280nm	**Included** in standard QC
capillary gel electrophoresis, detection by UV absorbance and/or fluorescence	LabChip GXII Touch24	**Upon request**
Analytical SEC (HPLC)	Ultimate 3000 UHPLC system (Thermo Fisher Scientific).	**Upon request**
Analytical SEC (HPLC) or **Titer determination** (HPLC/Prot.A))	Vanquish Flex Binary w/ DAD (Thermo Fisher Scientific).	**Upon request**
Titer determination in culture supernatant (antibodies)	BLItz™ System (Pall)	**Upon request**
LC/MS characterization of monoclonal antibodies (mAbs)	Q-Exactive Plus System and Vanquish Flex UHPLC (Thermo Fisher Scientific).	**Upon request** intact / deglycosylated as of today
endotoxin determination LAL assay (end-point or kinetic) *multiwell or single PTS cartdrige*	1) PTS cartdrige + Reader Endosafe® PTS 2) Kit Endochrome K256 + BioTek ELx808 plate reader (Charles River Laboratories)	**Upon request**
other	tbd	**Upon request**

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Example Documentation (Basic)

Gene-to-protein service 'scale'

Analysis certificate

ThermoFisher SCIENTIFIC

GeneArt No: 21xxx

Customer: Biotech – Dr. John Doe

Documentation created: 22/03/2017

Protein name:	**IgG1**
Vector backbone:	pcDNA3_4
Expression construct:	21xxx
Expression service:	GtP'scale'
Expression cells:	Expi293(TM)
Culture volume:	1 L
Harvest:	6 days post-transfection
Purification:	HiTrap Protein A HP
	binding: 20 mM sodium phosphate, elution: 0,1 M acetic acid pH 3 collection tubes containing 20% 1M Tris-HCl, pH 9
Dialysis:	16 h against 20 mM Tris, pH 7.4, 50 mM NaCl
Polishing:	HiLoad Superdex 200 26/600, prep grade according to customer-provided protocol
	followed by concentration to reach > 1.0 mg/ml if necessary
Purity:	evaluated by Coomassie Blue staining
Endotoxin:	<0.100 EU/ml equals <**0.096 EU/mg protein**
Monomer status:	**98.5 %** monomeric
Concentration:	1.0 mg/ml as determined by absorption at 280 nm
	using a Nanodrop device
Delivered material	**138.6 mg** protein (138.6 ml / 1.0 mg/ml)
	in 20 mM Tris, pH 7.4, 50 mM NaCl
	• 20 x 1.0 ml aliquots
	- sterile filtered -

Gene-to-protein service 'scale'

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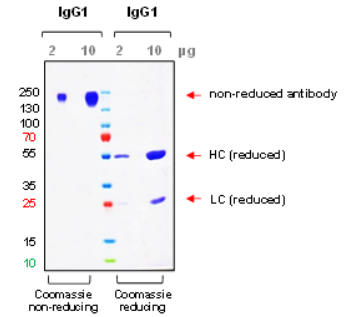
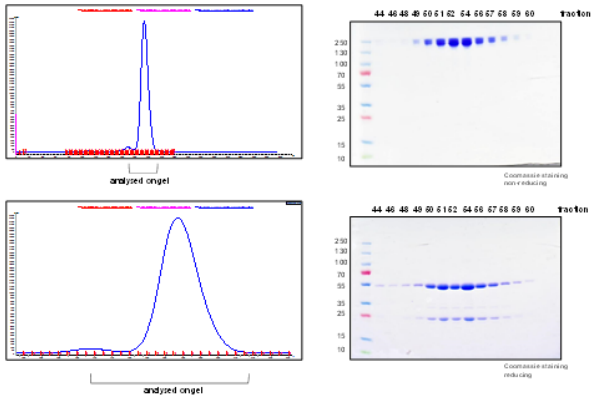
Certificate of Analysis

Coomassie-Gel:



Gelfiltration: HiLoad Superdex 200 26/600, prep grade



Additional note:

Fractions # 44 to 60 of the SEC run were analysed using Coomassie staining.

As specified by the customer, **fractions # 50 to 59** were pooled accordingly.

Gene-to-protein service 'scale'

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Analytical Size exclusion chromatography (SEC)

Column : TOSOH TSKgel G3000SWxl

Running buffer: 50 mM NaPhosphate, 300 mM NaCl, pH6.8

Flow = 1.0 mL/min

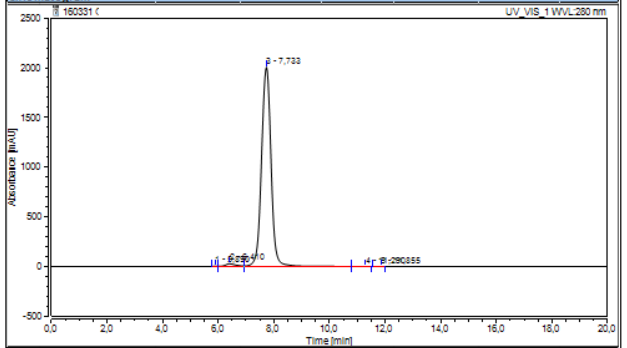
Sample: 50 µL undiluted sample

Chromatogram and Results

Injection Details

Injection Name:	IgG1	*Run Time (min):*	20,00
Vial Number:	BD5	*Injection Volume:*	50,00
Injection Type:	Unknown	*Channel:*	UV_VIS_1
Calibration Level:		*Wavelength:*	280,0
Instrument Method:	Tosoh_Isokratisch_1ml_min_20min	*Bandwidth:*	n.a.
Processing Method:	150516 GenMab SEC	*Dilution Factor:*	1,0000
Injection Date/Time:	31.Mrz.16 09:35	*Sample Weight:*	1,0000

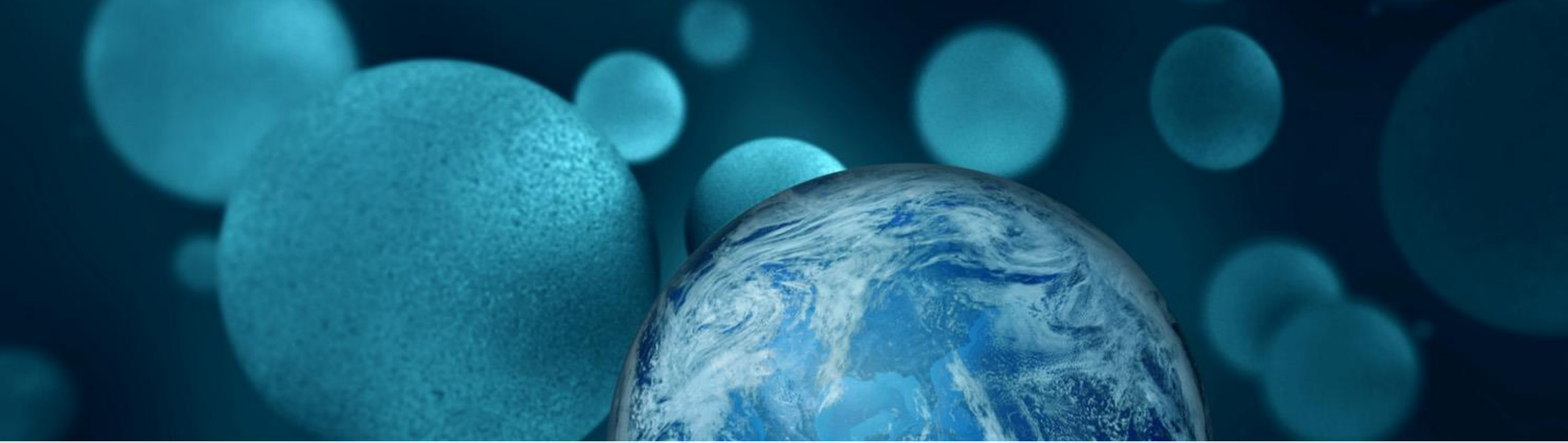
Chromatogram



Integration Results

No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount
1		5,890	0,204	0,971	0,03	0,05	n.a.
2		6,410	11,500	26,240	1,43	1,29	n.a.
3		7,733	791,931	2006,825	98,52	98,64	n.a.
4		11,290	0,134	0,274	0,02	0,01	n.a.
5		11,855	0,057	0,207	0,01	0,01	n.a.
Total:			803,826	2034,517	100,00	100,00	

Highly customized to your needs



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Customer Examples

Case Study: GeneArt Protein Purification Services, with ExpiCHO Expression System

Utilize Strategic Outsourcing: Delivering 50% more proteins/antibodies and saving >2,000 FTE hours/year

Situation

- a privately-held biotechnology company, explores numerous new and novel proteins/antibodies to test on their immunotherapy platform to fight various diseases including cancer.
- Using the Expi293 system for expression/purification of their proteins/antibodies of interest, they were looking to increase productivity. Specifically:
  - Increase protein/antibody production
  - Reduce FTE hours required

Our response

- Introduced ExpiCHO mammalian expression system. The system delivered higher yield, however many FTE hours were still required to perform expression/purification of targets in house.
- Introduced GeneArt Protein Purification services with proprietary GeneOptimizer technology to help save time and resources for producing relevant protein/antibody targets.

Value delivered

- Customer achieved productivity gains leading to faster turnaround on data, resulting in the identification of additional targets for screening, and the securing of private funding. Specific productivity gains:
  - Approximately **50% more proteins/antibodies delivered** through outsourcing the production of 90% of their proteins
  - **Saved > 2,000 FTE hours /year**
    (Equivalent of one FTE; 40 hrs/week x 52)

GeneArt Protein Service—Customer Success Story Examples

Non-Optimized (CHO)

	MAb 1 HC	MAb 3 HC	MAb 4 HC
MAb 1 LC	< 20 µg/L	n.d.	n.d.
MAb 3 LC	n.d.	0.35 mg/L	n.d.
MAb 4 LC	0.5 mg/L (medium scale 0.73 mg/L)	n.d.	1.65 mg/L (medium scale 1.65 mg/L)

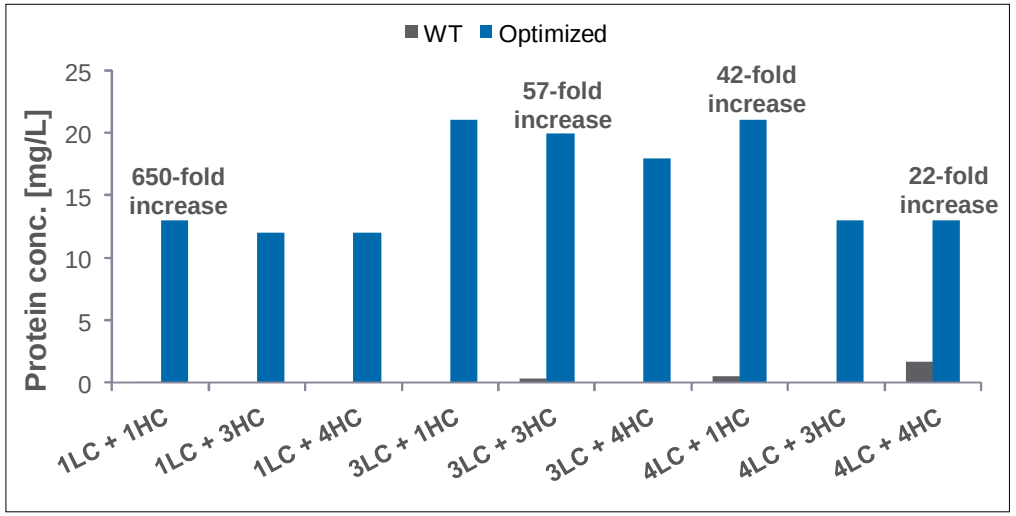
MAb 1
MAb 2
MAb 3
MAb 4

Optimized (CHO)

	MAb 1 HC	MAb 3 HC	MAb 4 HC
MAb 1 LC	13 mg/L 650-fold increase	12 mg/L	12 mg/L
MAb 3 LC	21 mg/L	20 mg/L 57-fold increase	18 mg/L
MAb 4 LC	21 mg/L 42-fold increase	13 mg/L	13 mg/L 22-fold increase

MAb 1
MAb 2
MAb 3
MAb 4

Work performed for a large pharmaceutical company

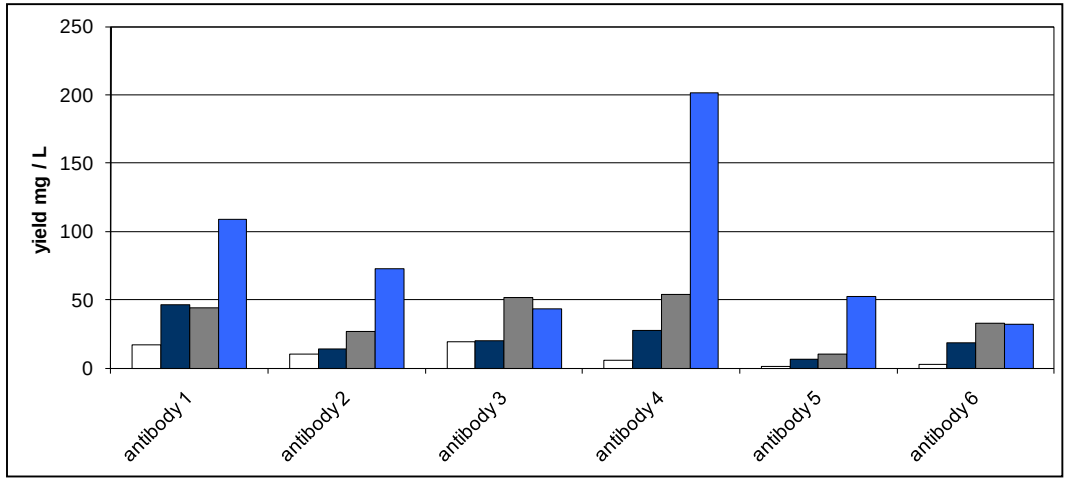


*All transfections were done with a 3:1 LC:HC ratio, 3 mL culture. Initial MAb 1 was <20 µg/L and large-scale production – no yield.

Gene Optimization Enhances Antibody Expression in CHO Cells

GeneArt Protein Service—Customer Success Story Examples

GeneArt™ optimized genes & advanced **HEK293** expression systems



- Wildtype gene, customer in-house production
- Optimized gene, customer vector, FreeStyle293
- Optimized gene, pcDNA3.3 vector, FreeStyle293
- Optimized gene, pdDNA3.3 vector, Expi293

	Pharmacuetical Customer X	Thermo Fisher Scientific
Antibody A	2 mg/L	252 mg/L
Antibody B	2 mg/L	272 mg/L
	Wild type HC & LC genes Customer‘s leader peptide pcDNA3.3 FreeStyle 293 system	Optimized HC & LC genes IgG kappa leader peptide pcDNA3.4 Expi293 system

- Substantial increase in expression levels by combining GeneOptimizer technology with advanced expression systems (Gibco™ FreeStyle™ 293 or Expi293 systems)
- Commercially available solution for **full transferability of processes & results**

This is the Thermo Fisher Scientific advantage

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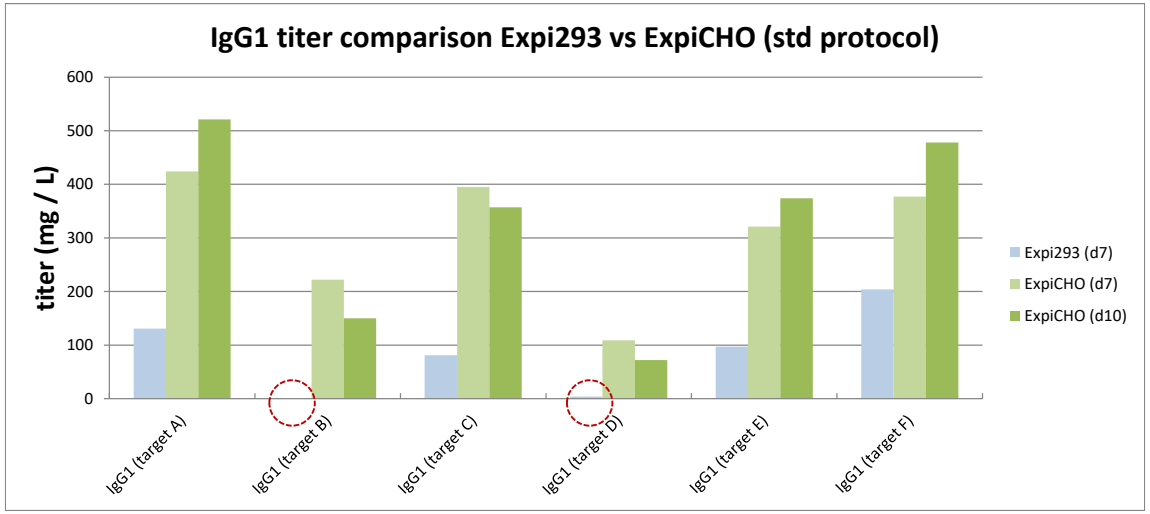
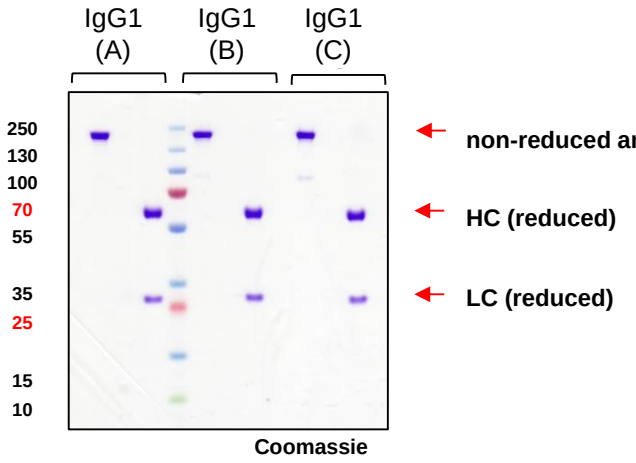
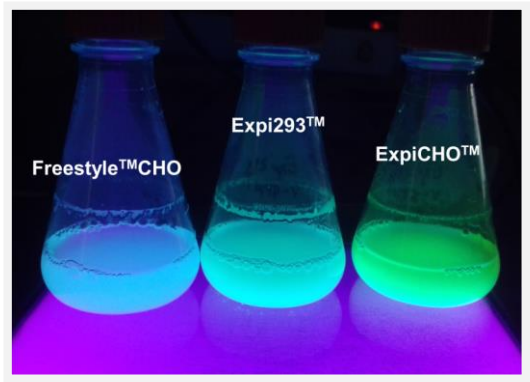
GeneArt Protein Service—Customer Success Story Examples

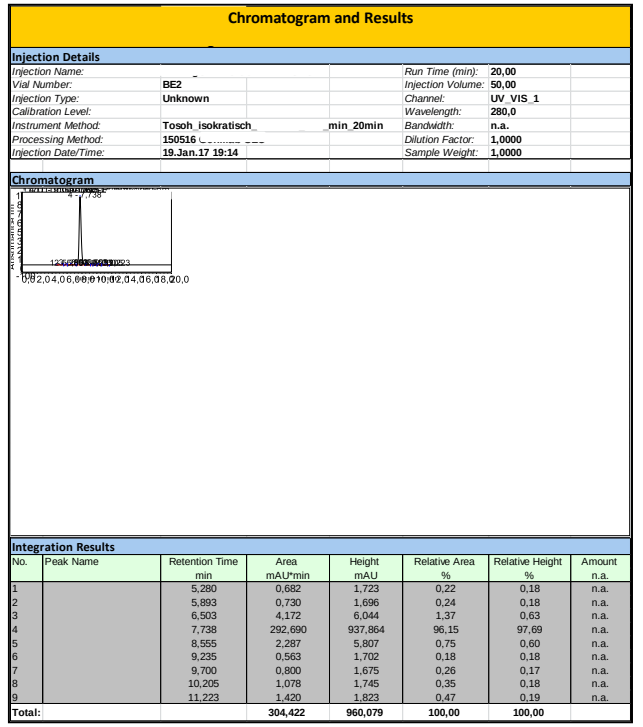
ExpiCHO™ Protein Service



"We are also excited about the expression levels of these proteins."
Customer quote, large biotech







Chromatogram and Results

Injection Details

Injection Name:		Run Time (min):	20,00
Vial Number:	BE2	Injection Volume:	50,00
Injection Type:	Unknown	Channel:	UV_VIS_1
Calibration Level:		Wavelength:	280,0
Instrument Method:	Tosoh_isokratisch_____min_20min	Bandwidth:	n.a.
Processing Method:	150516 _ _ _ _ _ _ _ _	Dilution Factor:	1,0000
Injection Date/Time:	19.Jan.17 19:14	Sample Weight:	1,0000

Chromatogram

Integration Results

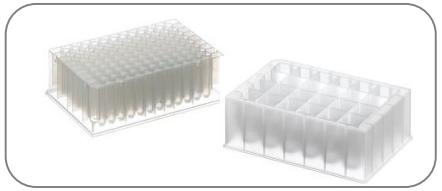
No.	Peak Name	Retention Time min	Area mAU*min	Height mAU	Relative Area %	Relative Height %	Amount n.a.
1		5,280	0,682	1,723	0,22	0,18	n.a.
2		5,893	0,730	1,696	0,24	0,18	n.a.
3		6,503	4,172	6,044	1,37	0,63	n.a.
4		7,738	292,690	937,864	96,15	97,69	n.a.
5		8,555	2,287	5,807	0,75	0,60	n.a.
6		9,235	0,563	1,702	0,18	0,18	n.a.
7		9,700	0,800	1,675	0,26	0,17	n.a.
8		10,205	1,078	1,745	0,35	0,18	n.a.
9		11,223	1,420	1,823	0,47	0,19	n.a.
Total:			304,422	960,079	100,00	100,00	

… works as well for *Fabs* or other secreted epitope-tagged *non-antibody targets*

Works as well for Fabs or other secreted epitope-tagged non-antibody targets

ThermoFisher SCIENTIFIC

ExpiCHO™ small-scale protein expression/purification service



Small-scale/24–96 multiwell expression

Yield in µg

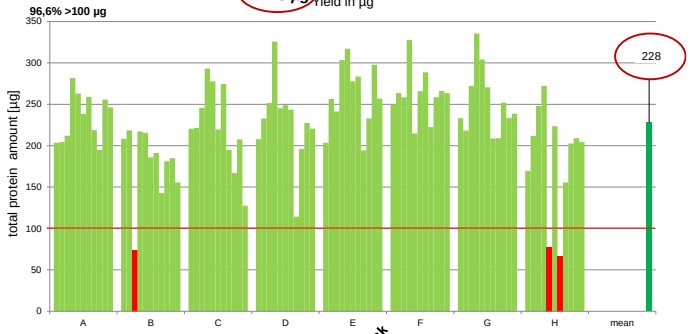
	1	2	3	4	5	6	7	8	9	10	11
A	204	204	212	282	263	238	259	219	195	256	246
B	208	219	74	217	216	186	191	143	181	185	156
C	220	221	246	293	278	220	275	195	167	208	128
D	208	233	251	326	245	249	243	114	196	227	221
E	204	256	241	303	317	278	283	194	233	298	257
F	250	263	258	328	215	266	289	223	258	266	263
G	233	218	272	336	304	270	209	209	252	233	238
H	170	212	248	272	78	224	67	156	203	209	204
mean											

Ø 228 µg

Recovery in % (compared to BLItz titer measurement)

	1	2	3	4	5	6	7	8	9	10	11
A	81	84	89	80	89	87	87	88	79	92	85
B	74	81	79	82	80	77	94	76	90	101	80
C	84	83	106	92	85	111	199	84	246	85	85
D	86	84	89	101	96	86	100	97	86	93	80
E	64	76	87	80	102	90	98	88	89	98	83
F	87	82	97	85	74	93	88	100	100	110	86
G	76	75	94	84	83	98	98	92	94	93	80
H	76	77	89	75	98	81	93	68	74	80	77
mean											

90 %



Yield in µg

	1	2	3
A	537	627	589
B	568	581	543
C	546	581	598
D	570	551	590
mean			

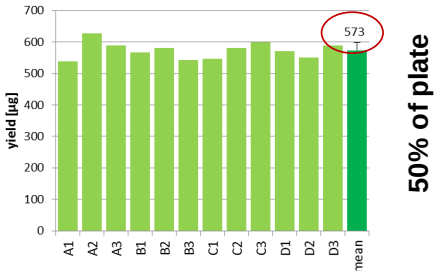
Ø 573 µg

Recovery in % compared to BLItz titer measurement)

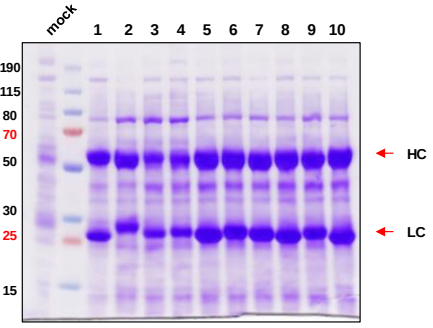
	1	2	3
A	72	84	79
B	76	78	73
C	73	78	80
D	76	74	79
mean			

Ø 77%

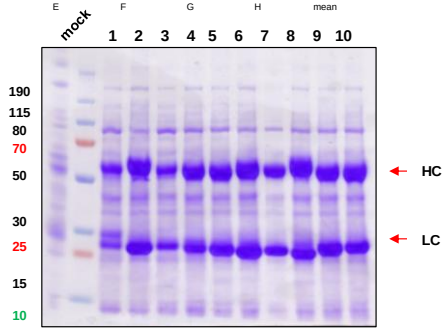
100% > 100 µg



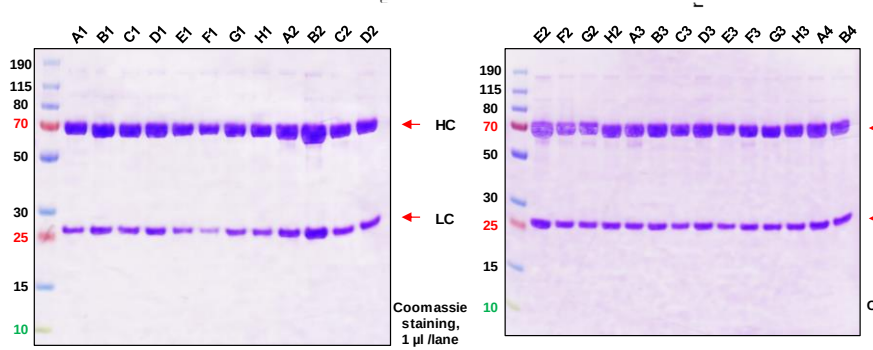
50% of plate



lane	well	GeneArt No	Protein	plate
1	A1	2779684	QV81	5
2	B1	2779685	QV82	5
3	C1	2779686	QV83	5
4	D1	2779687	QV84	5
5	A2	2779688	QV85	5
6	B2	2779689	QV86	5
7	C2	2779690	QV87	5
8	D2	2779691	QV88	5
9	A3	2779692	QV89	5
10	B3	2779693	QV90	5



lane	well	GeneArt No	Protein	plate
1	C3	2779694	QV91	5
2	D3	2779695	QV92	5
3	A4	2779696	QV93	5
4	B4	2779697	QV94	5
5	C4	2779698	QV95	5
6	D4	2779699	QV96	5
7	A5	2779700	QV97	5
8	B5	2779701	QV98	5
9	C5	2779702	QV99	5
10	D5	2779703	QV100	5



ThermoFisher SCIENTIFIC

Gene-to-Protein Expertise Provides Flexibility and Support

Complete service chain

All **in-house** production: each single step from oligo synthesis to the purified protein

Save time: go from **gene to protein** in as few as 30 days

Reliable performance

Proprietary, reliable, and advanced expression systems, **Expi293 and ExpiCHO systems,** all reagents commercially available

World-class expression optimization

Scalable and flexible

Range of scales: from 35 mL to 25 L

Customized service: ready-to-use customer purification protocols and expandable capabilities

Experienced and secure

Dedicated and experienced project management team: communication in all project phases

Secure e-business solutions: unique portal

Active MSA with pharma and biotech customers

Receive purified protein in a reasonable time frame with a fully transferable workflow

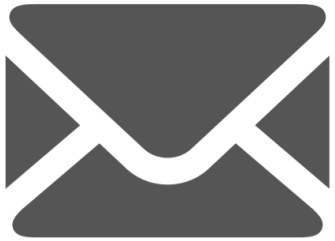
Why Partner with Thermo Fisher Scientific

- Benefit by outsourcing projects and then get access to commercially available reagents so you can replicate in-house; consistency and performance
- Expertise in the full workflow; from synthesis to protein production with a world-class optimization algorithm that consistently improves yield
- Expi293 and ExpiCHO media systems are produced by Thermo Fisher Scientific, so helps minimize licensing costs
- We have access to the highest titer system on the market
- Flexibility with offer HTP expression for screening up to WAVE for *in vivo* studies
- Complete communication, documentation and yield once pilot project performed
- Customizable purification for special proteins

How to Order GeneArt Protein Expression Service

thermofisher.com/genetoprotein

Contact your local sales representative



Email:
geneartprotein@thermofisher.com

Committed to Zero Waste

Zero Waste certified manufacturing sites

≥90% diversion from landfill of nonhazardous waste

Asheville, North Carolina

Bedford, Massachusetts

Bleiswijk, The Netherlands

Eugene, Oregon

Frederick, Maryland

Inchinnan, Scotland

Kiryat Shmona, Israel

Löhne, Germany

Marsiling, Singapore

Pleasanton, California

Regensburg, Germany

Tuas, Singapore

Warrington, UK

In Regensburg, 0% of our waste goes to landfill

Questions