A novel monoclonal antibody enhances phagocytosis and killing of *Mycobacterium tuberculosis* in macrophage cells

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Introduction

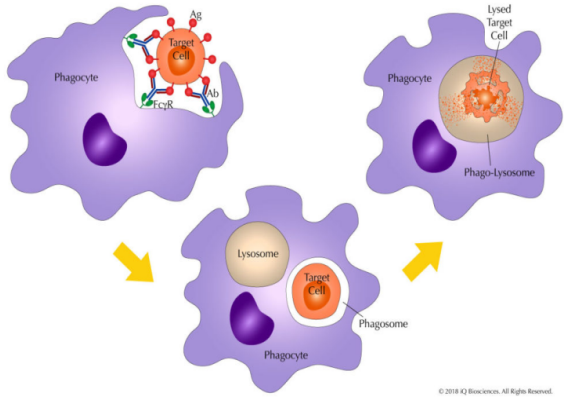
- Host-directed therapies in addition to or following anti-TB chemotherapy are increasingly being explored as an approach for enhancing treatment outcomes.
- Two novel MABs of the IgA and IgG classes have previously been shown to possess immunotherapeutic properties against *M. tuberculosis in vitro*, being reactive, not only with epitopes present on live and killed *M. tuberculosis,* but also on *M. smegmatis* (Balu *et al*. 2011; Welch *et al*. 2012).
- We evaluated a novel IgG mAb (JG7), selected from a broad panel of novel mAbs investigated earlier for binding activity to *M. smegmatis* and killed *M. tuberculosis,* to begin our studies in live *M. tuberculosis*.

Aim

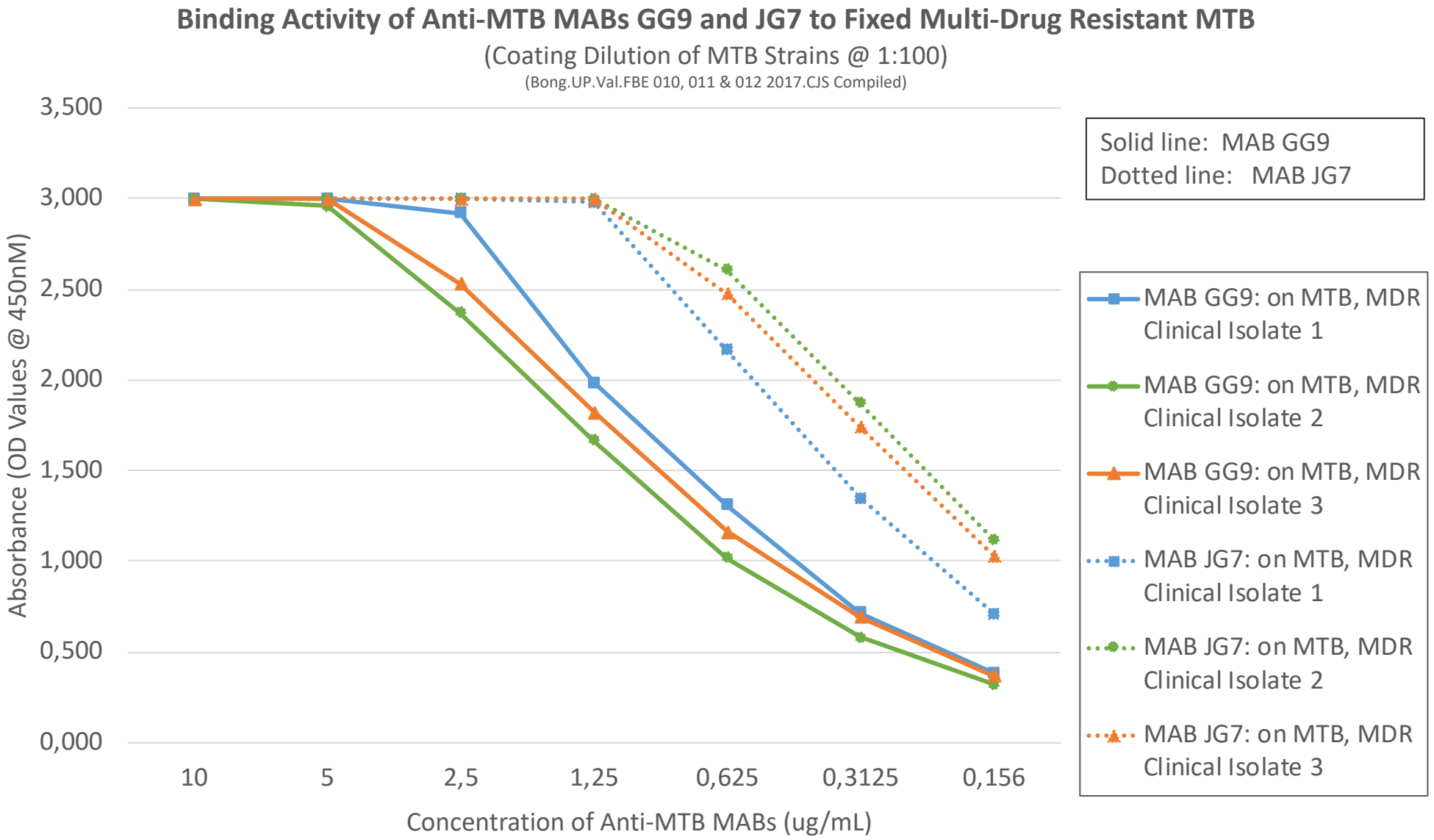
- To demonstrate the **binding activity** of novel anti-TB mAb, JG7, to live *Mycobacterium tuberculosis* (susceptible and resistant strains)
- To evaluate the functional capacity of JG7 to **enhance opsonic phagocytic killing activity** (OPKA) of live *M. tuberculosis* using macrophage cells (U-937)

Methods

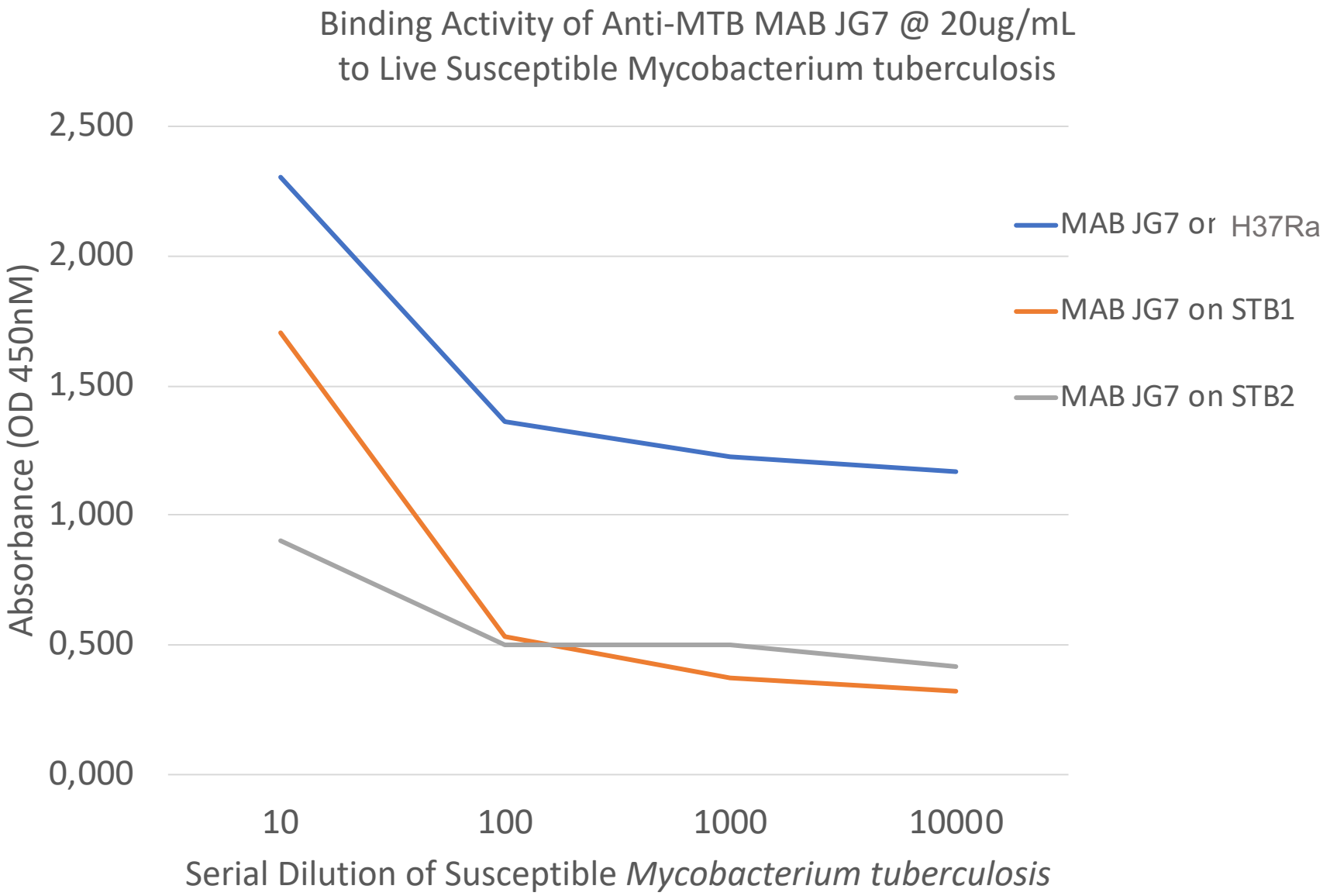
- Binding experiments
  - JG7 and GG9 analysed in alcohol-fixed-bacteria ELISA
  - JG7 + *M. tuberculosis* at mid-log growth phase for live-bacteria ELISA
  - 1 hour incubation, washing, secondary detection Ab, substrate
  - Absorbance determined at 450 nm
- Macrophage OPK *in vitro assay*
  - U-937 cells, differentiated for 72 or 96 hours
  - JG7 + *M. tuberculosis* at mid-log growth phase
  - 4 hour incubation, lysis of cells, plating on 7H10/7H11 agar
  - Plates read for CFU count 4-8 weeks later



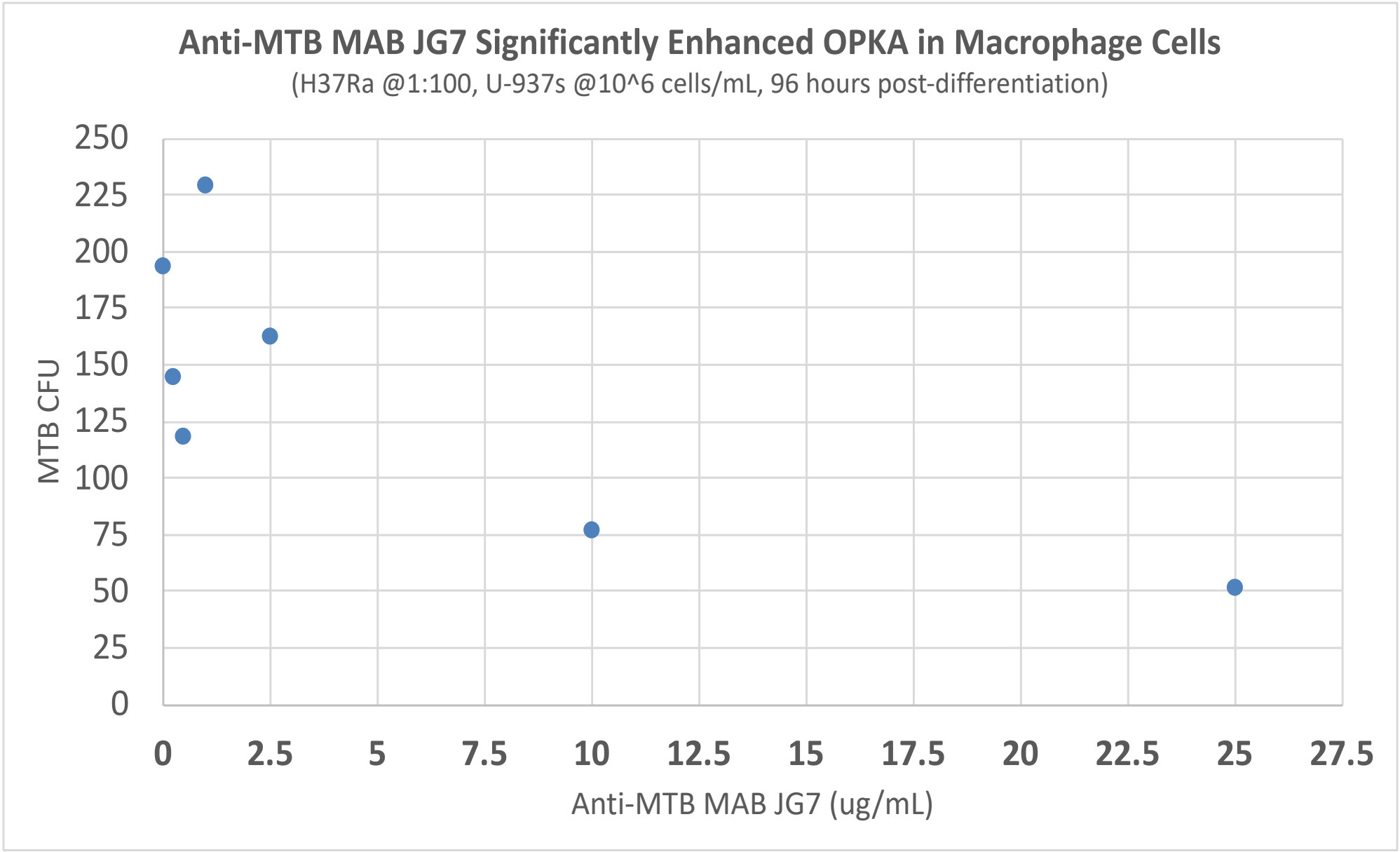
Fixed-bacteria ELISA results



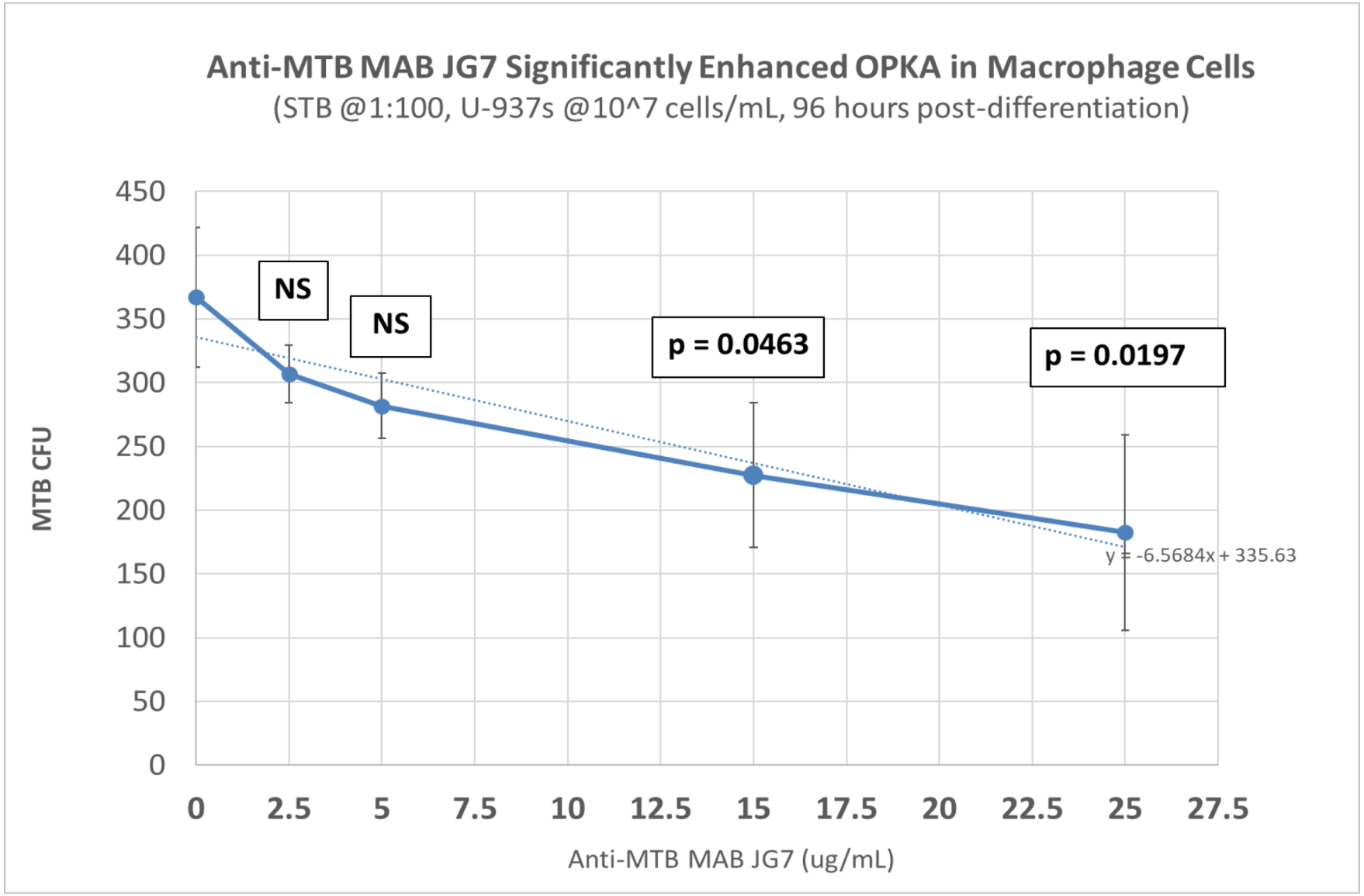
Live-bacteria ELISA results



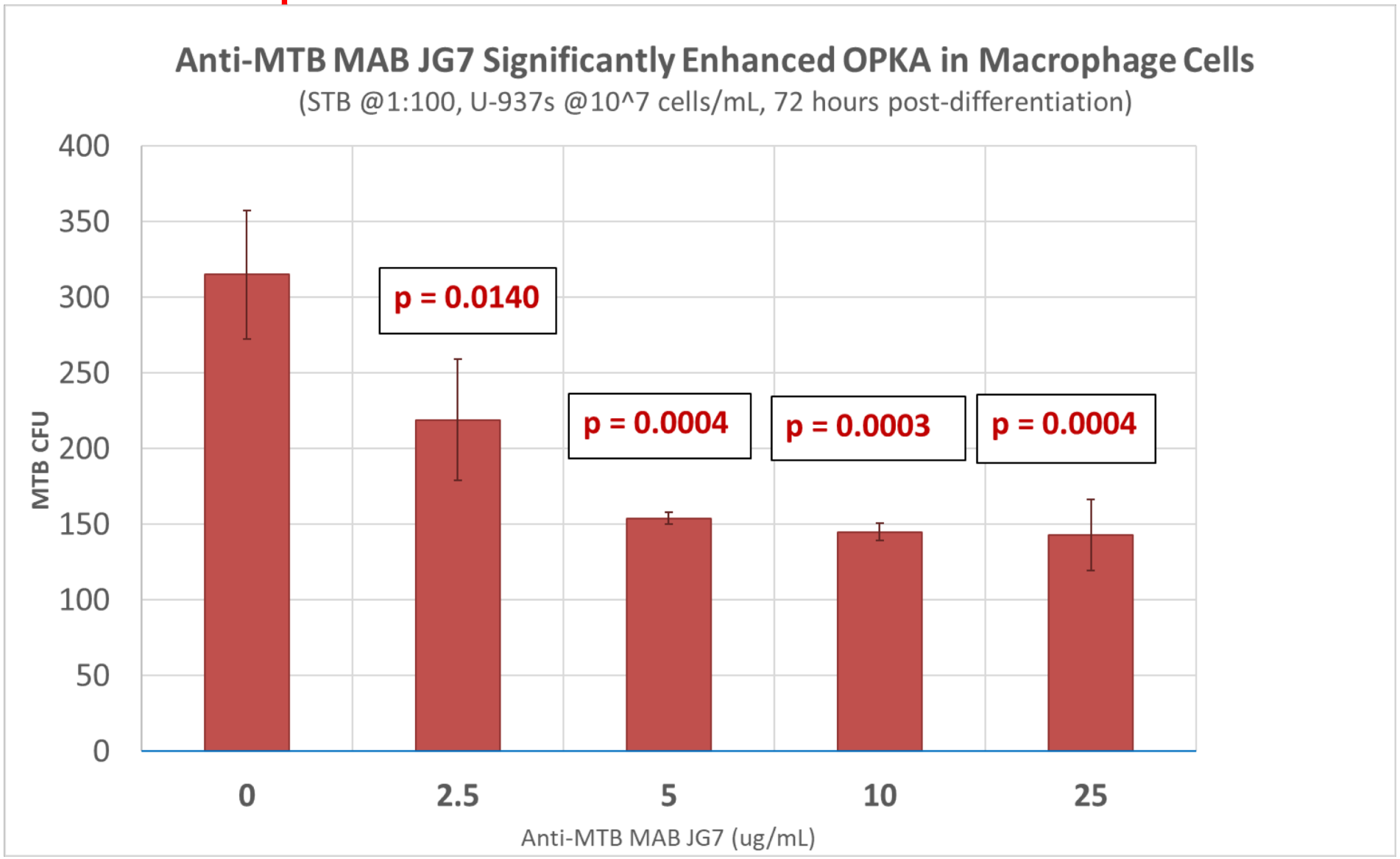
OPKA results: Strain H37Ra



OPKA results 96 hrs post-differentiation: Susceptible *M. tuberculosis* clinical isolate



OPKA results 72 hrs post-differentiation: Susceptible *M. tuberculosis* clinical isolate



Conclusions

- mAb JG7 binds to both sensitive and MDR *M. tuberculosis* strains
- JG7 enhances OPKA in macrophages
- Macrophage cells appeared optimal at 72 hours, post-differentiation
- Both binding and killing data suggest that opsonic mAbs, directed against *M. tuberculosis*, may be valuable for adjunctive treatment of TB, likely including MDR-TB

Ongoing studies

- Completing binding studies in resistant TB (MDR/XDR), including JG7 and an additional promising mAb currently under evaluation (GG9)
- OPKA against *M. tuberculosis* in granulocytes
- Cytokine response studies using both macrophages and granulocytes

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