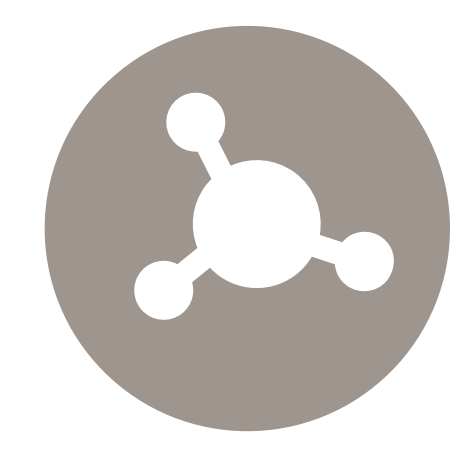


cQrex® peptides for increased performance in biopharma cell culture

The cell culture challenge

Optimized nutrient supply is key to successful cell culture and efficient production of high quality biopharmaceuticals such as therapeutic proteins, vaccines, gene therapies, and cell based therapies. As building blocks of proteins, amino acids are essential culture media ingredients. However, **some amino acids have properties that limit their cellular uptake and the bioprocess productivity.**

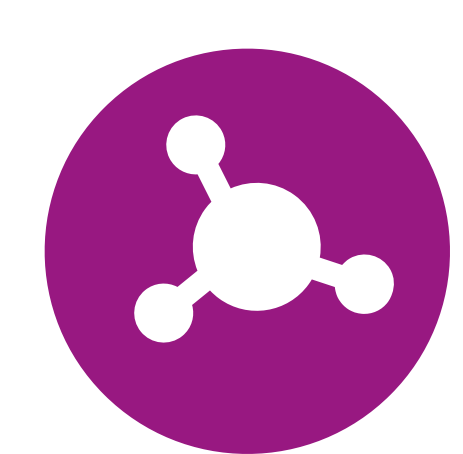
Target amino acid



L-glutamine
L-cystine
L-tyrosine

Insoluble or unstable

Carrier amino acid

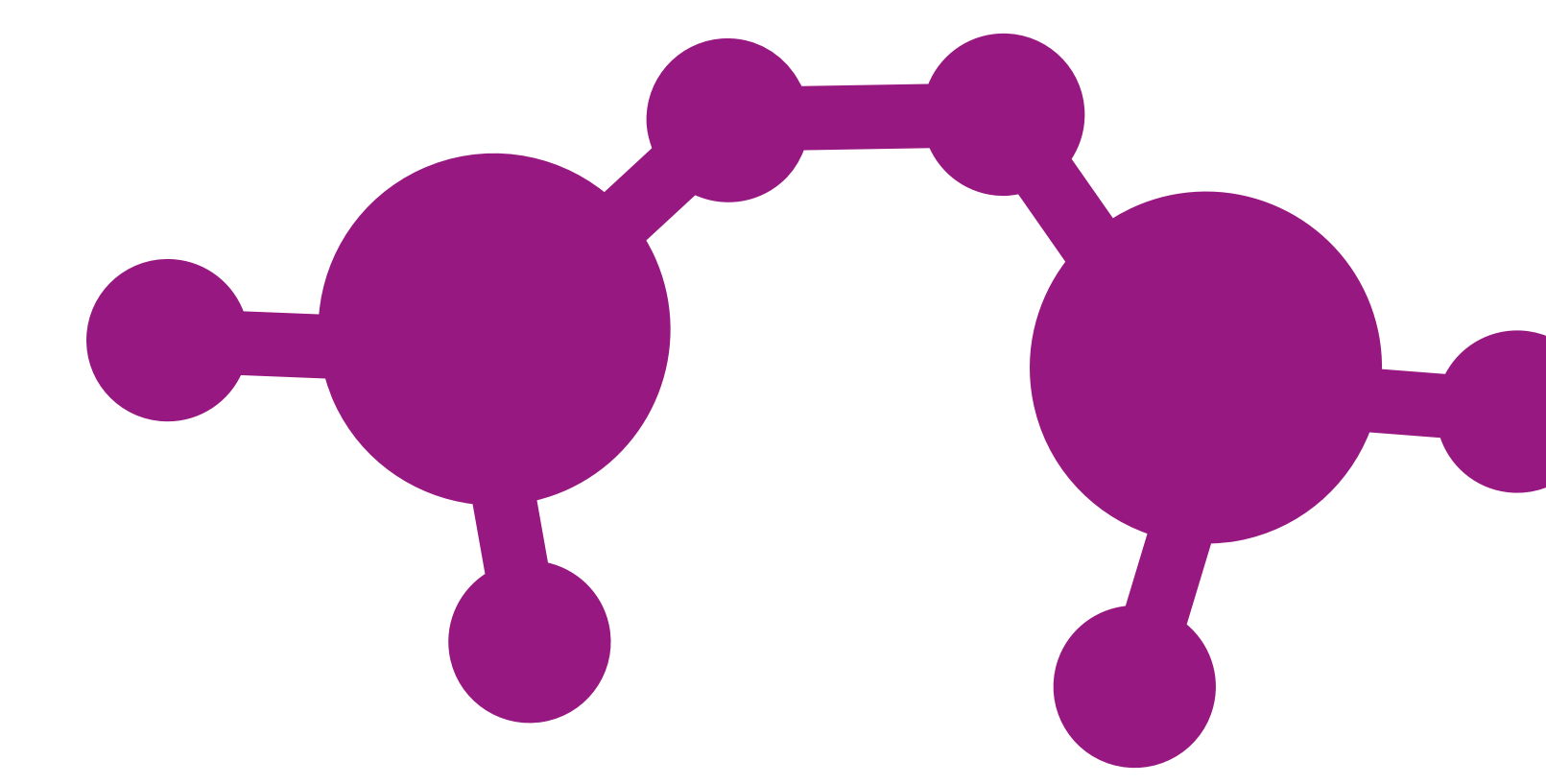


L-alanine
Glycine
L-lysine

Soluble and stable

PEPTIDE

SYNTHESIS



CELLULAR

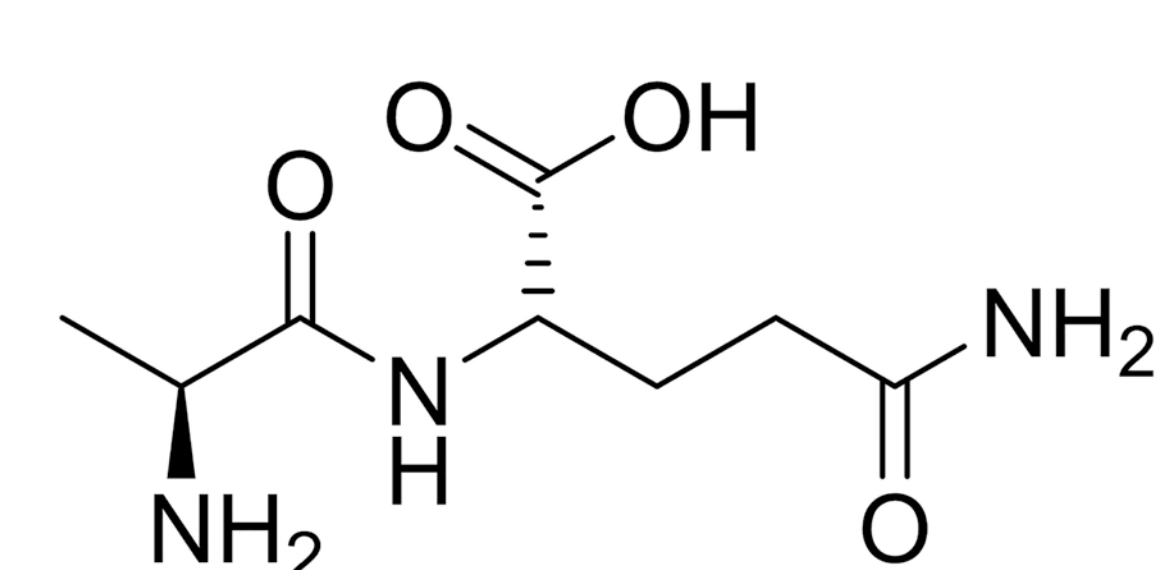
UPTAKE

Soluble and stable cQrex® peptide

AMINO ACID	ROLE	ISSUE
L-glutamine	Building block for proteins and major energy source (metabolites involved in the citric acid cycle)	L-Glutamine instability in cell culture media leads to pyroglutamic acid and ammonia formation. Rapid consumption in the cell also causes ammonia accumulation , which negatively impacts cell growth and lowers productivity.
L-cystine	Building block for proteins and the antioxidant glutathione (involved in redox balance)	In cell culture media, L-cystine is highly reactive and rapidly oxidizes into L-cystine . The latter is hardly soluble at neutral pH and cannot be provided in sufficient amounts to cells. This limits the bioprocess performance .
L-tyrosine	Building block for proteins	Because of its functional groups, L-tyrosine exhibits low solubility at neutral pH, resulting in high precipitation risks. Limited solubility lowers the amino acid's bioavailability , resulting in poor cell culture performance.

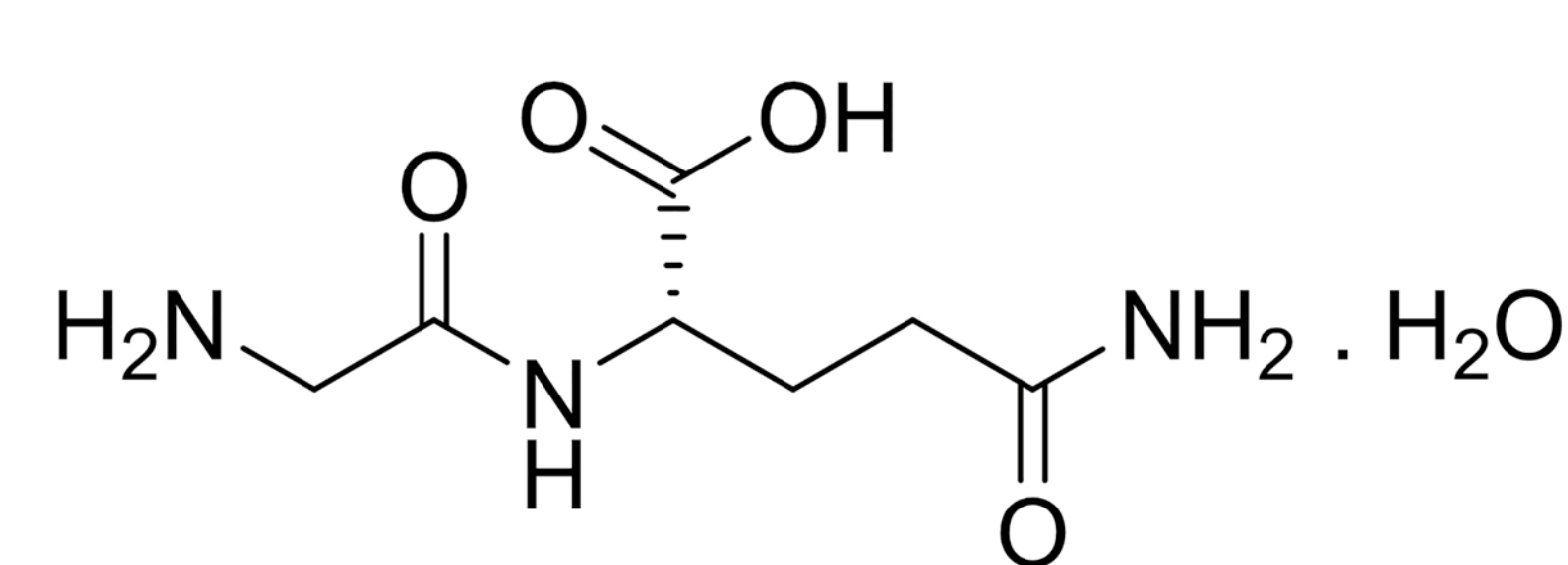
Our chemically defined cQrex® peptides overcome amino acids limitations in cell culture media

Gln GLUTAMINE PEPTIDES Highly stable



L-Alanyl-L-glutamine

cQrex® AQ



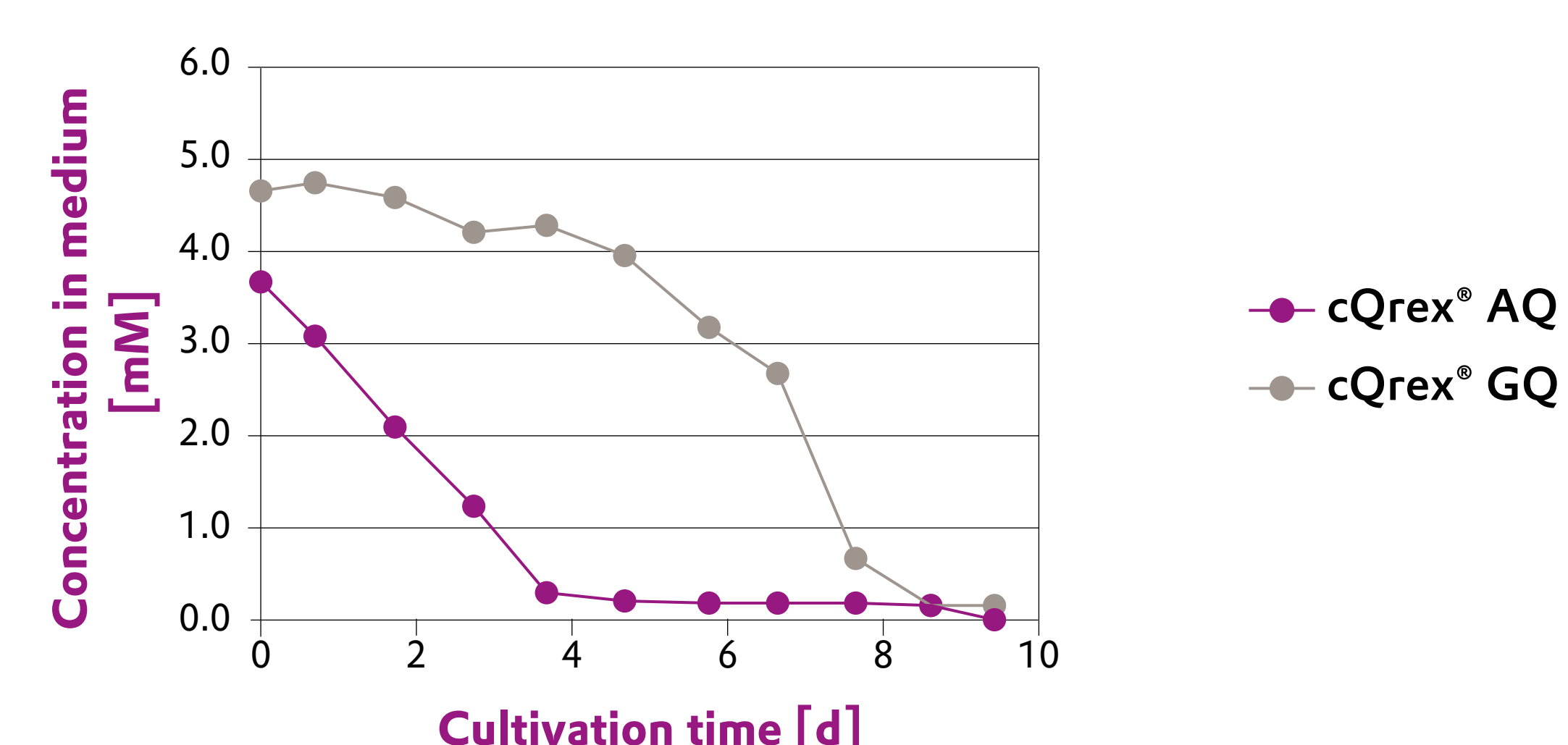
Glycyl-L-glutamine hydrate

cQrex® GQ

Increase flexibility with stable glutamine sources

- Ability to store media including cQrex® AQ or GQ without suffering from glutamine degradation
- Select the glutamine peptide that meets your needs:
 - Uptake rate depends on the carrier amino acid
 - Some cell lines are sensitive to L-alanine

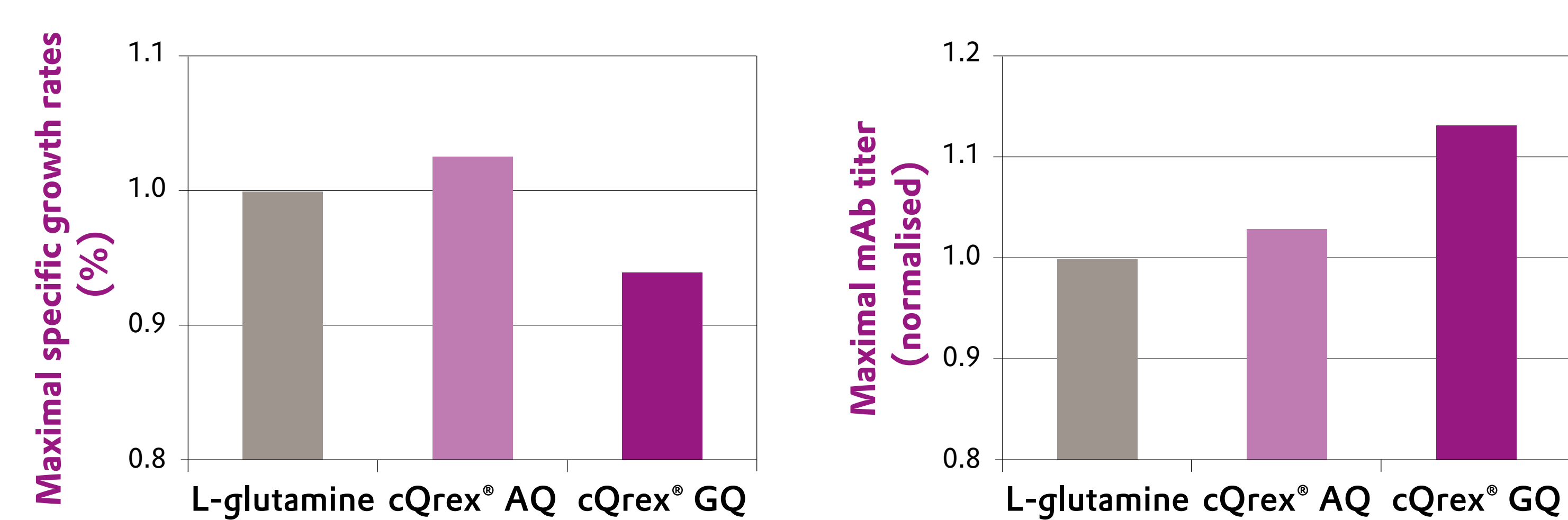
Batch cultivation of CHO DP-12 cells producing IgG1



Optimize cell growth and titer

Effects depend on the combination of cell line, process and selected cQrex® peptide

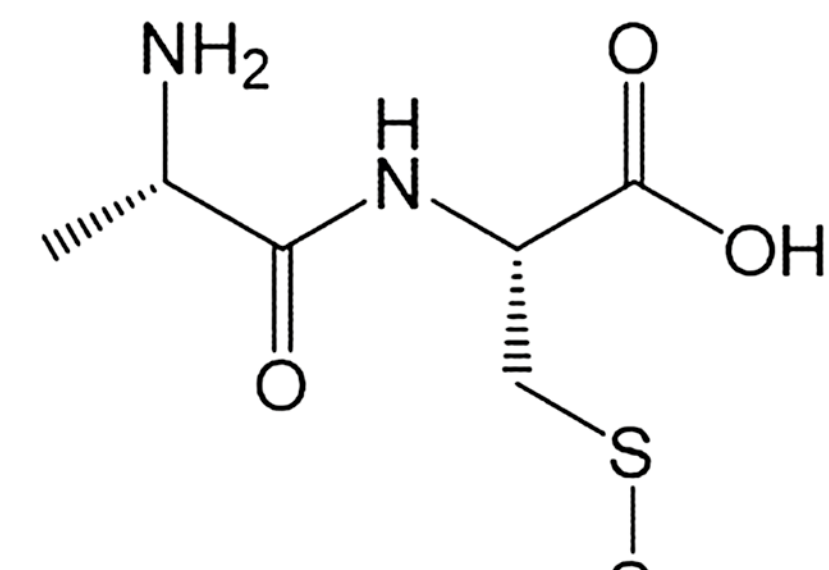
Batch cultivation of CHO DP-12 cells producing IgG1



cQrex® AQ: fast uptake
→ Beneficial for cell growth

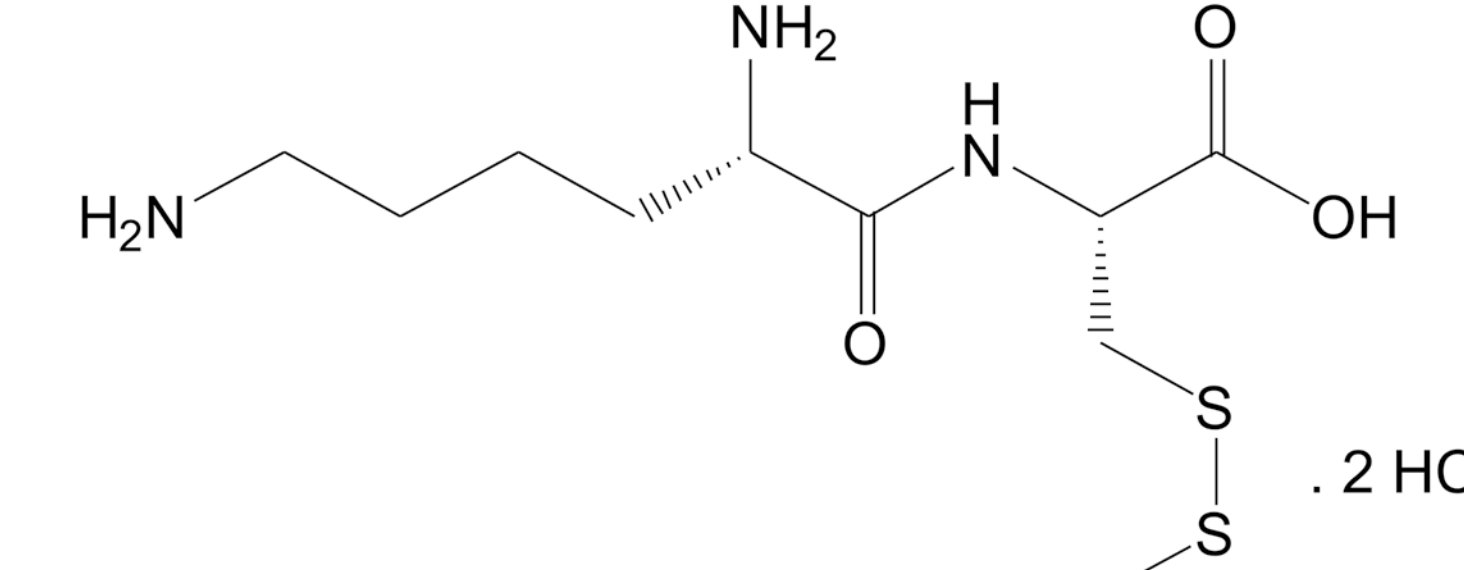
cQrex® GQ: slower uptake
→ Beneficial for titer

Cys CYSTINE PEPTIDES Highly soluble



N,N'-di-L-Alanyl-L-cystine

cQrex® AC



N,N'-di-L-Lysyl-L-cystine dihydrochloride

cQrex® KC

Intensify and simplify the bioprocess thanks to highly soluble peptides

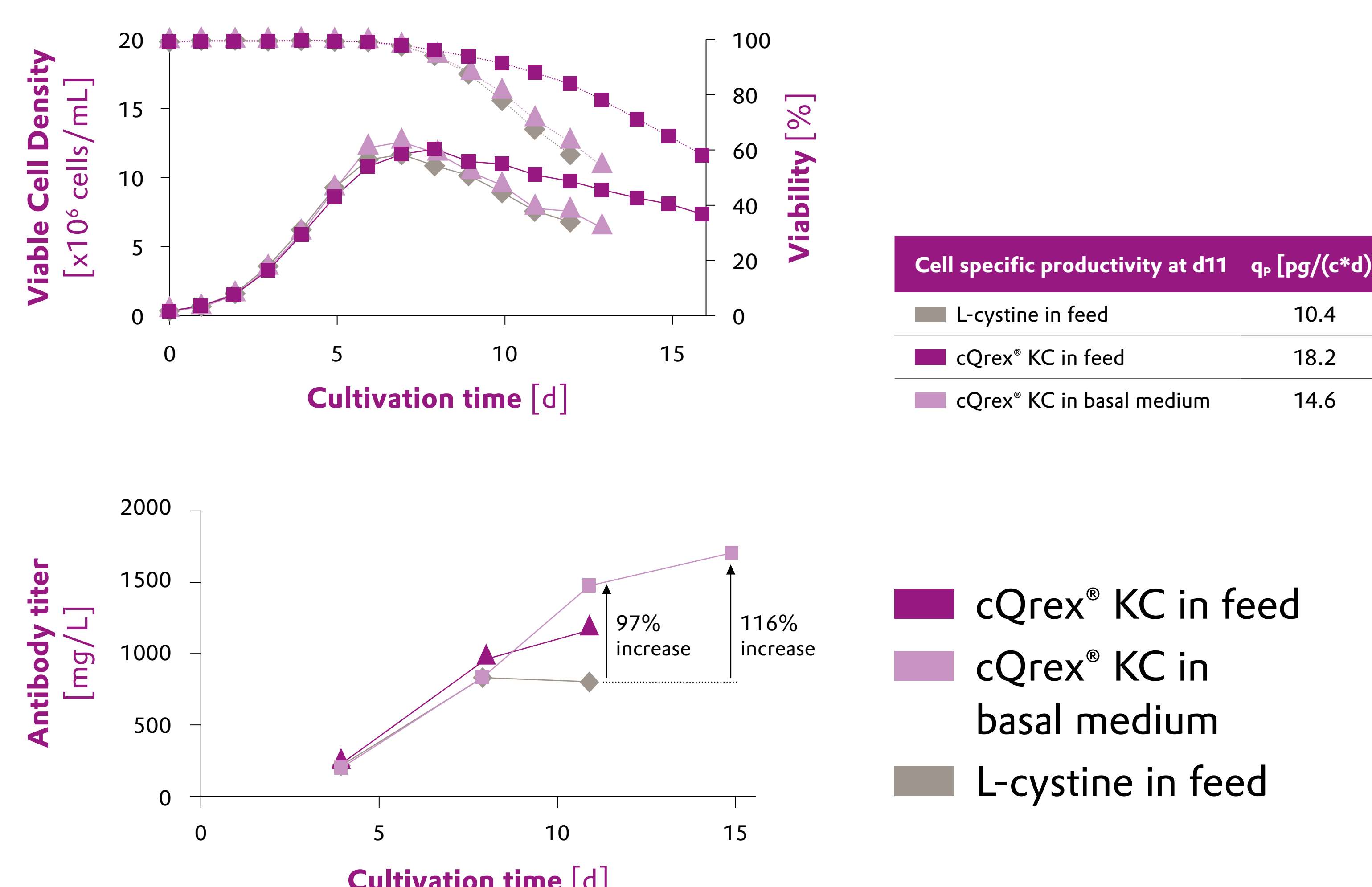
- Stable and highly soluble peptides at neutral pH: up to 1000 times higher solubility than L-cystine
- Enables high L-cystine concentrations in the basal, feed or perfusion medium
- Various formulation options to reduce bioprocess complexity and increase flexibility in media formulation and bioprocess design

Maximize bioreactor productivity and boost titers

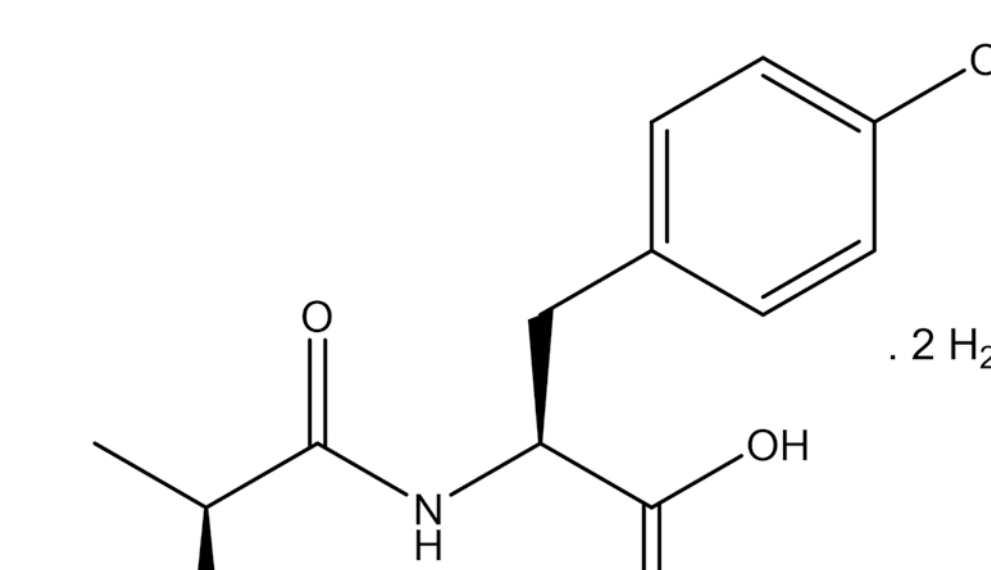
In bioreactors, cQrex® KC supplementation enables:

- Prolonged high cell viability
- Higher cell-specific productivity
- Strong increase in antibody titer

Fed-batch cultivation at bioreactor scale of CHO-GS cells producing an antibody (equimolar amounts of L-cystine and cQrex® KC, adjusted L-lysine concentration)

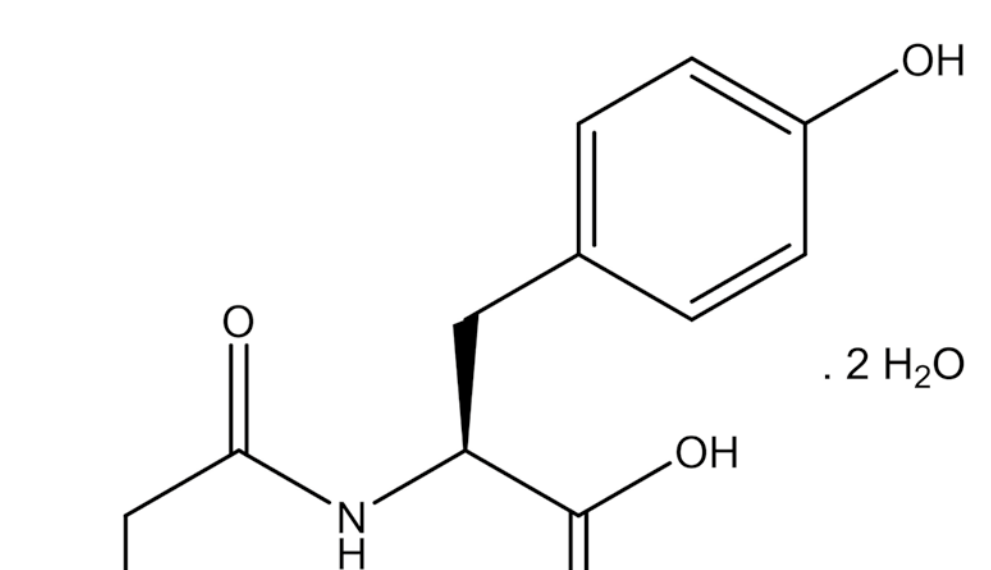


Tyr TYROSINE PEPTIDES Highly soluble



L-Alanyl-L-tyrosine dihydrate

cQrex® AY



Glycyl-L-tyrosine dihydrate

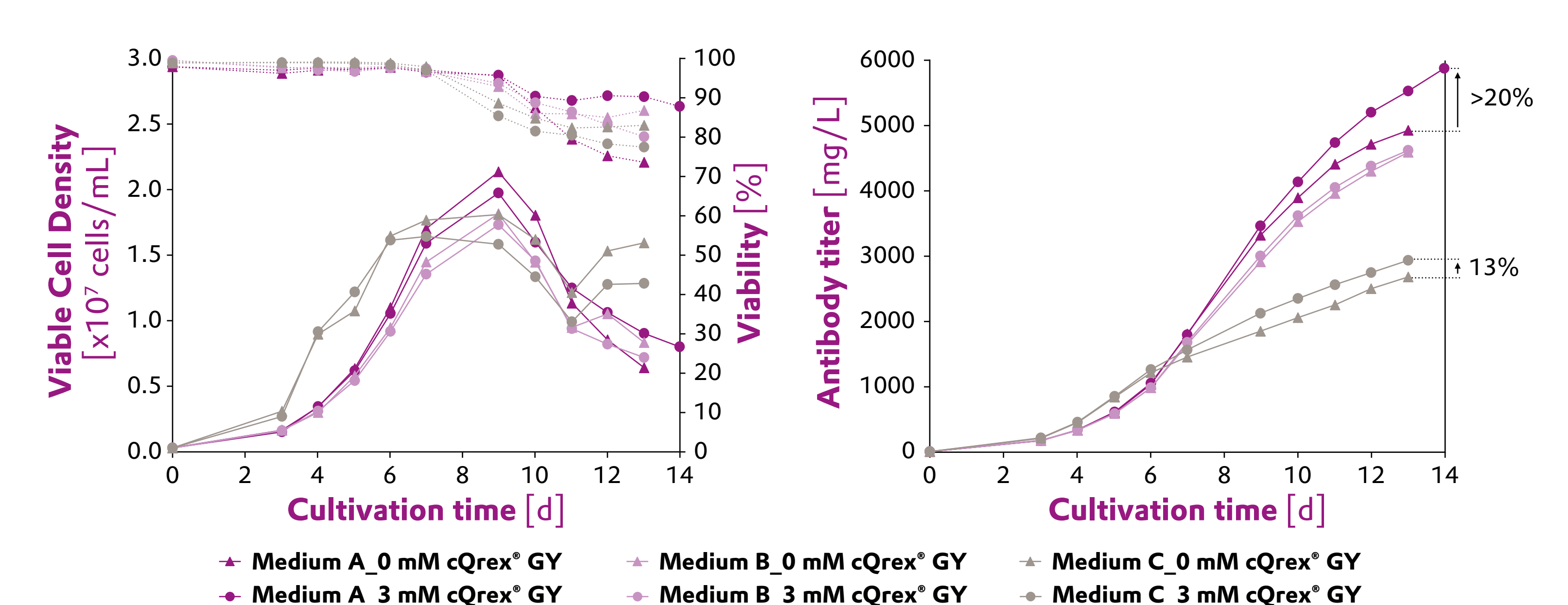
cQrex® GY

Boost the antibody titer with cQrex® supplementation

- Tyrosine peptides are stable and soluble in pH-neutral media (up to 110 mM)
- Possibility to include peptides in main feed or basal media enables simplified and risk-reduced bioprocess
- Additional benefits of cQrex® GY supplementation on cell culture performance:
 - Cell viability and growth: comparable or increased
 - Cell specific productivity: comparable or increased (data not shown)
 - Antibody titer: comparable or strongly increased – no negative effect

Fed-batch cultivation of CHO-K1 GS cells expressing IgG1 in 3 commercial media (basal and feed)

cQrex® GY stock solution added to commercial basal media



The cQrex® effect: greater cell culture performance with high-quality peptides

CHEMICALLY DEFINED
STABLE
BIOAVAILABLE
SOLUBLE
ANIMAL ORIGIN FREE

cQrex®



PRODUCTIVITY INCREASE

- Bioreactor used at its full capacity
- Efficient production of biopharmaceuticals



PROCESS INTENSIFICATION

- Higher concentrations of ingredients
- Boost in cell growth and viability



PROCESS SIMPLIFICATION

- No need for extreme pH
- Can be included in feed or basal media

cQrex® ingredients



Selection of performance-boosting ingredients:

cQrex® AQ, GQ, AY, GY, KC (10 g samples)
cQrex® AC (6 g sample)
cQrex® AKG (5 g sample)

Get in touch with our experts:
cQrex@evonik.com

EVONIK
Leading Beyond Chemistry