Mabqi

CASE STUDY

# DEVELOPMENT OF CONDITIONALLY ACTIVE PH-SENSITIVE ANTI-HER2 ANTIBODIES TO OPTIMIZE THE THERAPEUTIC INDEX

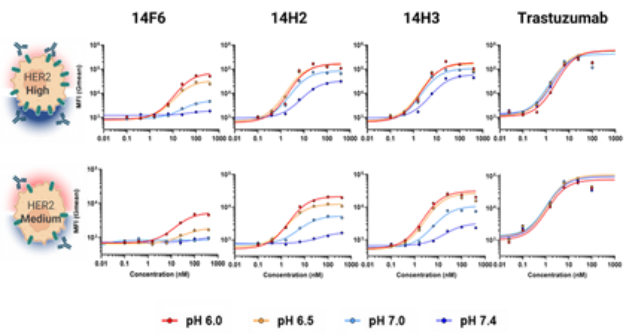
## METHOD

Antibodies were selected from Mabqi's **pHusci2™ library**, a synthetic human antibody library dedicated to the discovery of conditionally active pH-sensitive antibodies.
**pH-sensitivity is key to enhancing the drug's safety and efficacy profile** by improving its ability to bind to the intended target specifically in low pH environments (i.e. acidified tumor microenvironment of solid tumors). This results in an **increased therapeutic index** and **reduces on-target off-tumor toxicities**.

After discovery process, 92 positive scFv against recombinant HER2 at pH 6.5 were identified after dual-pH HTRF screening. A selection of pH-sensitive clones was further characterized as IgGs.

## RESULTS

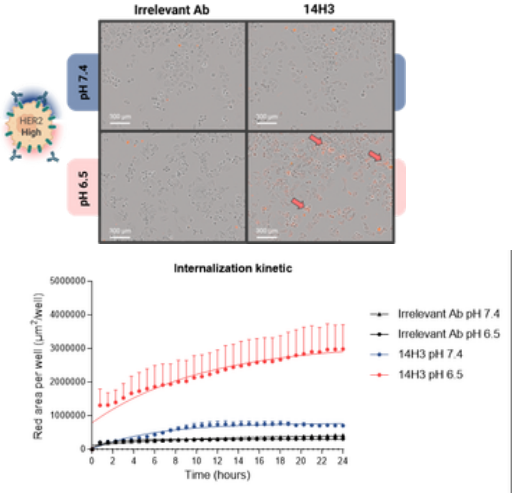
### 1. pH-sensitive targeting of HER2-expressing cancer cells




*IgGs binding on high and medium expressing HER2 cancer cells from pH 6.0 to 7.4 by flow cytometry*

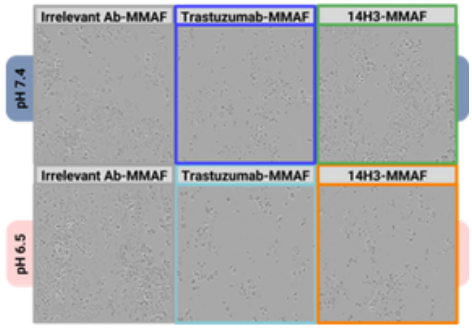
All IgGs exhibit a strong binding at acidic pH (6/6.5) and a low or very low binding at pH 7.4.

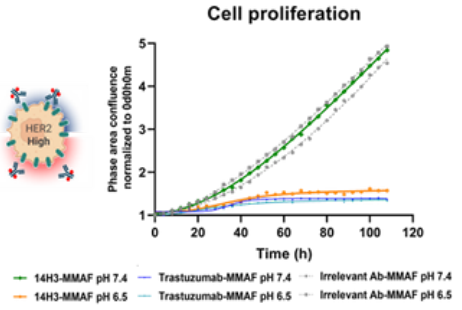
### 2. Specific internalization of IgG at acidic pH




IgG internalization on high HER2-expressing cancer cells by live imaging on HER2-expressing cells using Incucyte® FabFluor reagent.

### 3. Potent pH-sensitive cytotoxicity on HER2-expressing cancer cells




IgG-MMAF proliferation inhibition on high HER2-expressing cancer cells at acidic pH, by live imaging using Incucyte S3 device.

## CONCLUSIONS

- **Antibodies selected from Mabqi's pHusci2 library, bind to HER2 target with high affinity within TME acidic environment and with a strongly reduced affinity on healthy tissue at physiological pH.**
- **Identification of different types of highly pH-dependent anti-HER2 IgG:**
  - internalizing antibodies such as 14H3, for ADC format development
  - non-internalizing antibodies for TCE/CART development

*References : Collaboration with IRCM, France. Presented at 10th Antibody Industrial Symposium, 2022 - Festival of Biologics Basel, 2023*


CONTACT
France | @ business@mabqi.com

FOLLOW US
mabqi.com |