

CTP Synthase 1 (CTPS1) is a Potential New Therapeutic Target in Graft versus Host Disease

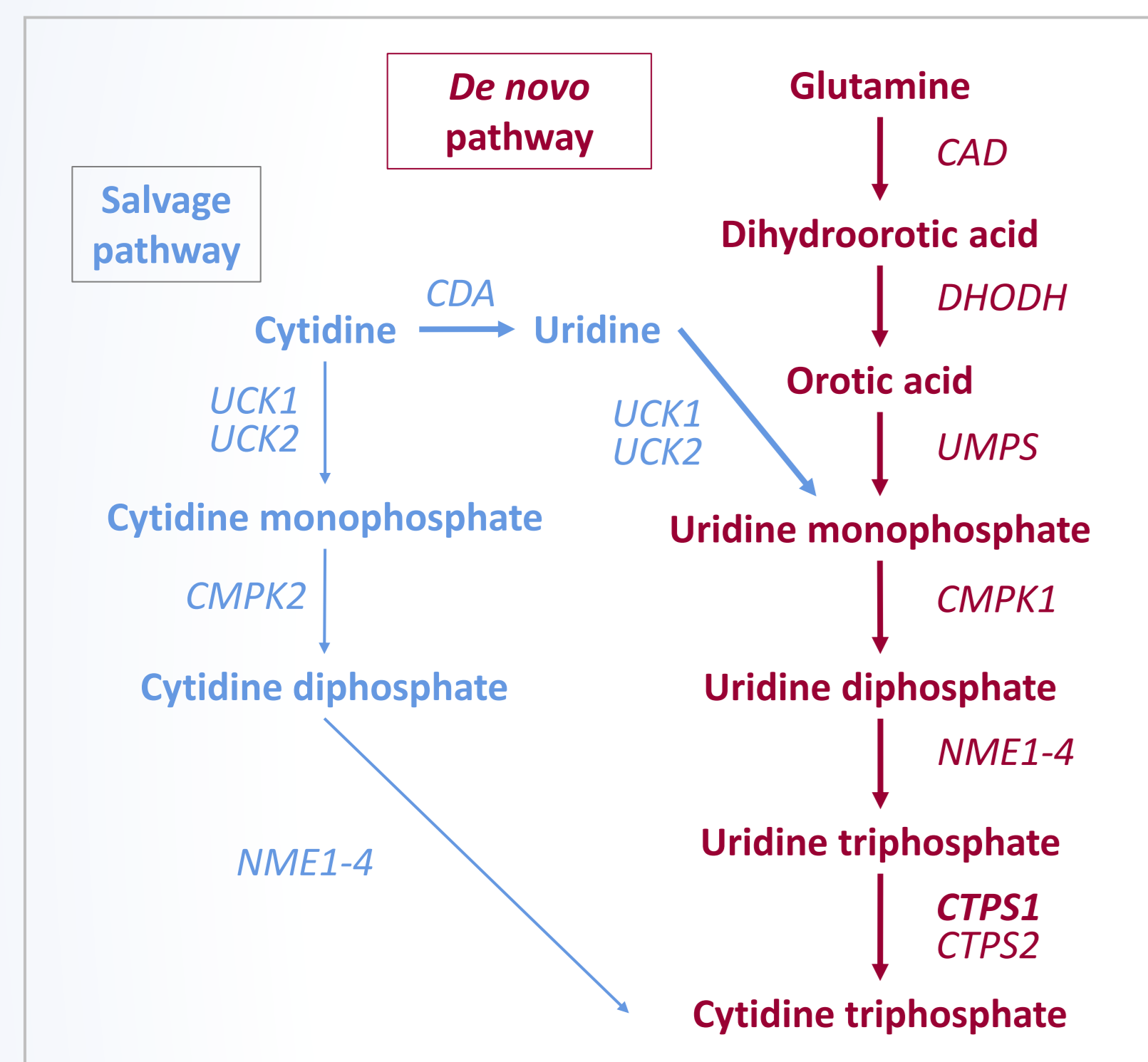
P1308

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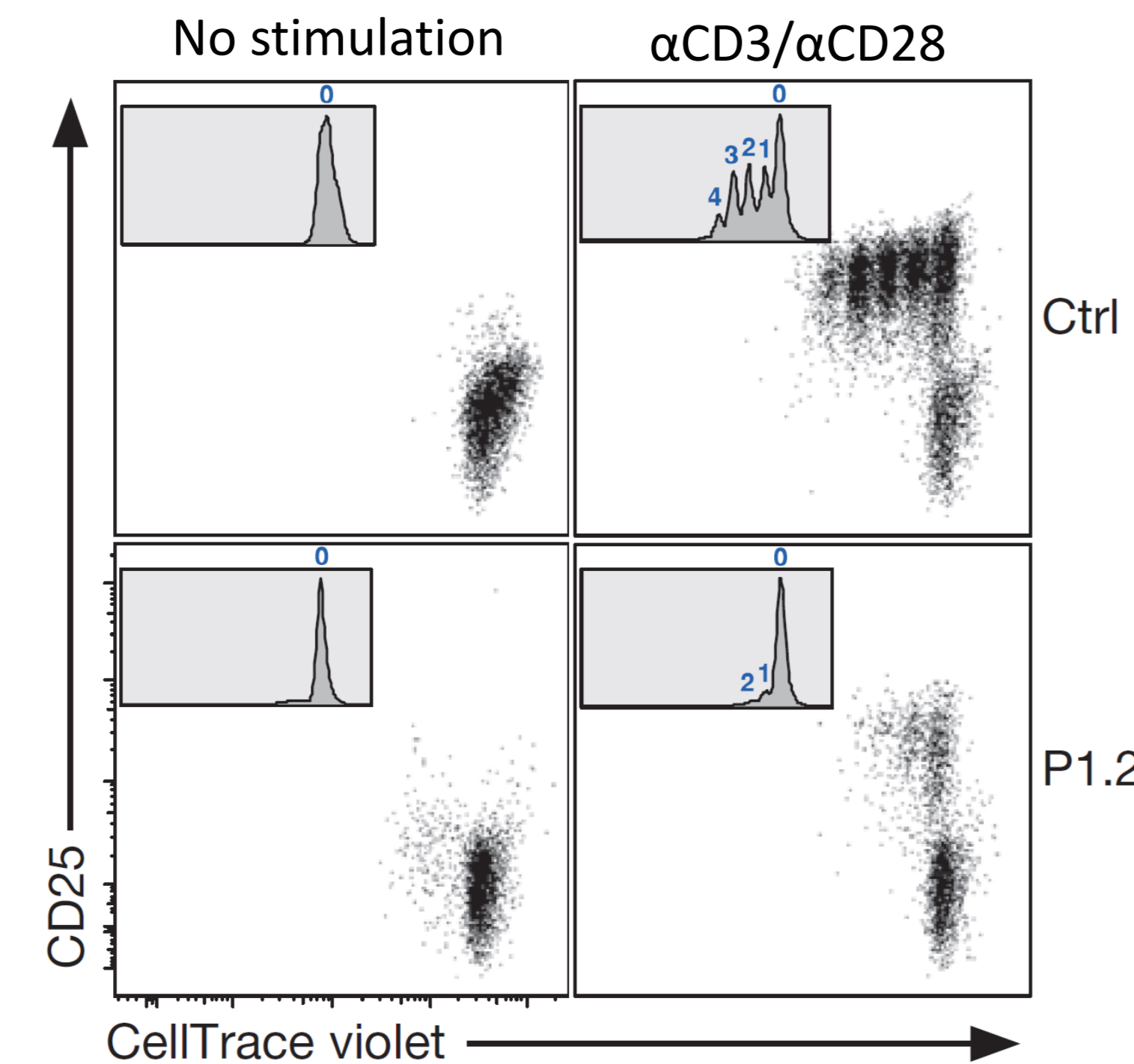
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CTPS1 is required for the proliferation of activated T and B cells

Pyrimidine synthesis pathway:



Inherited CTPS1 deficiency:

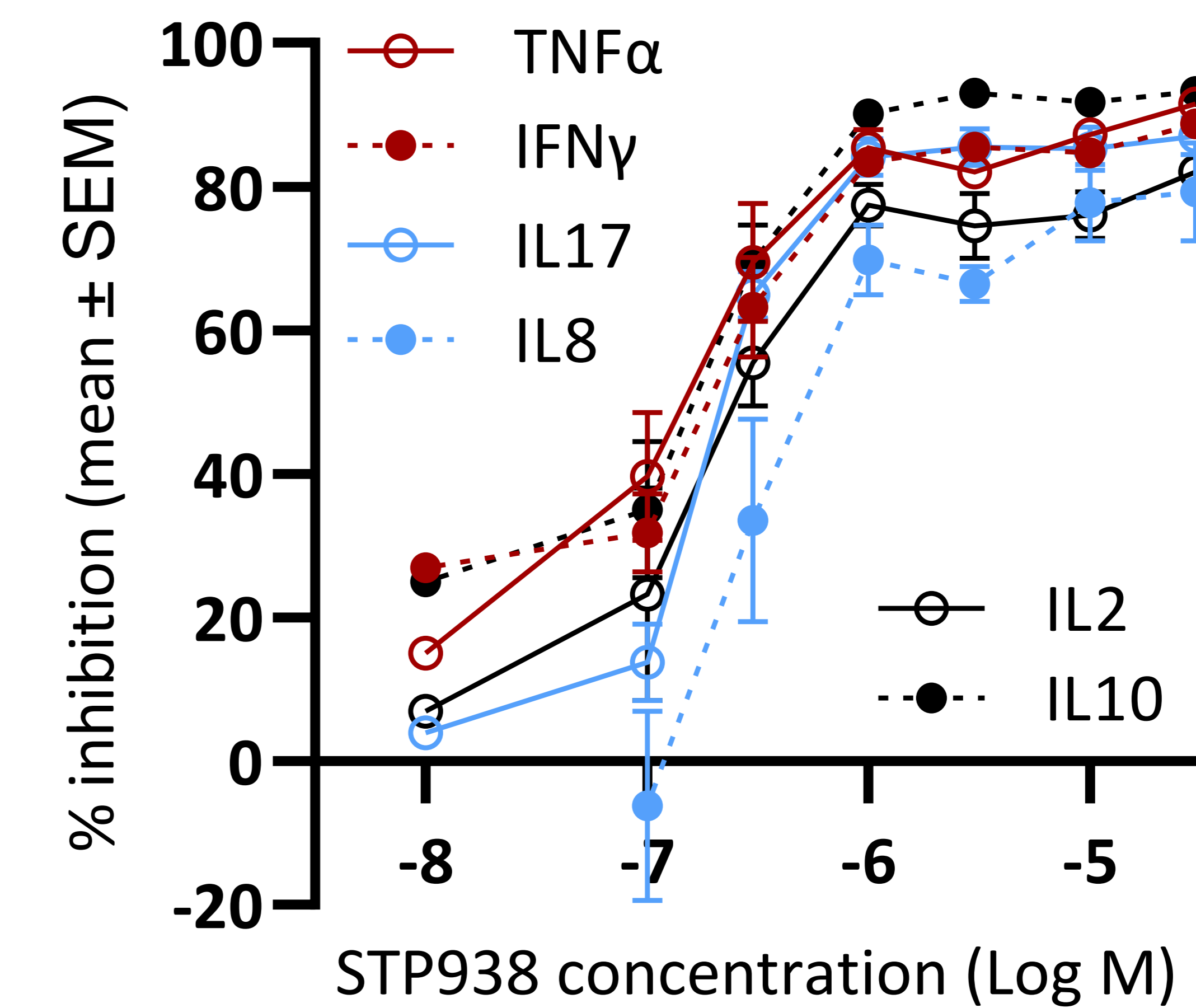


Nature. 2014 Jun 12;510(7504):288-92

Summary & Conclusions

- STP938 is a **potent and highly selective** small molecule inhibitor of **CTPS1**
- STP938 inhibits **T cell proliferation**
- STP938 inhibits **cytokine release** from stimulated T cells
- STP938 shows favourable preclinical **safety and drug-like properties**
- STP938 will enter **clinical development** as an **oral drug** for lymphoma late 2022

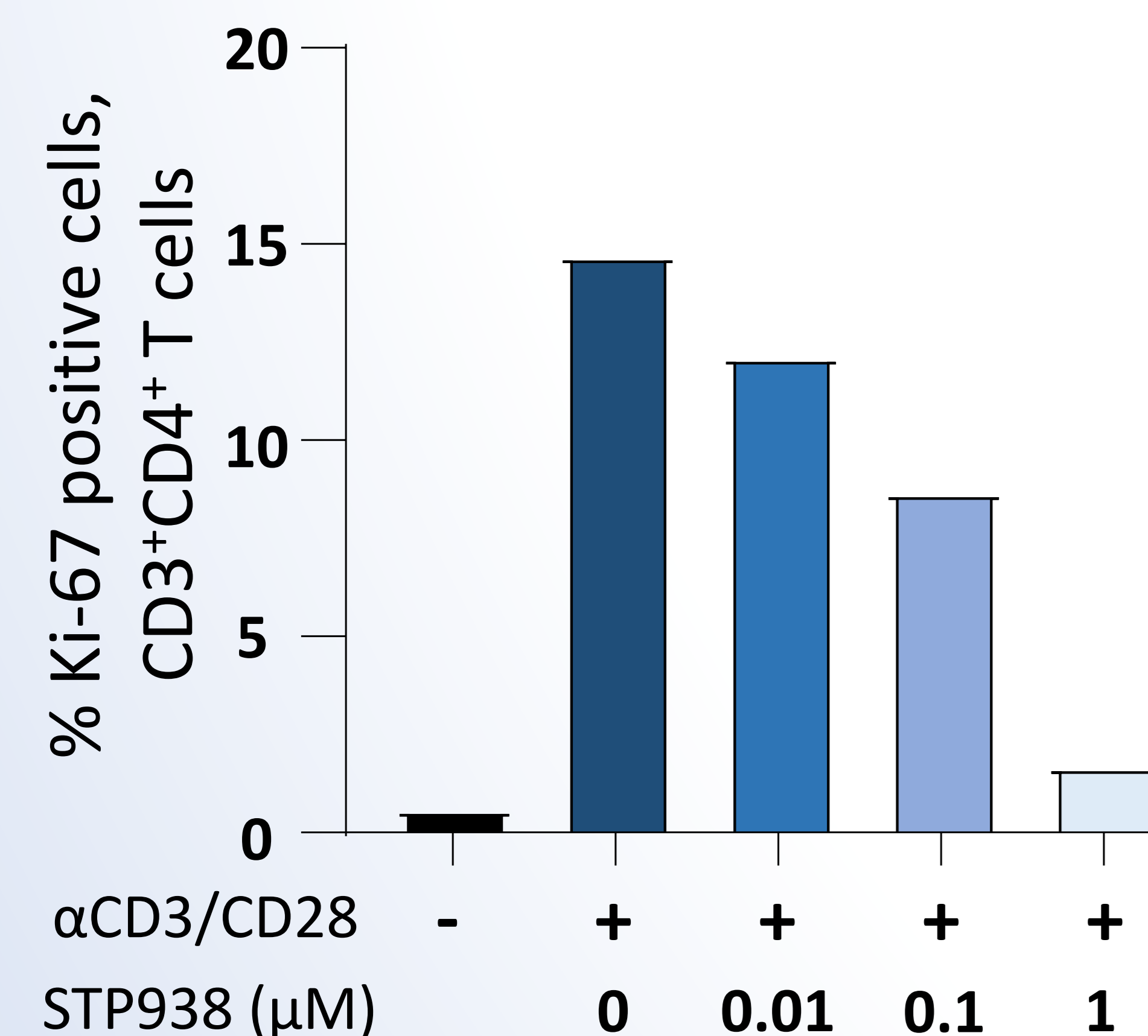
STP938 inhibits T cell cytokine release



- Whole blood, 10 normal donors, CD3/CD28 stimulation, 48 hr incubation
- Concentration dependent inhibition of cytokine release
- Highest concentrations of STP938 produce near-complete suppression of cytokines at STP938 levels achievable in humans

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STP938, a potent and selective CTPS1 inhibitor, blocks T cell proliferation



- Whole blood, representative donor from four studied, CD3/CD28 stimulation, 48 hr incubation
- Concentration dependent inhibition of Ki-67 expression also observed with CD8⁺ T cells
- Inhibition of proliferation also demonstrated by ³H-thymidine incorporation studies

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Other STP938 posters at EHA

P1248: STP938 is a novel target in T cell malignancy, showing cytotoxic activity *in vitro* and inhibiting neoplastic T cell growth *in vivo*.

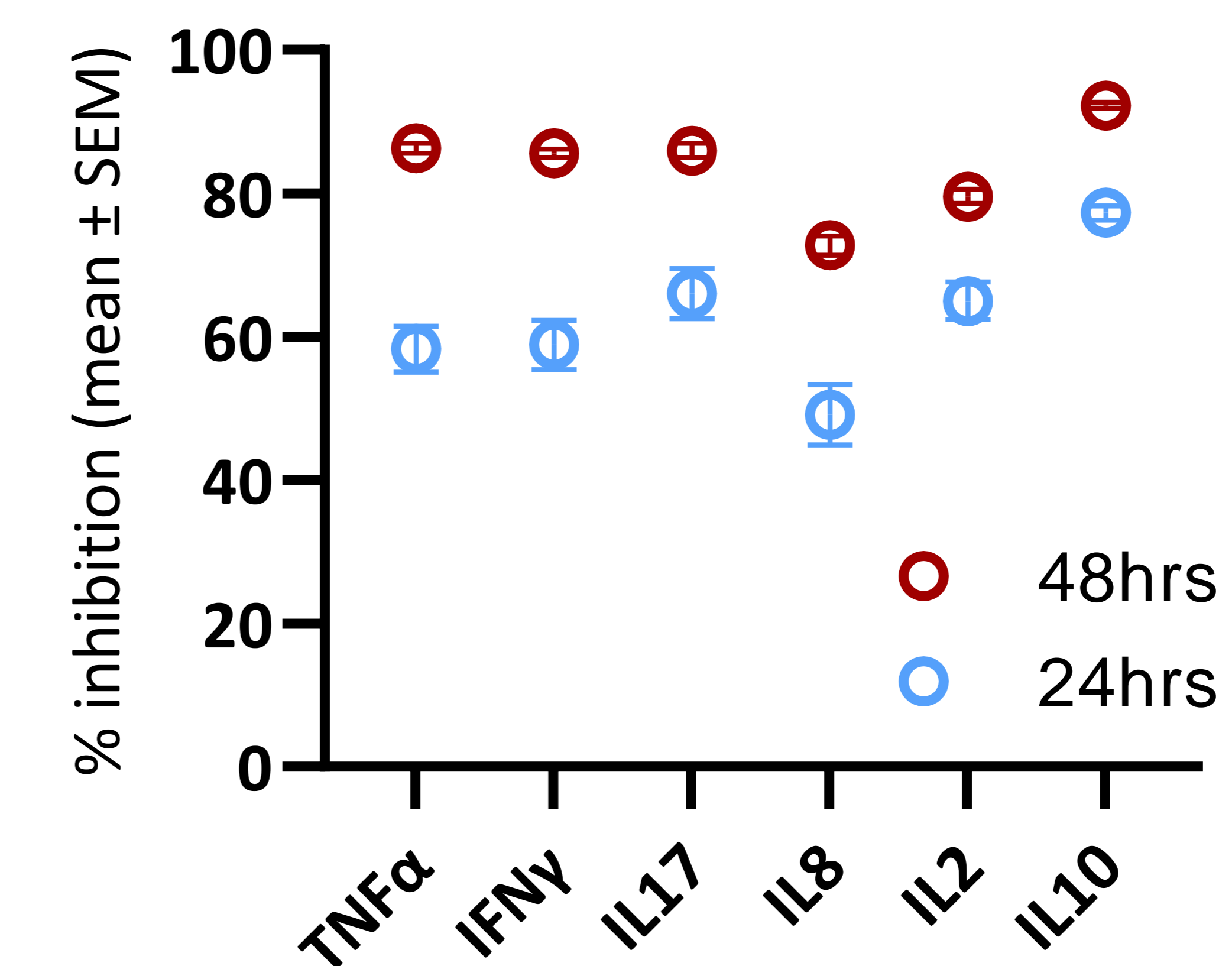
P864: STP938 shows single agent efficacy and synergy with ATR inhibition in multiple myeloma.

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Poster download:



Cytokine suppression by STP938 is independent of cell division



- Whole blood, 7-10 normal donors, CD3/CD28 stimulation, 1 μM STP938
- Partial inhibition of cytokine release at 24 hrs, prior to earliest cell division which occurs after 40 hrs in this system

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