Enabling a Healthier World
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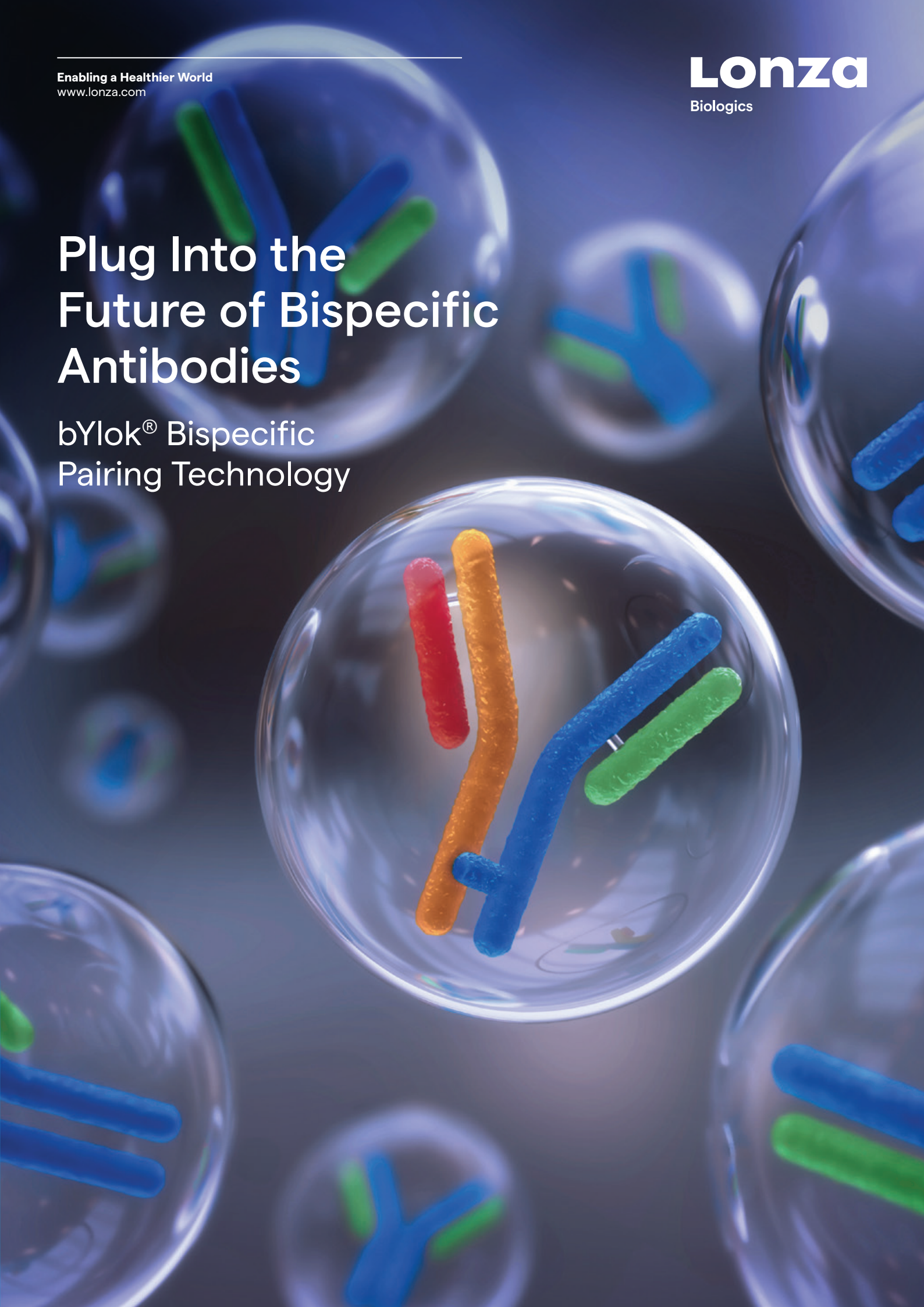
Lonza
Biologics

Plug Into the Future of Bispecific Antibodies

bYlok® Bispecific Pairing Technology



bYlok® Technology

is a New Design Engineering Approach for Developing Bispecific Antibodies

bYlok®

Precision Pairing that Links You...

Solving the HC-LC pairing challenge in bispecific antibodies

bYlok® is changing the way bispecific antibodies are designed. Achieving the correct heterodimerization of light and heavy chains during bispecific production can be challenging, and whilst the knobs-into-holes technology solves heavy chain mispairing, bYlok® offers a solution to address HC-LC mispairing.

bYlok® technology delivers >95% correct HC-LC pairing efficiency. It works on the principle of being closer-to-nature by design, reducing the risk of any unwanted immunogenicity, whilst offering superior manufacturing efficiencies to ease bispecific production at scale.

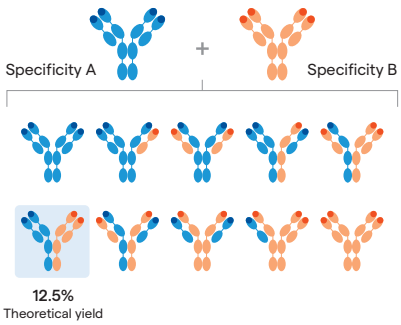
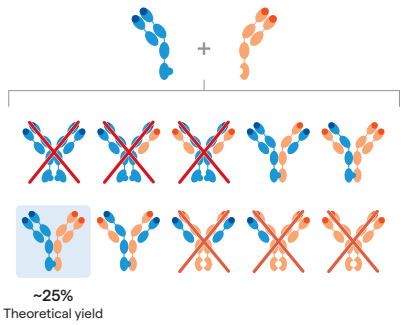
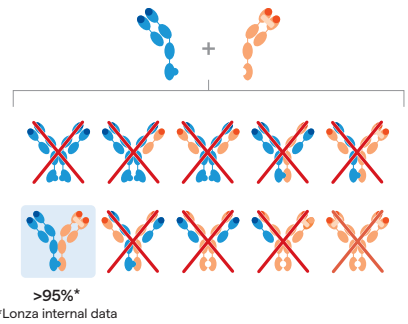
Heterogeneous mixture of very similar species	Partial solution: Knobs-into-Holes Technology	Complete solution: bYlok® Technology
		
Highest probability of mispairing events	Solves heavy chain mispairing. Knobs and holes are positioned in the CH3 region of antibodies in such a way that hinders formation of homodimers.	Disulfide Bridge is moved in one of the 'half mAbs' from constant domains (CH1/CL) to variable domains (VH/VL). Favours formation of a heterodimer.
Can require **two separate cell lines** (one for each 'half mAb'); followed by assembly and further downstream processing		Only one cell line required and simplified downstream processes.

Figure 1: How bYlok® overcomes the limitations of existing bispecific pairing solutions.

...to More Therapeutic Possibilities!

Elevated pairing precision to unlock the therapeutic future of bispecifics

HC-LC mispairing is a major challenge during bispecific antibody production. To solve HC-LC mispairing, the bYlok® technology involves the engineering of the native disulphide bridge, moving it from the constant domains (CH1/CL) to the variable domains (VH/VL). This minor modification favours the formation of correct HC-LC heterodimers.

bYlok® delivers >95% HC-LC accuracy in a true 'plug-and-play' format, unlocking new possibilities for discovery phase customers, from small biotech to big pharma. The technology can be easily implemented to build and retrofit bispecific antibodies through a research license from Lonza.

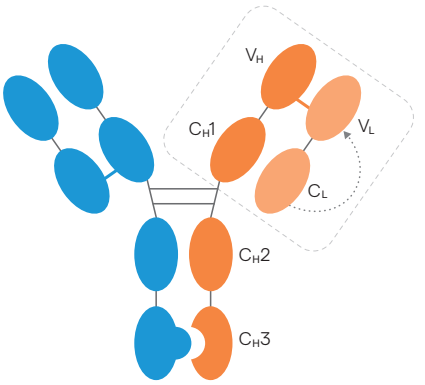


Figure 2: bYlok® design involves moving one of the disulfide bonds from the constant region to the variable domains.

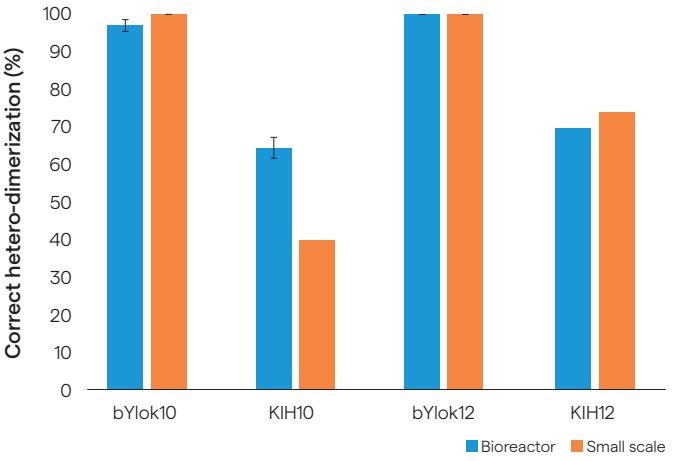


Figure 3: bYlok10 and bYlok12 are bispecific antibodies created using the bYlok® technology. KIH10 and KIH12 are their respective controls with knobs-into-holes only. Bispecific antibodies generated using bYlok® technology display >95% correct HC-LC pairing.

Scan the QR code to learn more about bYlok®.

Technology that Enables ‘Plug-and-Play’ Bispecific Antibodies

A new design engineering approach for bispecifics

1. **Simple engineering that can be retrofitted**
   The platform technology can be used to generate IgG-like bispecific complexes and other types of complexes from IgGs already being used in the clinic. By combining bispecific pairing precision with reduced risk of further impact on immunogenicity*, bYlok® technology can help you to develop better products.

2. **No compromises to the bispecific design**
   You don’t have to settle for a common LC approach. Also, the bYlok® mutation is a minor modification to the original mAb design, enabling a closer-to-nature approach to reduce the risk of unwanted immunogenicity.

3. **Standard product purification methods**
   Unlike other technologies, you don’t have to sacrifice yields to purify the correct bispecific format. With bYlok® technology, you can use standard purification methods.

4. **An easily implemented solution for everybody to use**
   Try bYlok® for yourself with Lonza in Your Lab™. A license also grants access to the bYlok® Sequence Editor, our online tool that guides you on how to introduce the required sequence modification. You will also get access to know-how and expert support to implement the technology in your lab.

Challenges of bispecifics production	Lonza’s solution
Low HC-LC pairing accuracy	Lonza’s bYlok® HC-LC pairing solution, combined with the knobs-into-holes technology, offers >95% pairing precision.
Risk of unwanted immunogenicity	Design by nature approach reduces risk of unwanted immunogenicity. The bYlok® modification causes no observed elevation in predicted immunogenicity.*
Difficult to express	Combining bYlok® with tools such as our GSquad® vectors and GS piggyBac® transposase technology enables increased efficiency and higher titers, at both small scale and bioreactor scale.
Complex downstream purification	Bispecifics containing the bYlok® modification can be purified using standard methods with high yields.

*Lonza internal data.

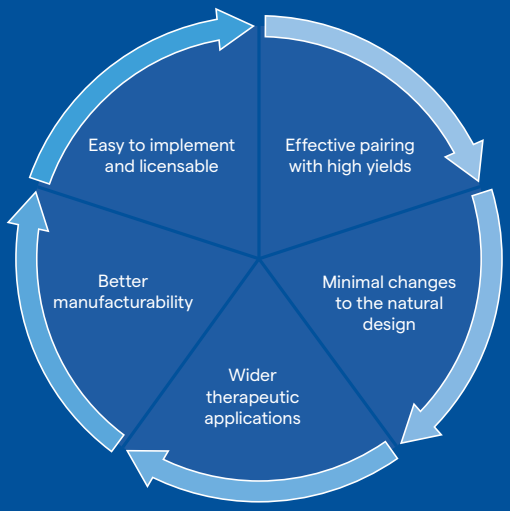
bYlok® Technology Widens Therapeutic Possibilities

Lonza's bYlok® technology: a true plug-and-play solution to bispecific antibody engineering – high product quality, simplified processes, unlocking the future

Precision pairing...
bYlok® links you to more therapeutic possibilities. The new technology solves one of your biggest manufacturing challenges, enabling >95% correct HC-LC pairing.

...that links partners...
Licensing solutions unlock our technology for everyone to take into the lab, making scalability simple and accessible.

...to better possibilities
Widen the therapeutic applications of your antibodies with bYlok® technology. Our focus on minimal structural modification and streamlined manufacturing processes ensures optimal conditions for your clinical products in development.



Bispecific antibodies generated using bYlok® technology display >95% correct HC-LC pairing*

*Lonza internal data.

Contact us

To find out more about our game changing **bYlok® technology**, visit **www.lonza.com/biologics/expression-technologies/bYlok** or scan the QR code.

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