

# Anti-Human Claudin-18.2 Monoclonal Antibody As Cancer Therapeutics

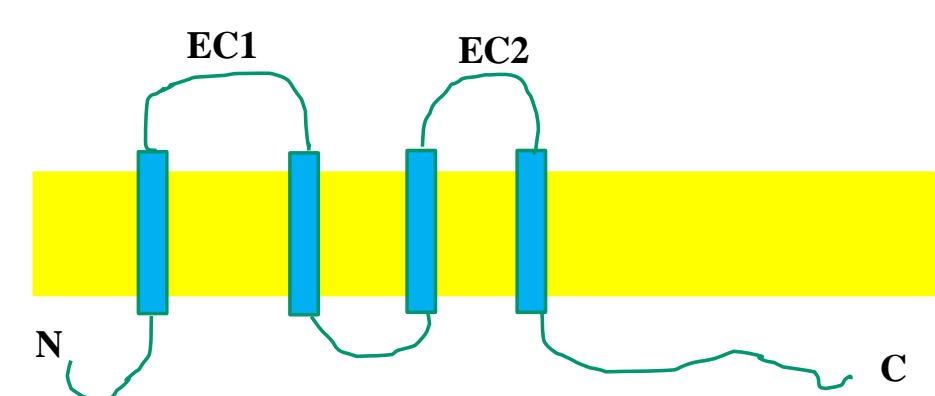
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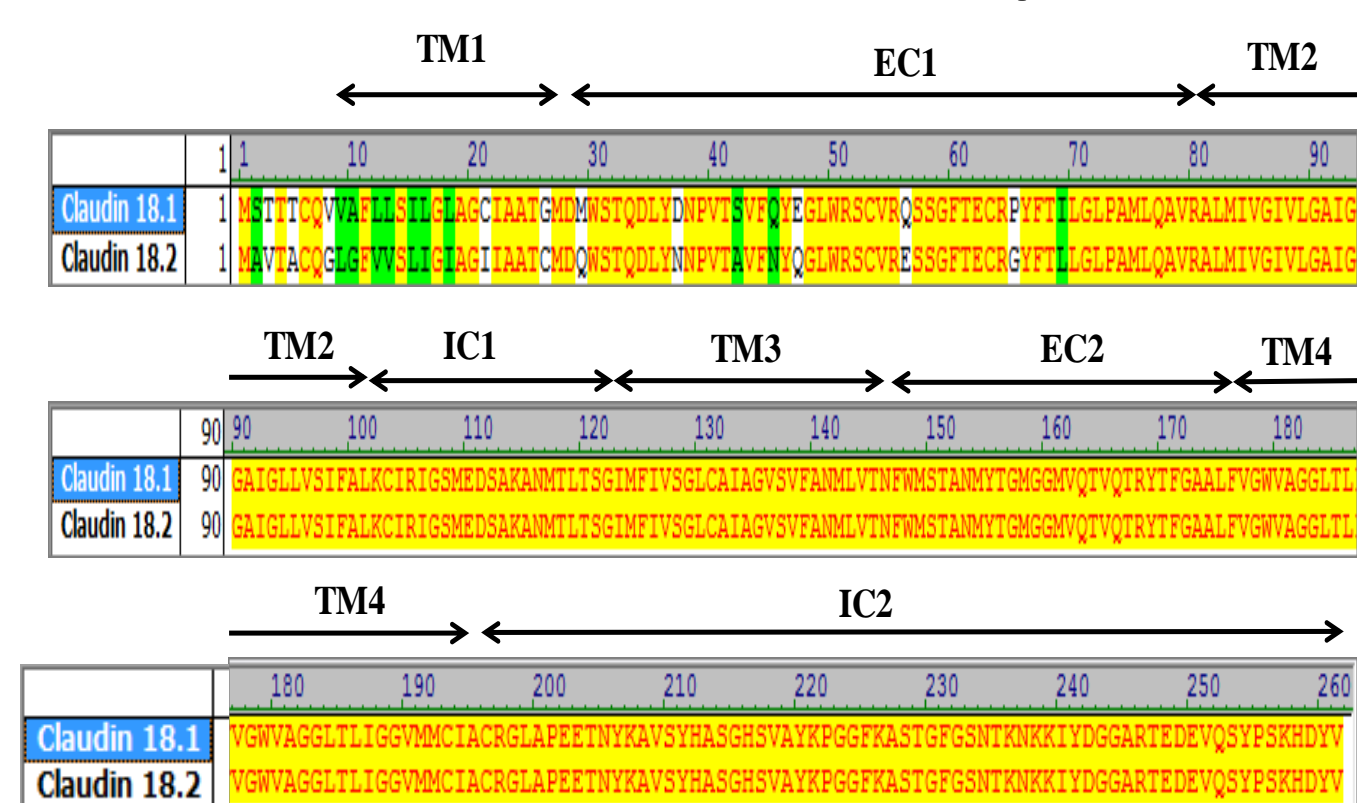
## BACKGROUND

- Claudin-18 (CLDN18) is a member of a large family of four-span transmembrane proteins, Claudins, which are the essential components of the mammalian tight junctions (TJs) in the epithelial cells.
- Claudin-18 has two splice variants, 18.1 and 18.2. While CLDN18.1 is specifically expressed in the lung tissue, CLDN18.2 expression in normal tissue is more restricted and is only detected in small patches of stomach mucosal.
- CLDN18.2 expression is elevated in many types of epithelial cancers including stomach, esophagus, pancreatic and ovarian cancers. The expression of CLDN18.2 is not only detected in primary tumors, but also in the metastatic sites. Therefore, CLDN18.2 is an ideal target for monoclonal antibody-based cancer therapies.
- CLDN18.2-specific antibodies are difficult to generate due to its high homology to CLDN18.1. There are only 7-8 amino acid differences between these two splice variants in the first extracellular loop.
- Using a combination of DNA, protein, and transfected cells as immunogens, coupled with high-throughput FACS-based hybridoma screening approach, we have generated a panel of mouse monoclonal antibodies highly specific for CLDN18.2.

CLDN 18.2 is a multi-span transmembrane receptor

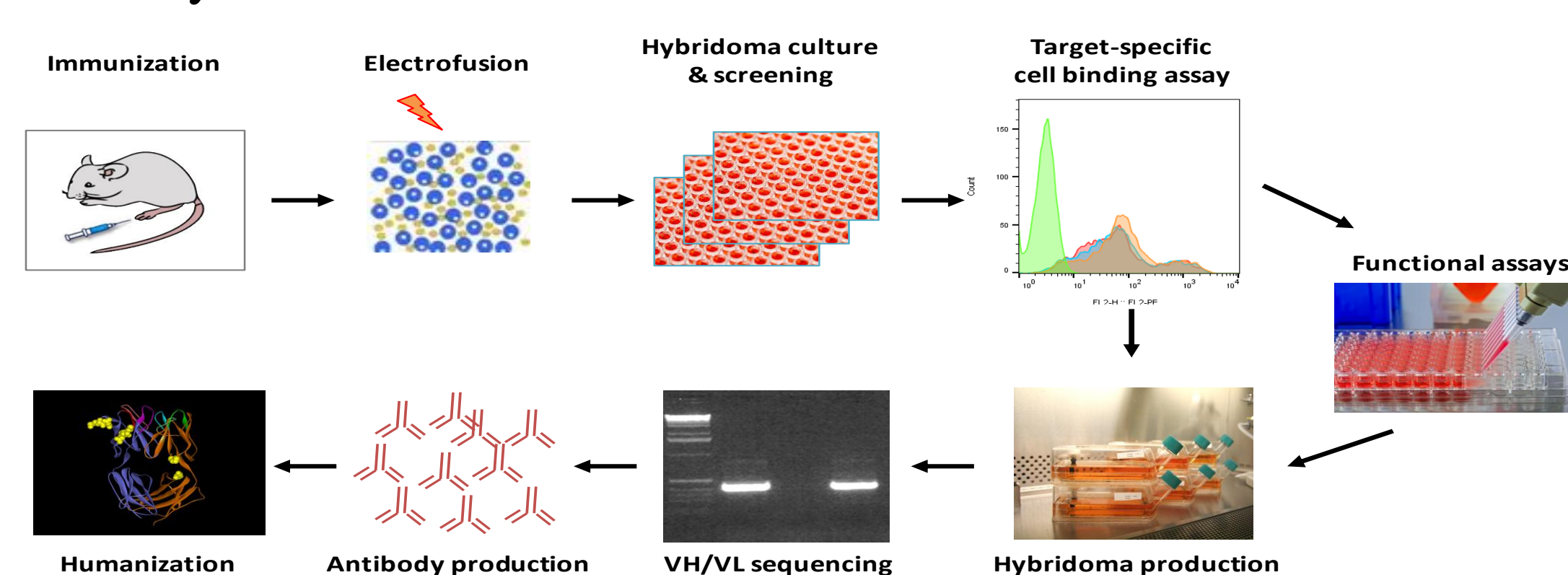


CLDN 18.2 is identical to CLDN 18.1 except in TM1 and EC1



## APPROACHES

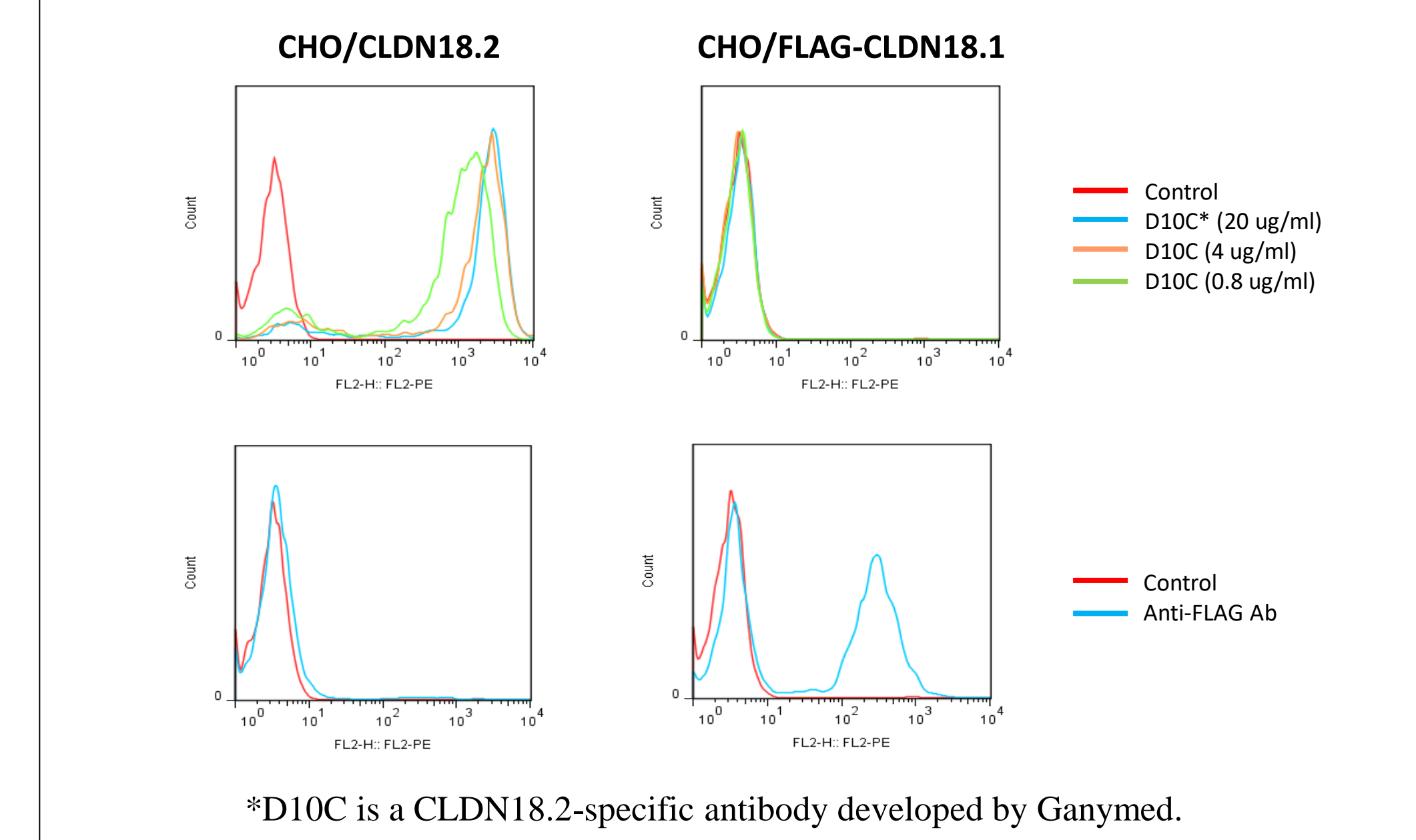
- Generation of mouse anti-human CLDN18.2 mAbs through our Therapeutic Antibody Discovery Platform
- Mouse immunization with DNA, protein and cell immunogens
- Screening for mAbs binding to CLDN18.2 expressing cells
- Counter-screen for mAbs binding to CLDN18.1 expressing cells
- Evaluation of mAbs binding to cancer cells
- Determination of anti-CLDN18.2 antibody-induced receptor internalization
- Antibody humanization



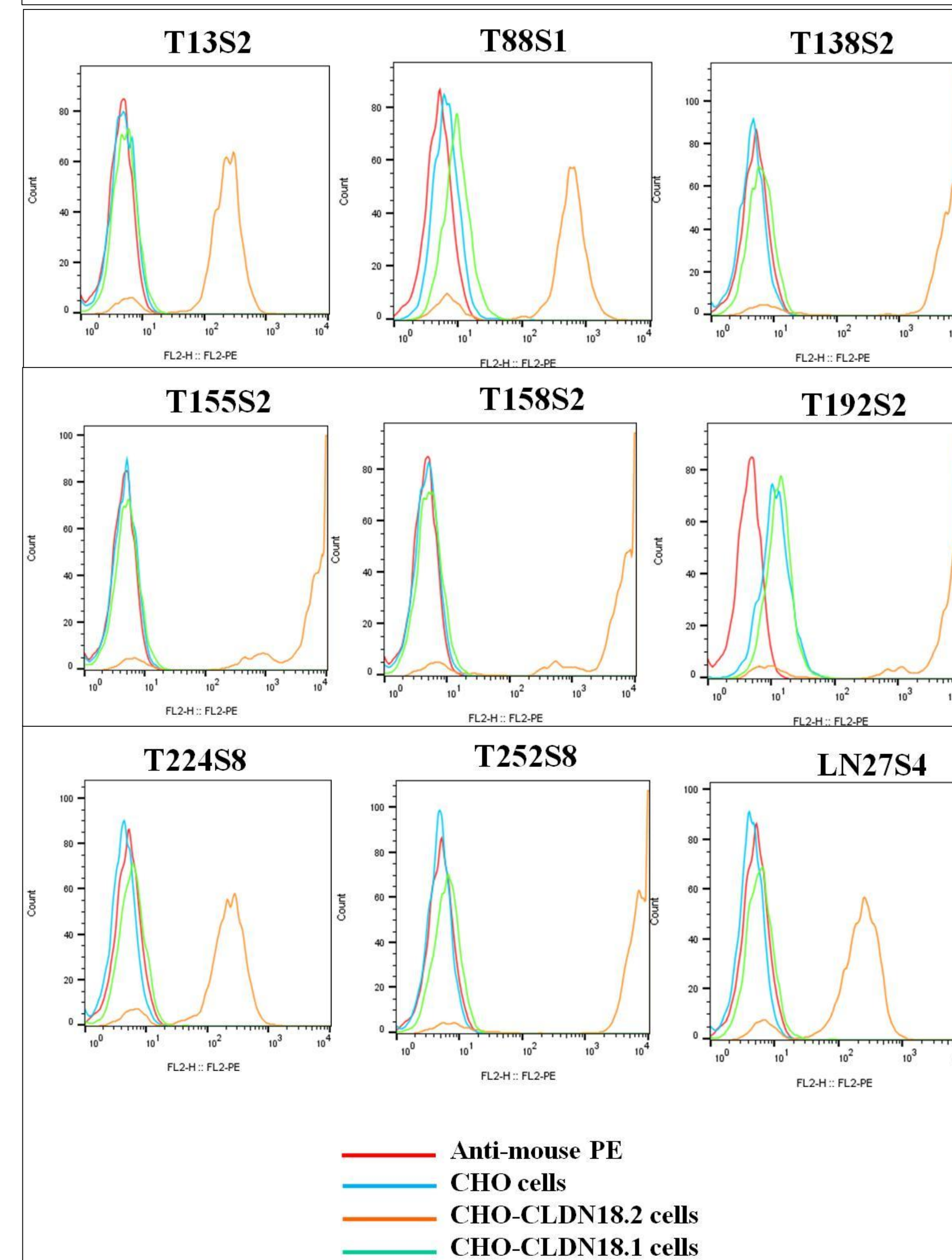
Our Platform for Therapeutic Antibody Discovery

## RESULTS

### Generation of CHO Cell Lines Expressing CLDN18.2 and FLAG-CLDN18.1

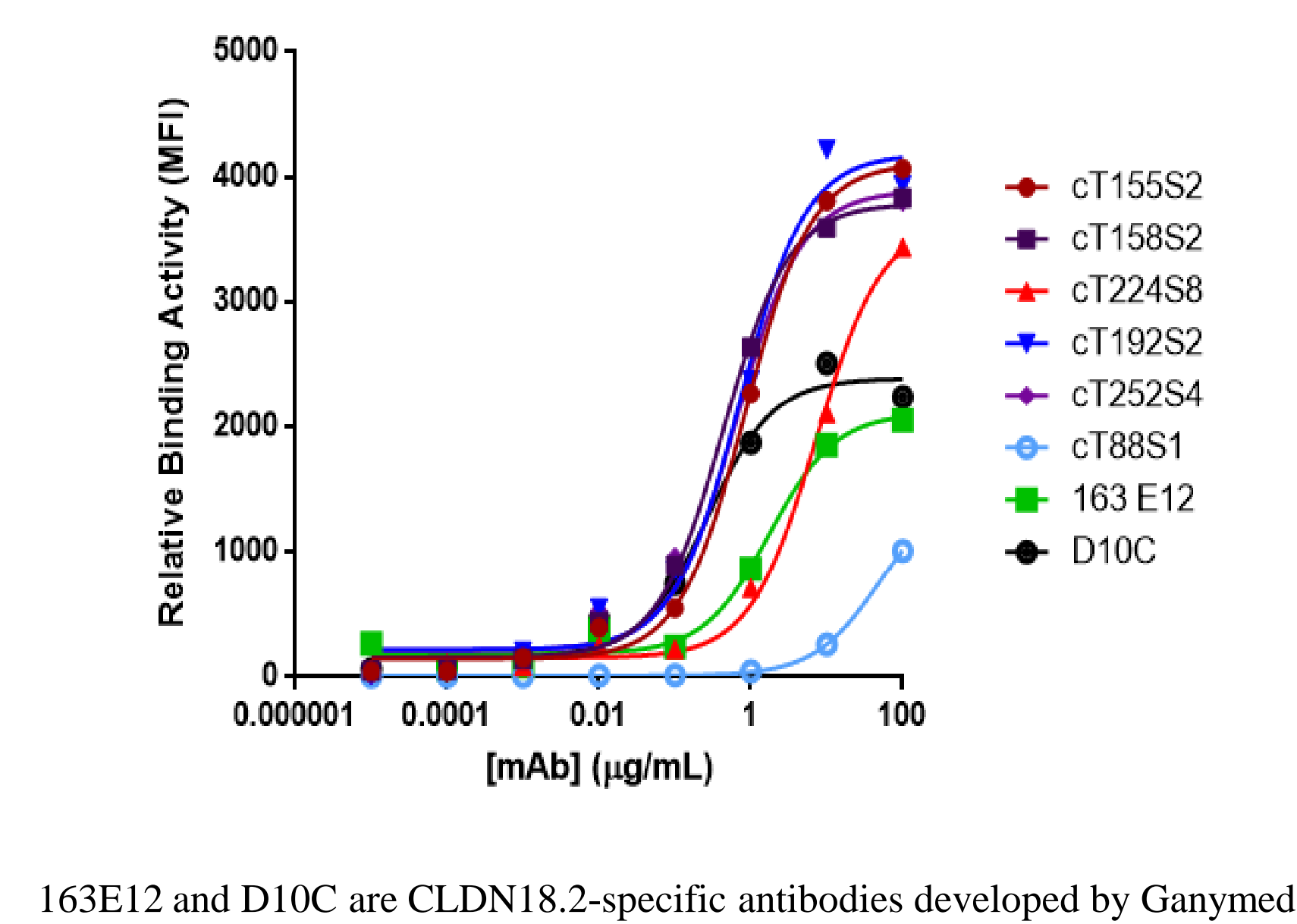


### Binding Specificity of Anti-CLDN18.2 mAbs

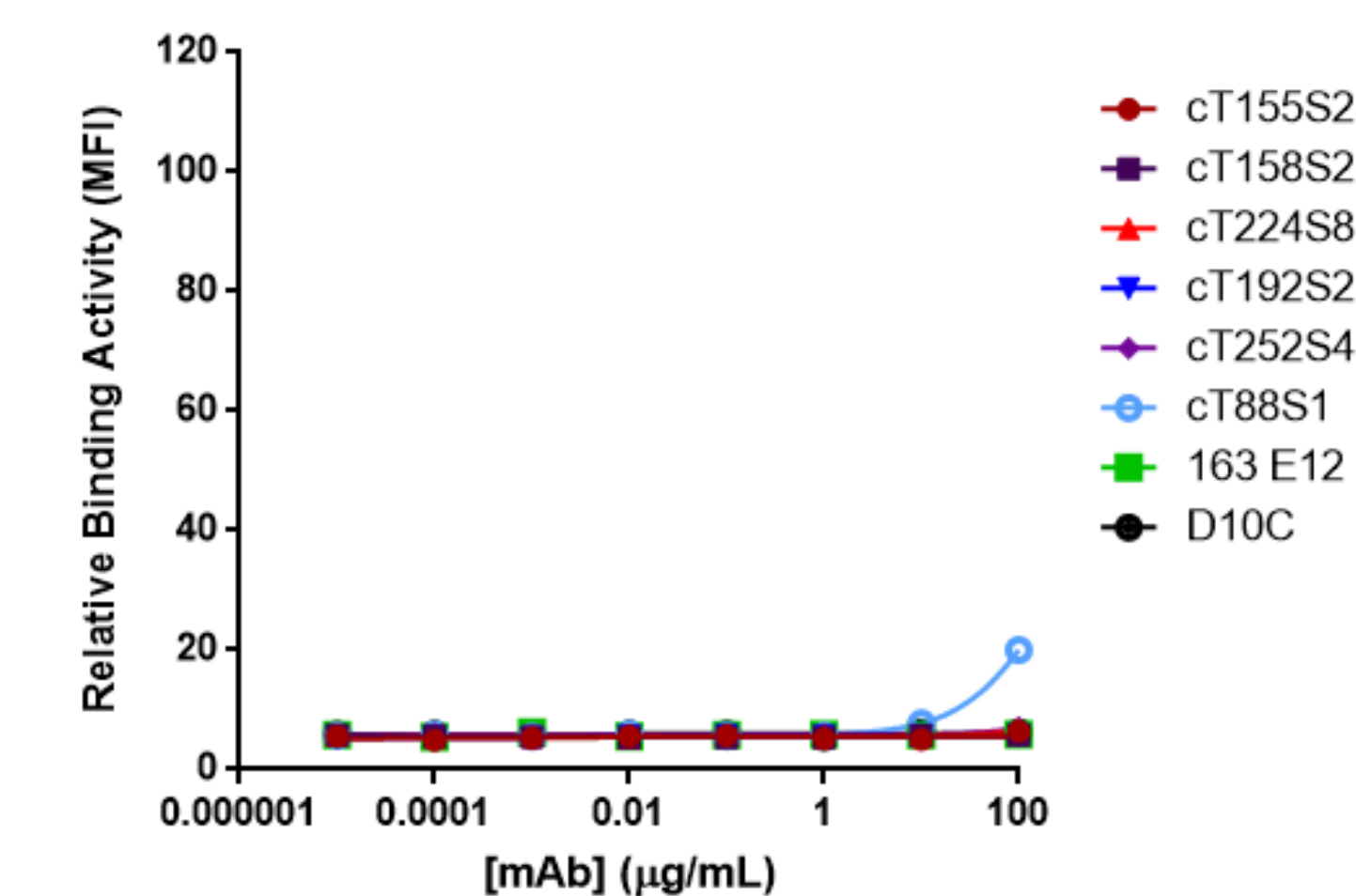


## RESULTS

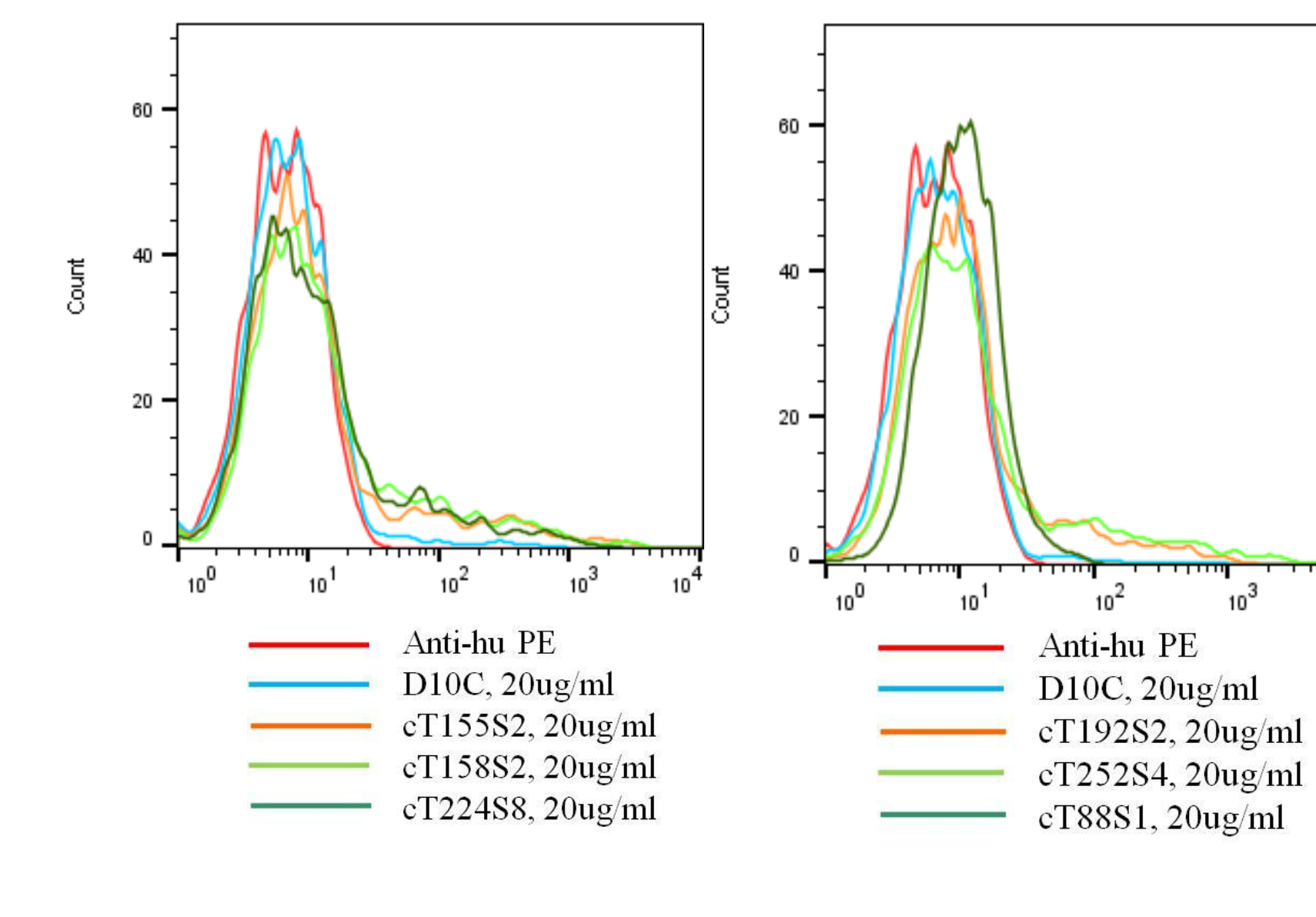
### Anti-CLDN18.2 Chimeric Antibodies Bind to CHO-CLDN18.2 Cells with High Affinity



### Anti-CLDN18.2 Chimeric Antibodies Did Not Bind to CHO/FLAG-CLDN18.1 Cells

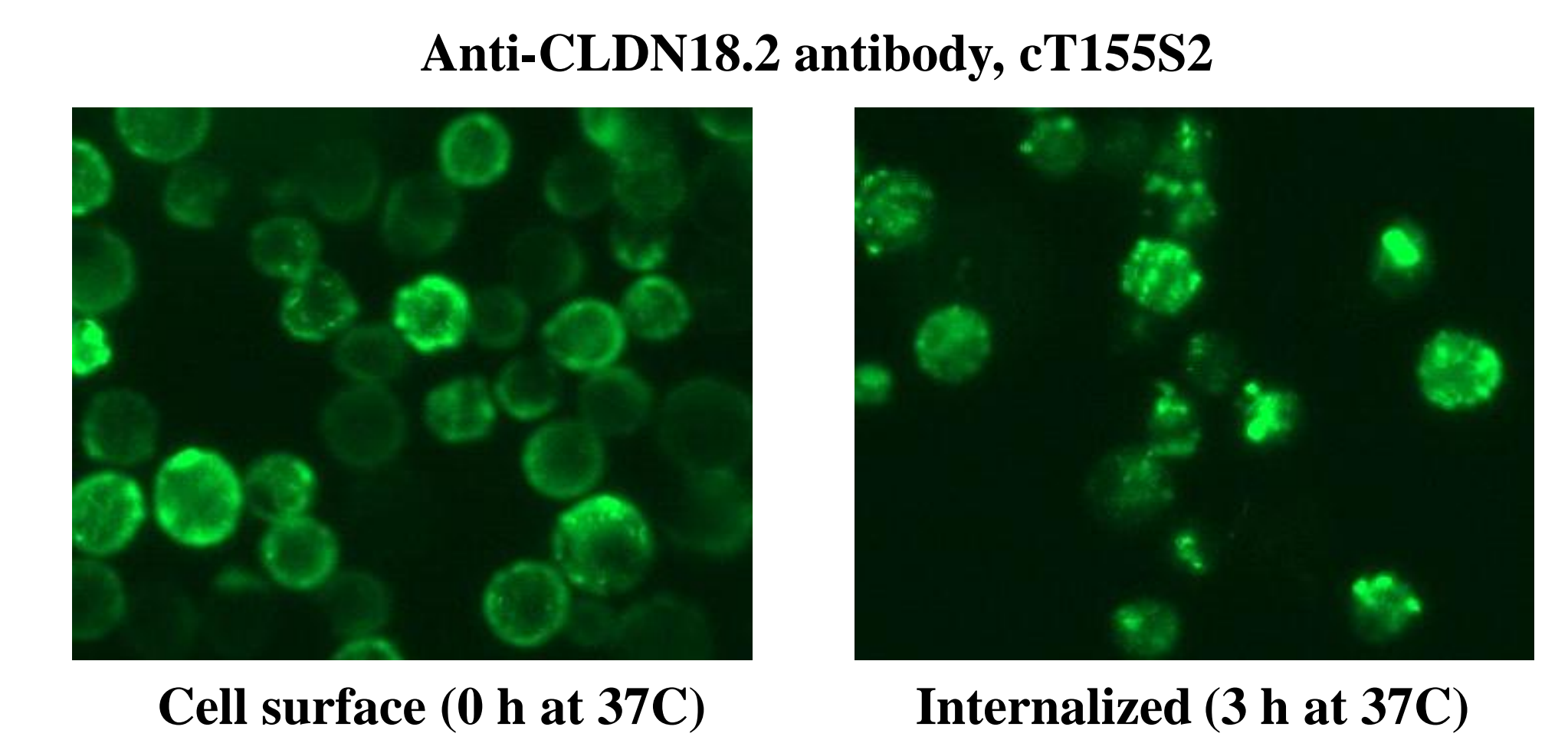


### Binding of Anti-CLDN18.2 Chimeric Antibodies to KATO III cells

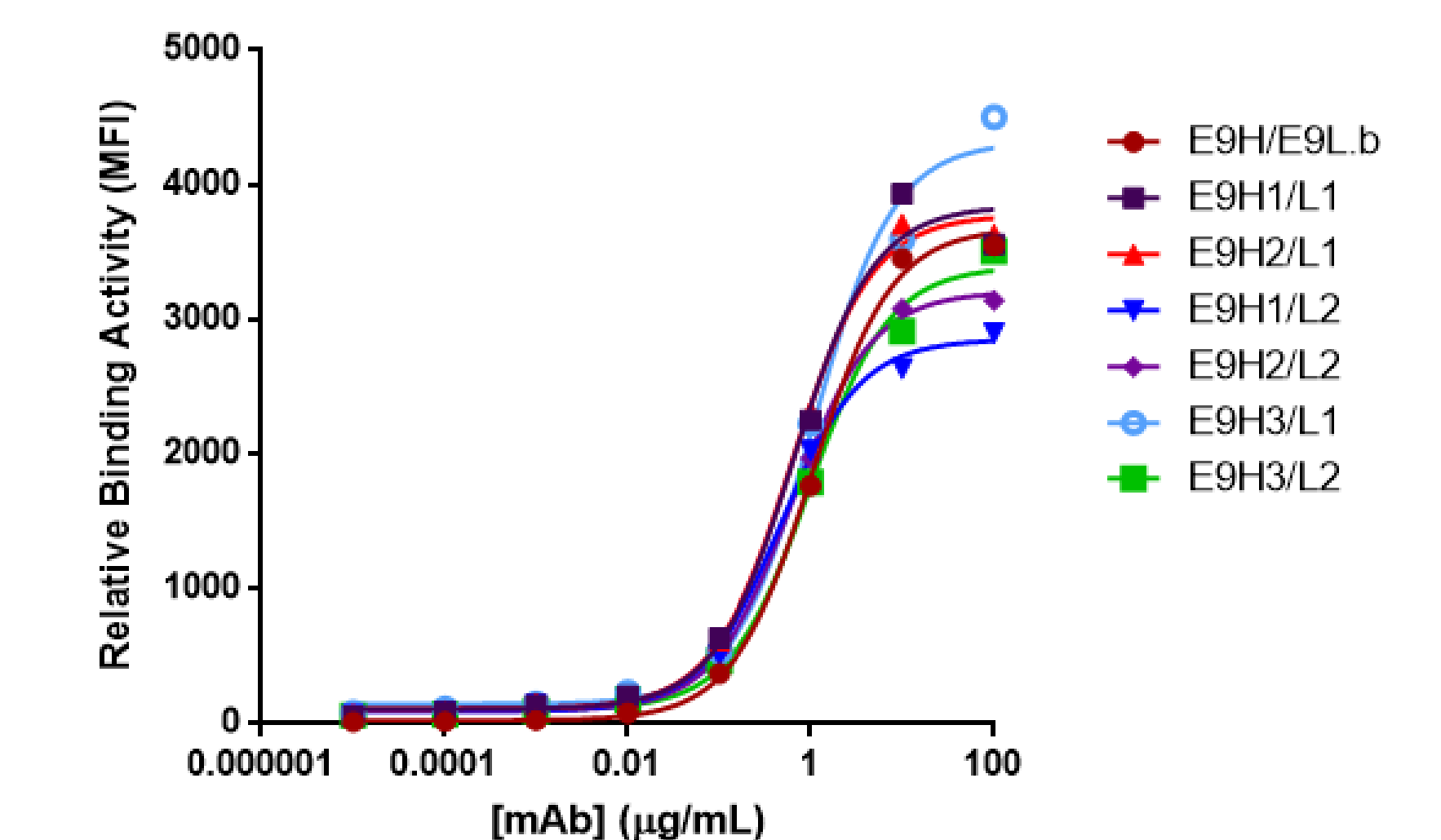


## RESULTS

### Anti-CLDN18.2 Antibody Induced Receptor Internalization in CHO-CLDN18.2 Cells



### Binding of Humanized Anti-CLDN18.2 Antibodies to CHO/CLDN18.2 Cells



## SUMMARY

- We have generated a panel of high affinity anti-human CLDN18.2 monoclonal antibodies via the mouse hybridoma approach.
- These antibodies are highly specific for CLDN18.2 and do not bind to CLDN18.1.
- These antibodies bind to human gastric cancer cell line KATO III and can induce CLDN18.2 internalization
- One of the lead antibody has been humanized and is under evaluation in preclinical animal models.

\*This program is available for licensing and collaboration. For further information, please contact us at [hlin@accurusbio.com](mailto:hlin@accurusbio.com) or [richard@accurusbio.com](mailto:richard@accurusbio.com)