The current study shows mechanisms of IGM-55.5 binding to the surface of Nalm-6 cells (control), Nalm-7 cells (control), Nalm-6 or -6 D cells (control), and Splenic B cells treated with HuMab 216 for 15 minutes lead to pore formation (SEM). White arrows indicate observable pores.

**CDIM Expression on Human Hematologic Cell Lines**

**Background: CDIM & IGM-55.5**

- **HuMab 216** is a human natural antibody isolated from patient.
- HuMab 216 recognizes a linear asparagine epitope structurally similar to the Y* neonatal blood group antigen, CDIM.
- HuMab 216 is poly-reactive.
- Functionally, HuMab 216 binds and kills patient-derived malignant B cells, normal human B cells, and murine B cell lines, and extended overall survival in an acute lymphoblastic leukemia model.
- HuMab 216 was tested in a Phase I clinical trial with an excellent safety profile and functional capacity to ablate leukemic blasts in ALL.
- IGM-55.5 was engineered to have similar antigen specificity and restricted polyreactivity.
- IGM-55.5 has improved preclinical potency.
- The current study shows mechanisms of action of IGM-55.5 and demonstrates its efficacy on human B cell lines in vitro, in xenograft mouse models, and in normal human and patient-derived samples.

**IGM-55.5, a novel monoclonal human recombinant IgM antibody with potent activity against B cell leukemia and lymphoma**

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**Abstract**

IGM-55.5 is an engineered monoclonal human recombinant IgM antibody that was derived from a natural monoclonal antibody 216 isolated at Stanford University from the supernatant of a patient with Non-Hodgkin’s lymphoma. HuMab 216 was previously used in a B cell leukemia and lymphoma Phase I trial and was demonstrated to be well tolerated with significant decrease in peripheral blood blasts observed (Liebler et al. Haematologica, 2012). IGM-55.5 has been engineered to be non-reactive in recognition of a carbohydrate determinant as an epitope on normal human B cells as well as B cell lymphomas and B progenitor lymphoblastoid lines.

Here, we report new preclinical studies that describe the mechanism of action and patient activity of IGM-55.5. In vitro analysis of IGM-55.5 was found to have high surface binding on a broad panel of B cell leukemias and lymphoma cell lines by flow cytometry. IGM-55.5 binding leads to the disruption of the plasma membrane and formation of large membrane pores resulting in cell death. This non-classical apoptosis occurs in the absence of complement fixation but in vitro cytotoxicity is increased in assays in the presence of human complement. Studies with expression depleted tumor xenograft models (Namalwa, Granta, and Nalm-D) demonstrated that IGM-55.5 bound to Namalwa cells, normal human B cells, and human and murine B cell lines, and reduced B cell viability as determined by flow cytometry (propidium iodide staining & normalization; n=4 normal healthy donors shown.)

**CDIM-55.5 mediated CDC on Tumor Cell Lines**

**Summary**

- IGM-55.5 5k cells by at least two mechanisms, pore formation and complement dependent cytotoxicity.
- IGM-55.5 binds and kills B cell lines in vitro and in vivo models.
- IGM-55.5 5k cells and B cells from normal and patient donors.

**References**


**Figure Legends**

**A) HuMab 216 & B) IGM-55.5 bind to the surface of Nalm-6 cells (Control), Nalm-6 D cells (Control), Nalm-7 cells (Control) and Splenic B cells treated with HuMab 216 for 15 minutes lead to pore formation (SEM). White arrows indicate observable pores.**

**CDIM-55.5 Purified B cells treatment with IGM-55.5 for 24 hours in the absence of complement leads to reduced B cell viability as determined by flow cytometry (propidium iodide staining & normalization; n>4 normal healthy donors shown).**

**Background: CDIM & IGM-55.5**

- **HuMab 216** is based on natural human antibody isolated from patient.
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