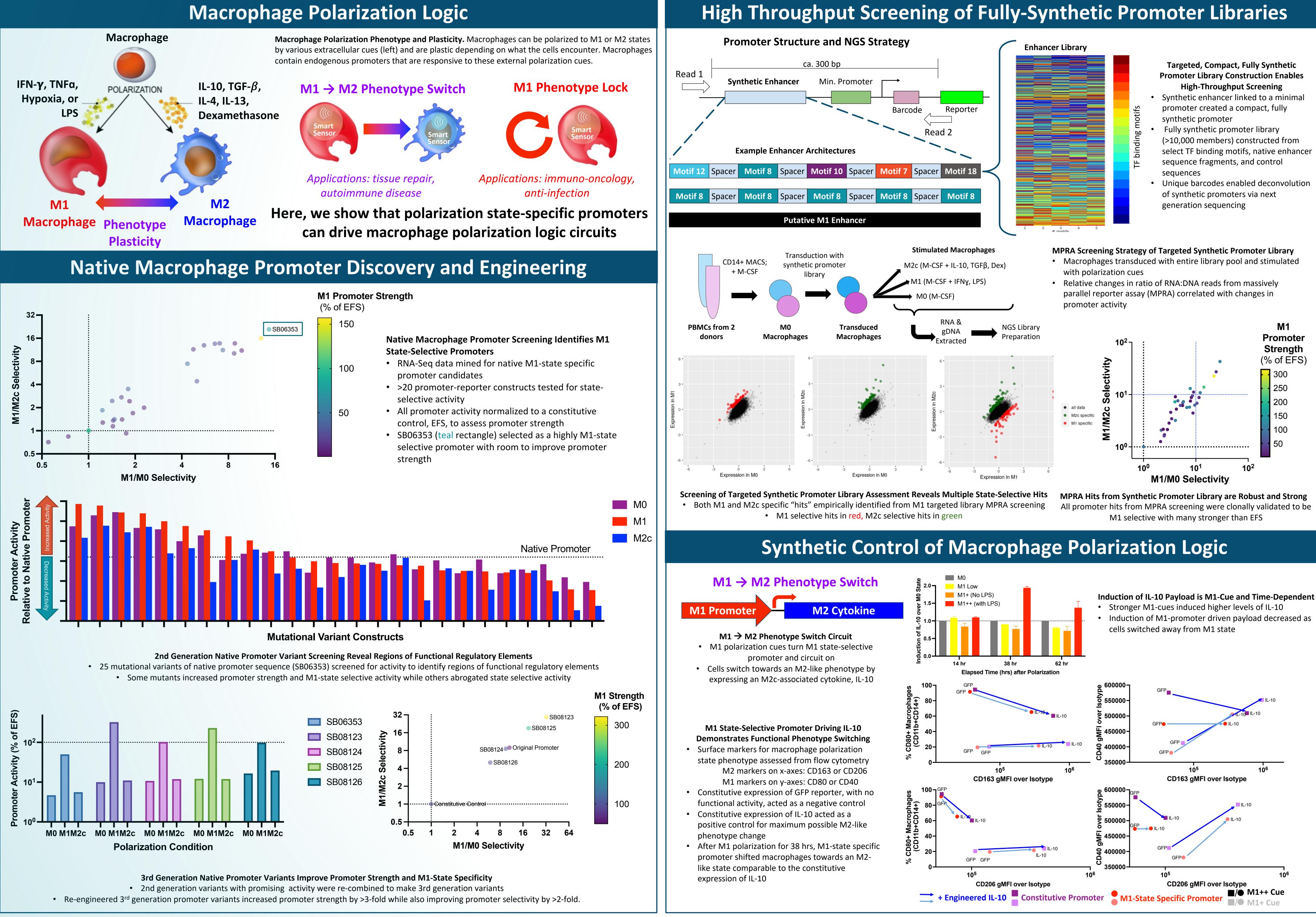
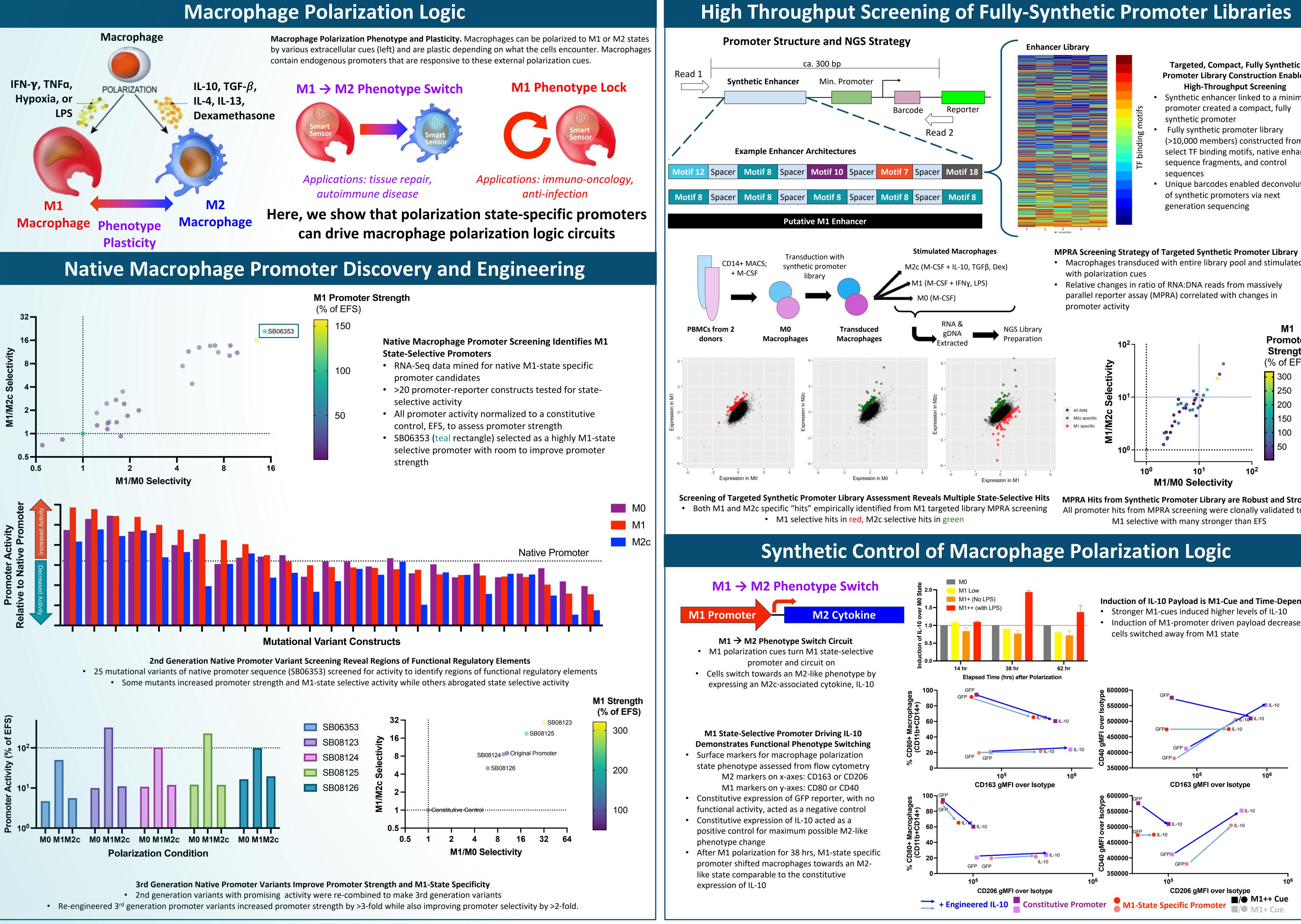


Designing Cell-State-Specific Synthetic Promoters as Smart Sensors to Control Macrophage Polarization

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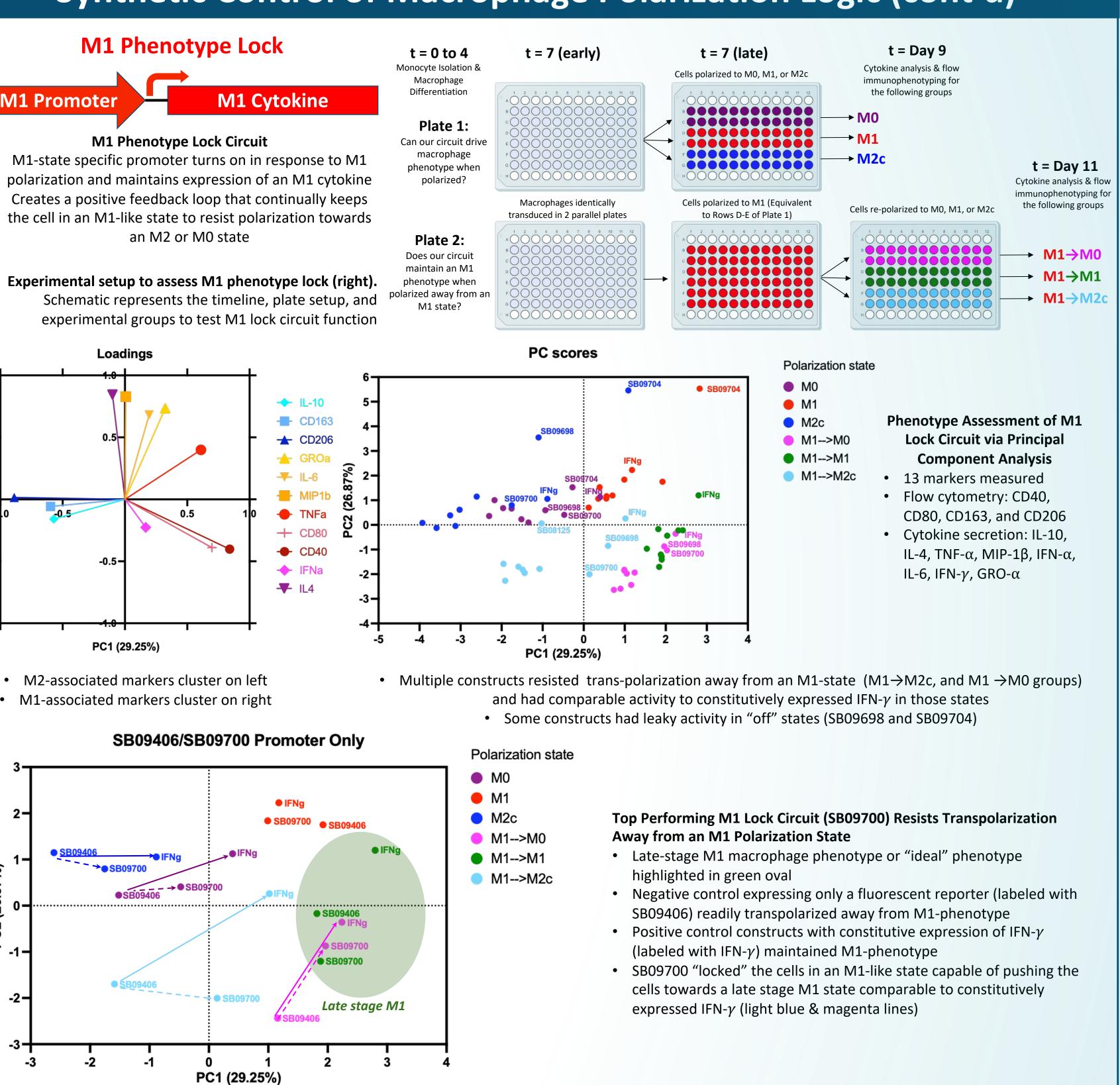
¹Senti Biosciences, Inc. South San Francisco, CA ²BlueRock Therapeutics LP

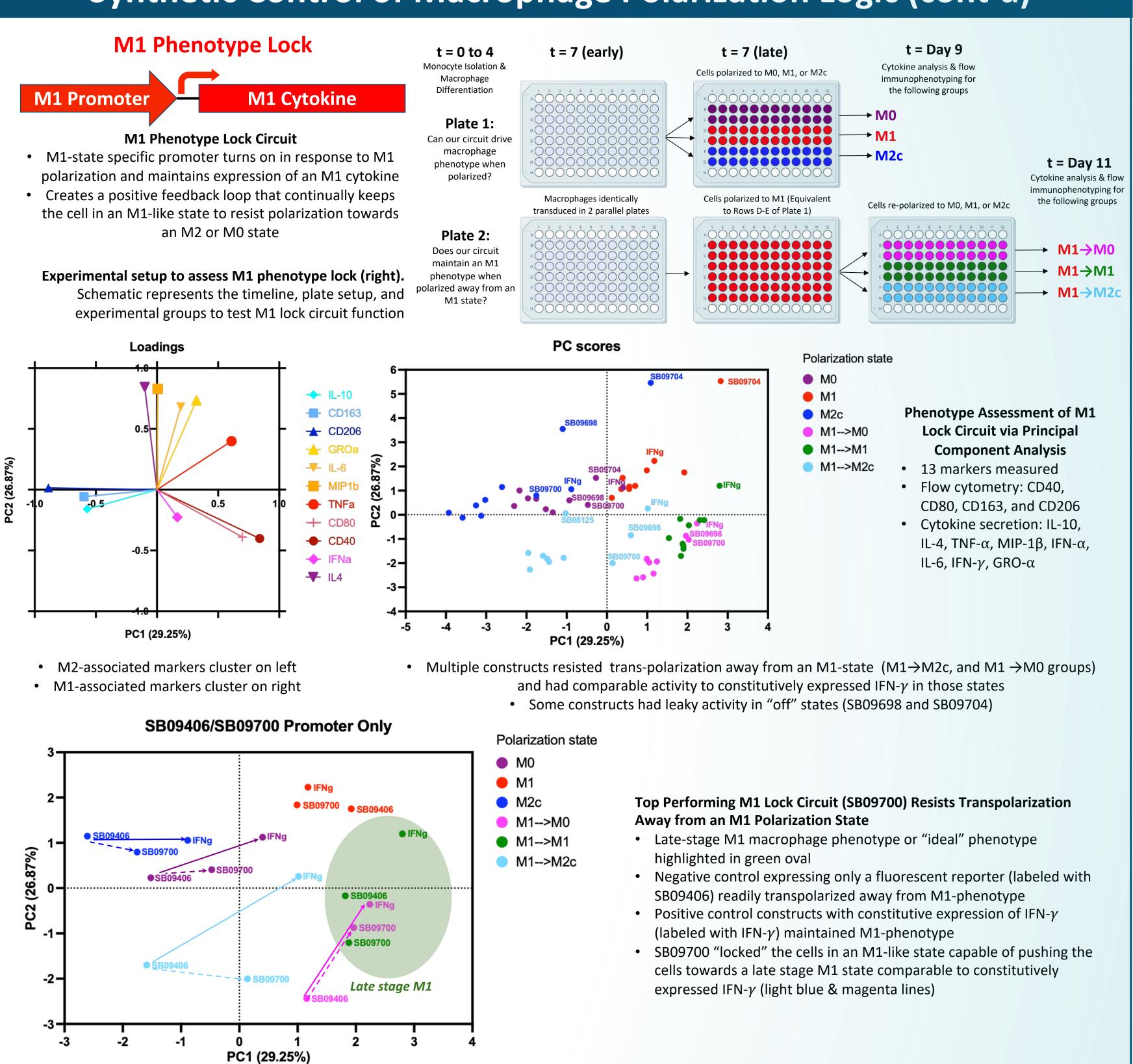
MPRA Hits from Synthetic Promoter Library are Robust and Strong All promoter hits from MPRA screening were clonally validated to be

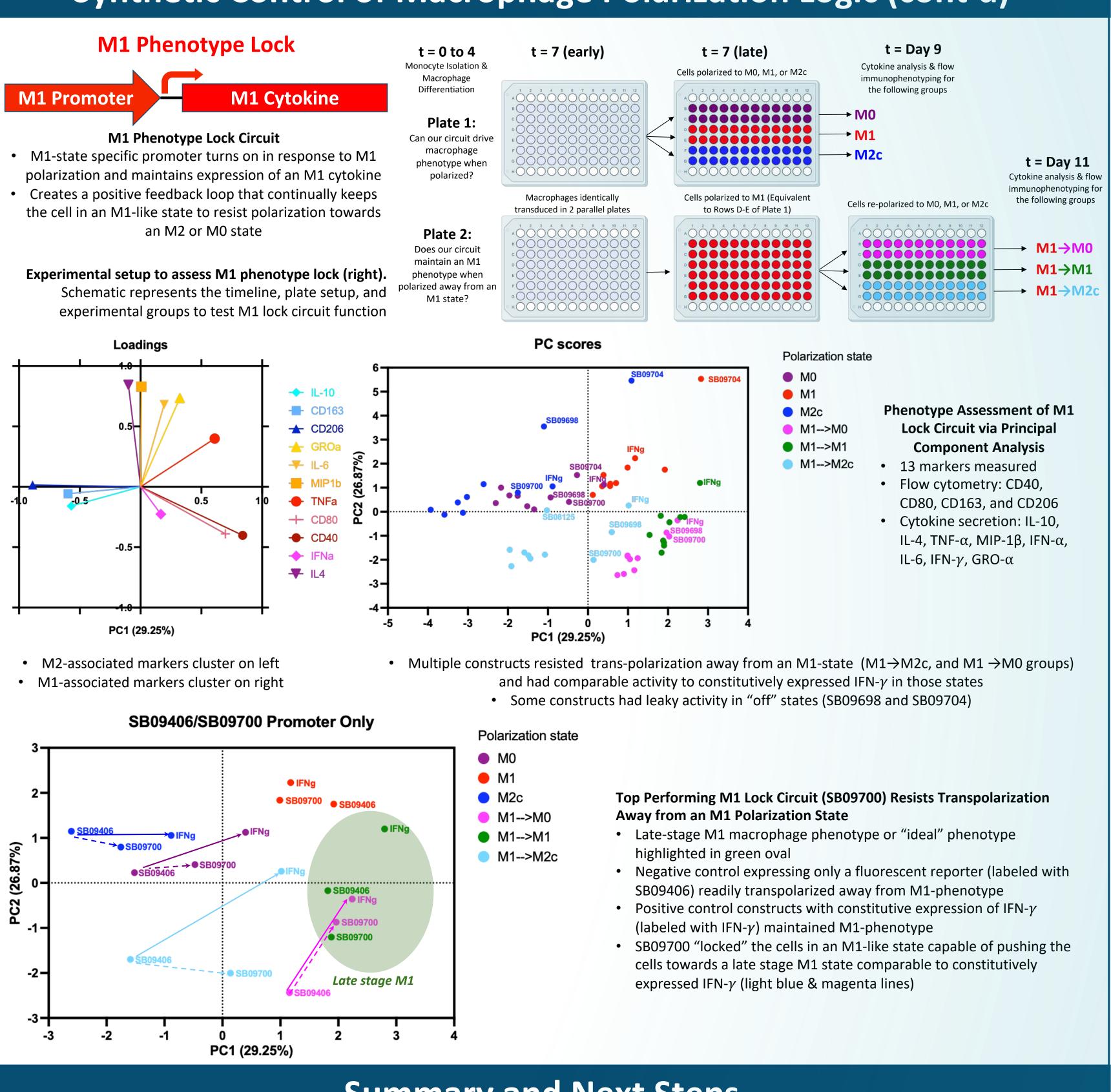
New York, NY

- Targeted, Compact, Fully Synthetic Promoter Library Construction Enables
- Synthetic enhancer linked to a minimal
- (>10,000 members) constructed from select TF binding motifs, native enhancer
- Unique barcodes enabled deconvolution

Synthetic Control of Macrophage Polarization Logic (cont'd)







- of macrophage cell state

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Summary and Next Steps

Native M1 state-specific macrophage promoters were discovered and can be rationally reengineered to improve promoter strength and M1 state-specific activity

• Fully synthetic state-specific promoter libraries were bioinformatically designed for highthroughput MPRA screening (>10⁴ variants per screen)

Re-engineering of natural promoters and high throughput screening of synthetic promoters both yielded strong and selective Smart Sensors

State-specific promoters can be built into Smart Sensor circuits to control macrophage polarization logic (e.g. Phenotype "Switch" or Phenotype "Lock" circuits)

Next step: Generation of alternative state-specific promoters that are highly selective for additional macrophage states and therapeutically relevant environmental cues

Next step: Optimize pairs of engineered promoters and payloads for enhanced dynamic control