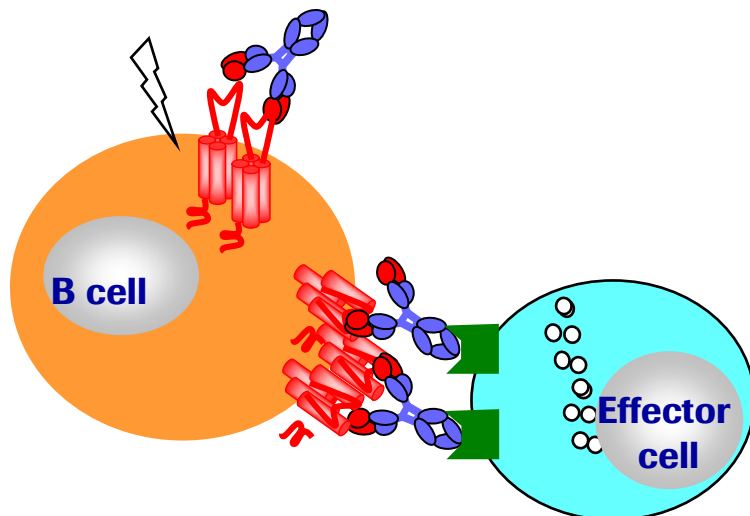


# ***Therapeutic Antibody Engineering for Enhanced Cell Death Induction and Immune Effector Functions***

*Pablo Umaña*

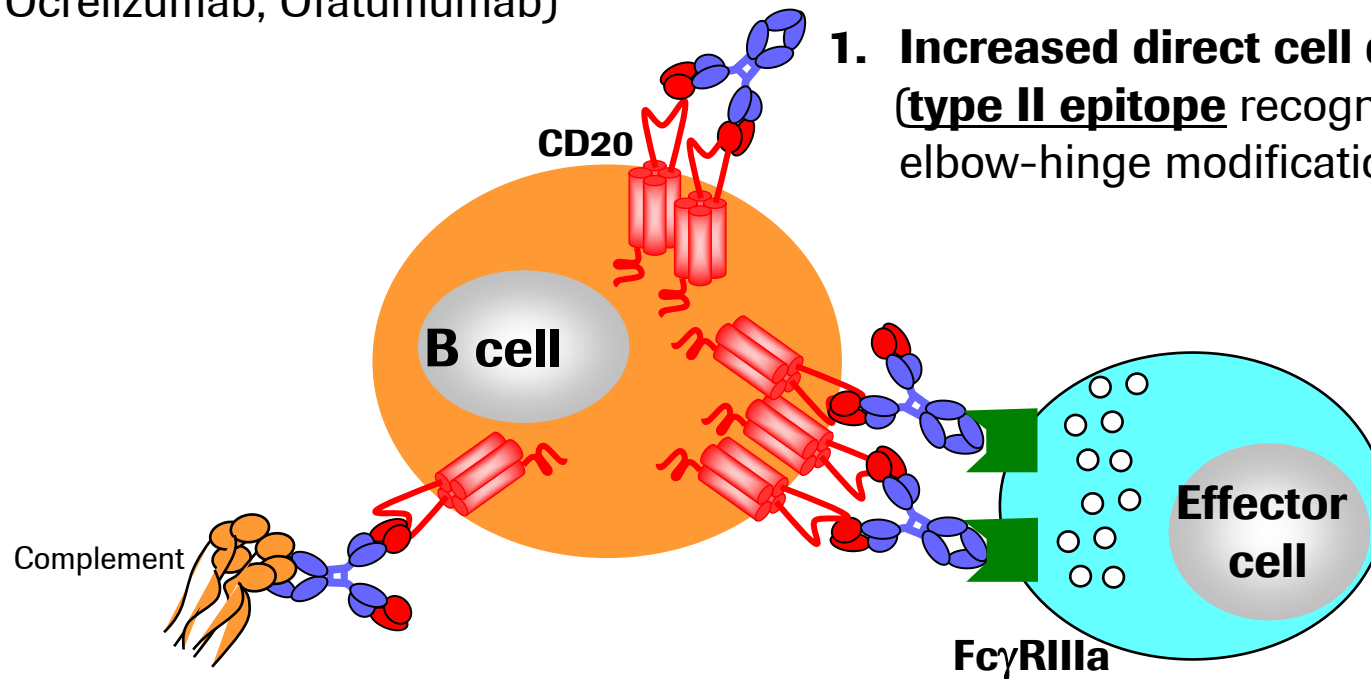


# Overview of mechanisms of action of GA101

## Mechanisms of action of GA101 (Type II Ab)

### vs. Type I Abs

(Rituximab, Ocrelizumab, Ofatumumab)



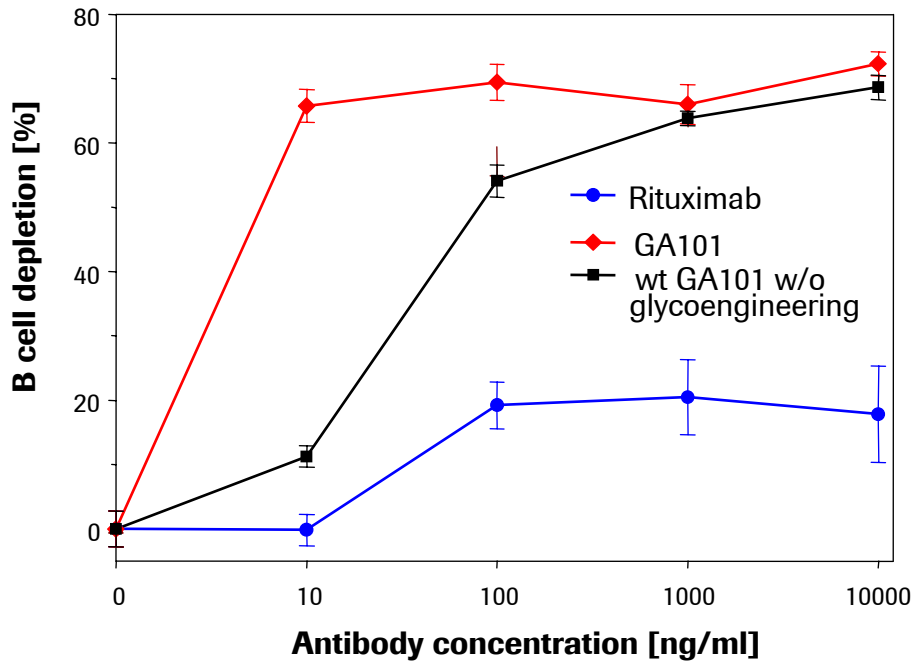
1. **Increased direct cell death**  
(type II epitope recognition & elbow-hinge modification)

3. Unlike Rituximab (type I epitope) **lower CDC** activity due to recognition of type II epitope

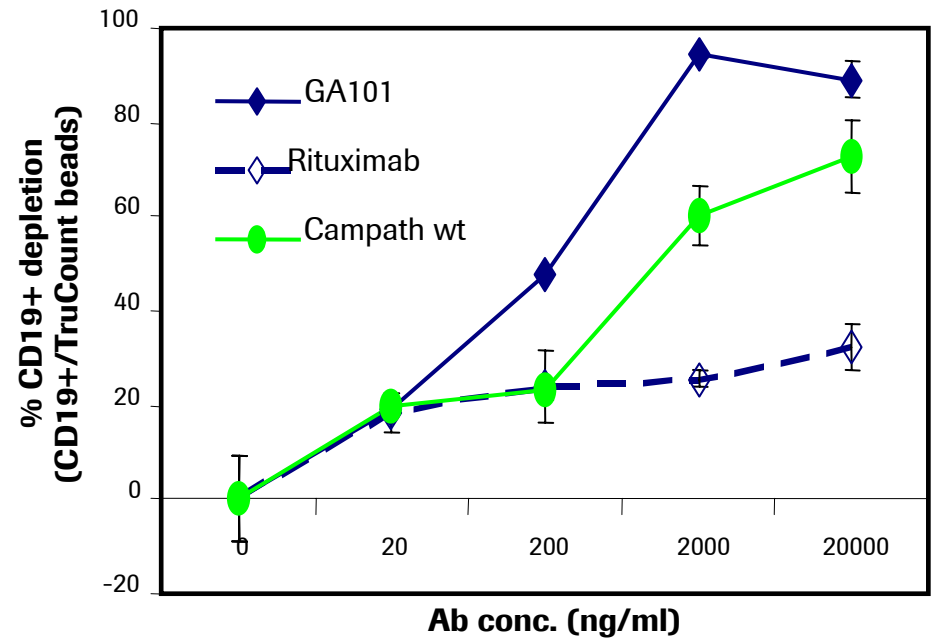
2. **Increased ADCC**  
via increased affinity to the 'ADCC receptor' FcγRIIIA

# GA101 is superior to Rituximab in Whole blood assays

**B-cell depletion - Whole blood Assay (24h)**  
**Healthy volunteer (FcγRIIIA genotype: F/F)**

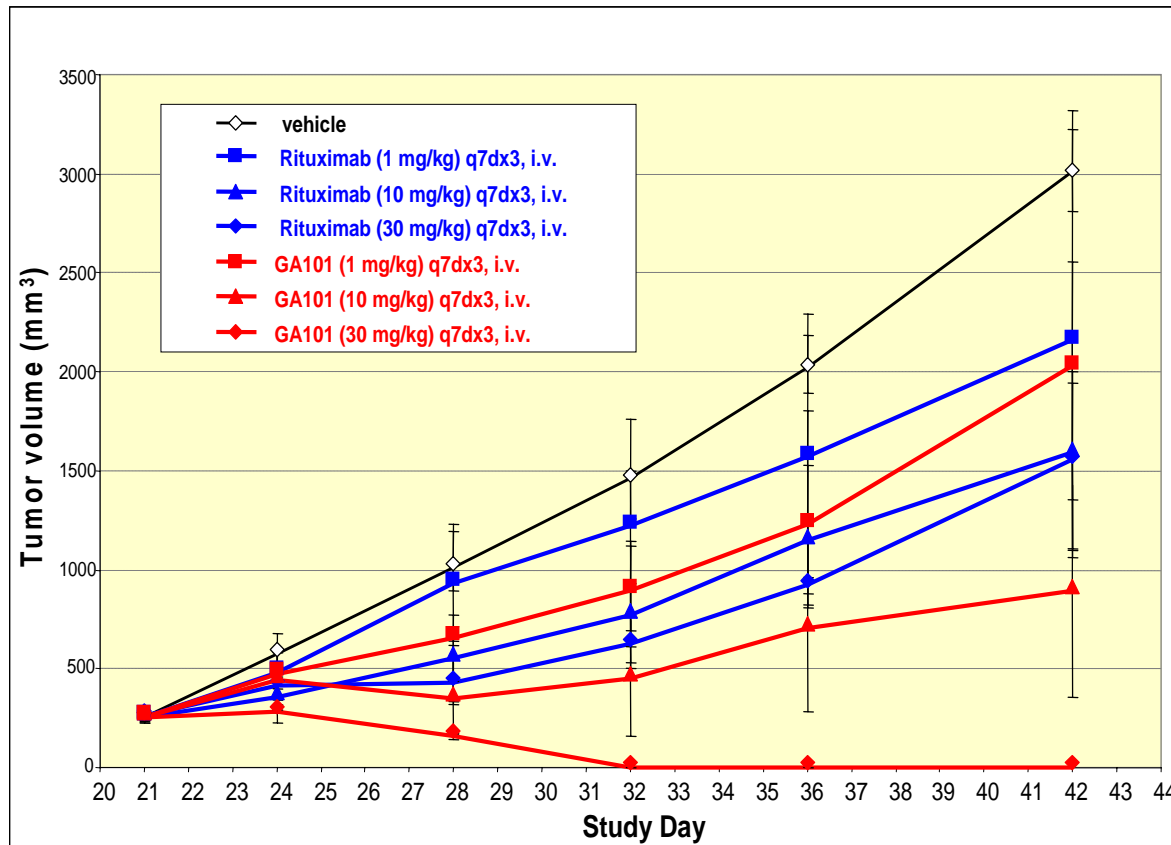


**B-cell depletion Whole blood Assay (24h)**  
**B-CLL Patient Blood**



- Superior B-cell depletion of normal and malignant B-cells relative to Rituximab

# Superior efficacy & complete tumor remission in aggressive s.c. SU-DHL-4 DLBCL xenograft model



Treatment with GA101 (1, 10, 30 mg/kg, 3x, q7dx4, i.v.) resulted in dose-related **superior** efficacy in terms of tumor growth inhibition and complete tumor remission compared to Rituximab

# GA101: A differentiated 3rd generation CD20 MAb

- **Fully humanized MAb recognizing a CD20 type II epitope**
- **Superior ADCC & superior direct cell death induction**
- **Reduced CDC**
- **Superior B-cell depletion in whole blood assay**
- **Superior efficacy in various NHL xenograft models (incl. DLBCL, MCL, FL)**
- **Superior efficacy for tissue B-cell depletion in Cynomolgus monkeys and huCD20 tg mice**
- **Currently in Phase I trials**

