

Systemic Immune Modulation Alters Local Bone Regeneration in a Delayed Treatment Composite Model of Non-Union Extremity Trauma

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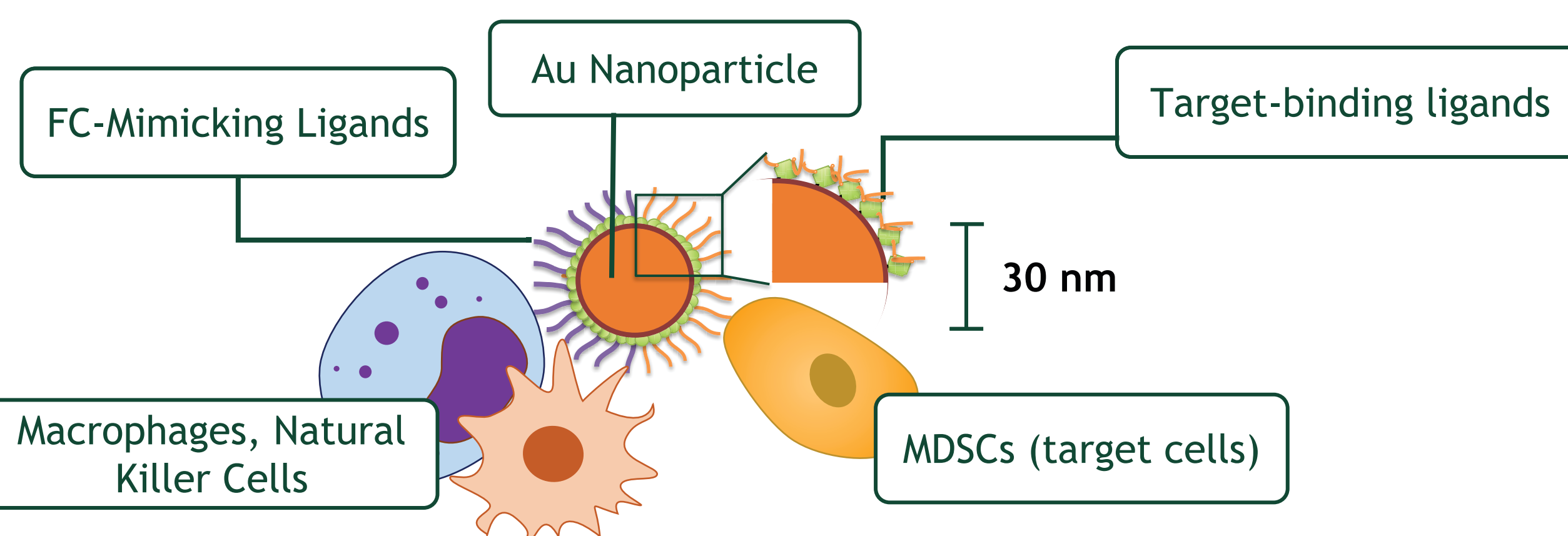
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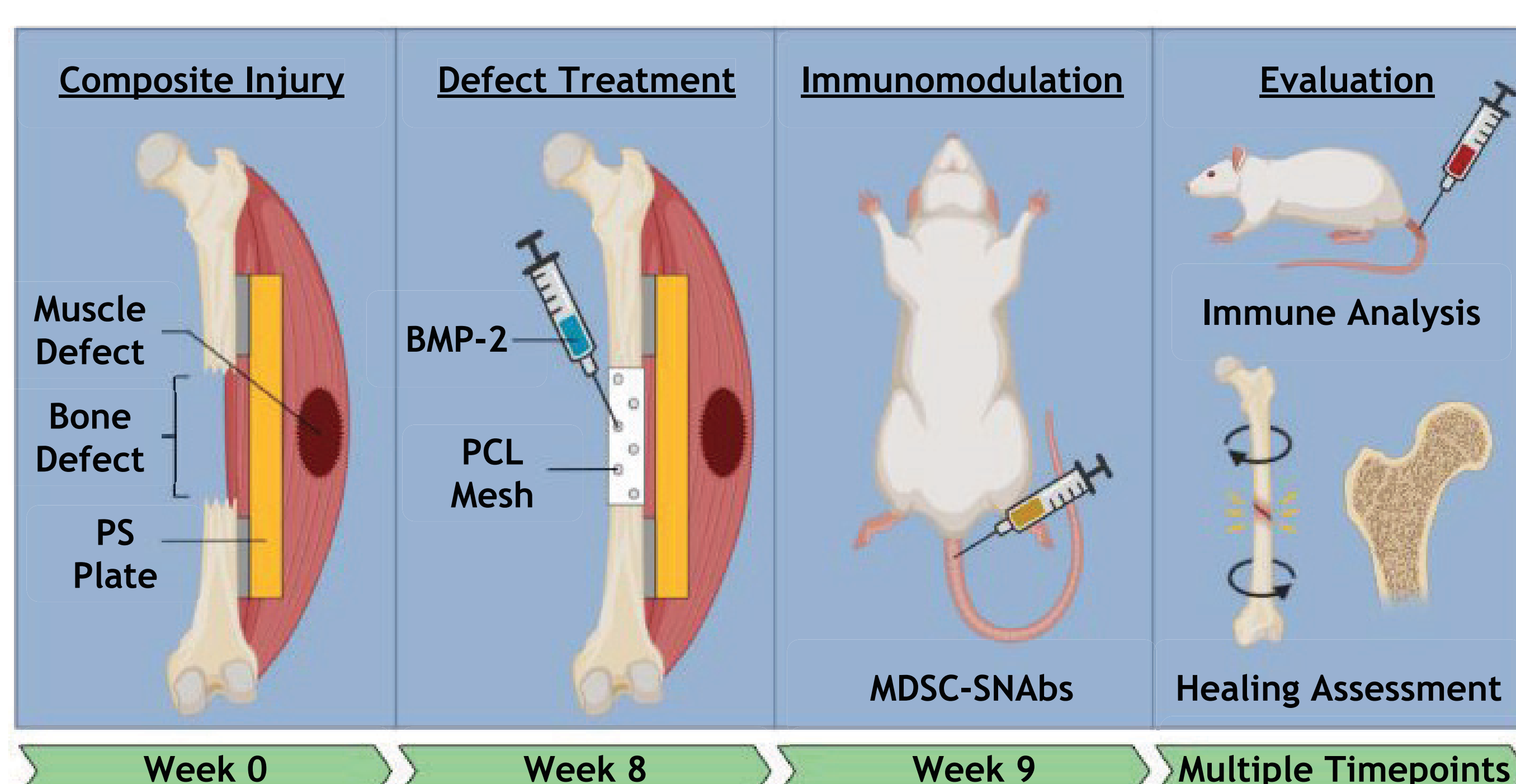
BACKGROUND AND APPROACH

Severe musculoskeletal trauma is exceedingly common and frequently presents challenging clinical scenarios such as bone non-unions and infections. Chronic immunosuppression after trauma has previously been linked to poor outcomes. Most notably, systemic myeloid-derived suppressor cells (MDSCs), which expand rapidly after trauma and suppress other immune cells, have been directly correlated to impaired bone regeneration.¹ In this study, we aimed to deplete MDSCs after trauma using Synthetic Nanoparticle Antibodies (SNABs), a therapeutic platform consisting of gold janus nanospheres that mimic the structure and function of antibodies to deplete a cellular target.² Here, rats being treated for musculoskeletal trauma were arterially injected with SNABs targeting S100A8/A9, a protein expressed by MDSCs. Blood immune cells were evaluated at multiple timepoints via flow cytometry, and healing was assessed by micro-CT imaging and torsional testing of regenerated bones. **We hypothesized that treatment with SNABs would deplete blood MDSCs and improve bone healing.**

Synthetic Nanoparticles for MDSC Depletion

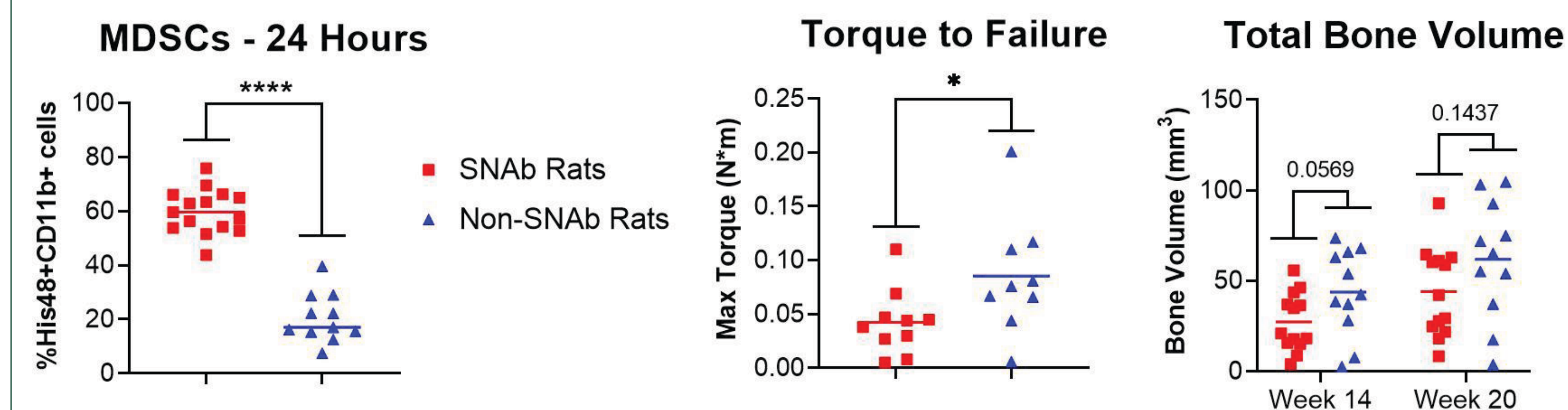


METHODS

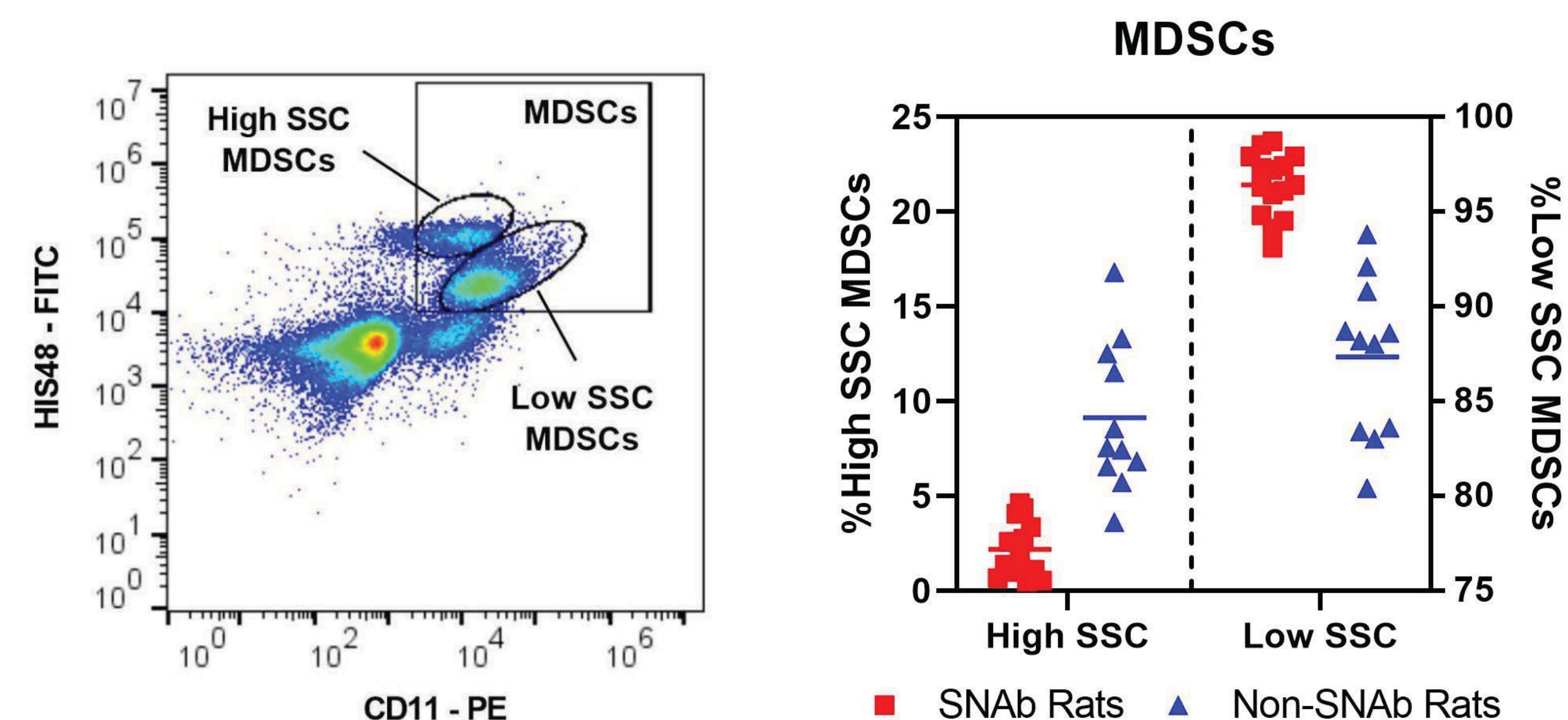


- 1 Unexpectedly, treatment with SNABs resulted in an increase in total blood MDSCs and worse bone healing.
- 2 Closer examination revealed that a high sidescatter sub-population of MDSCs was depleted, while a low sidescatter sub-population expanded.
- 3 MDSC sub-populations exhibit differential expression of the target protein S100A8/A9, possibly explaining their variable depletion.

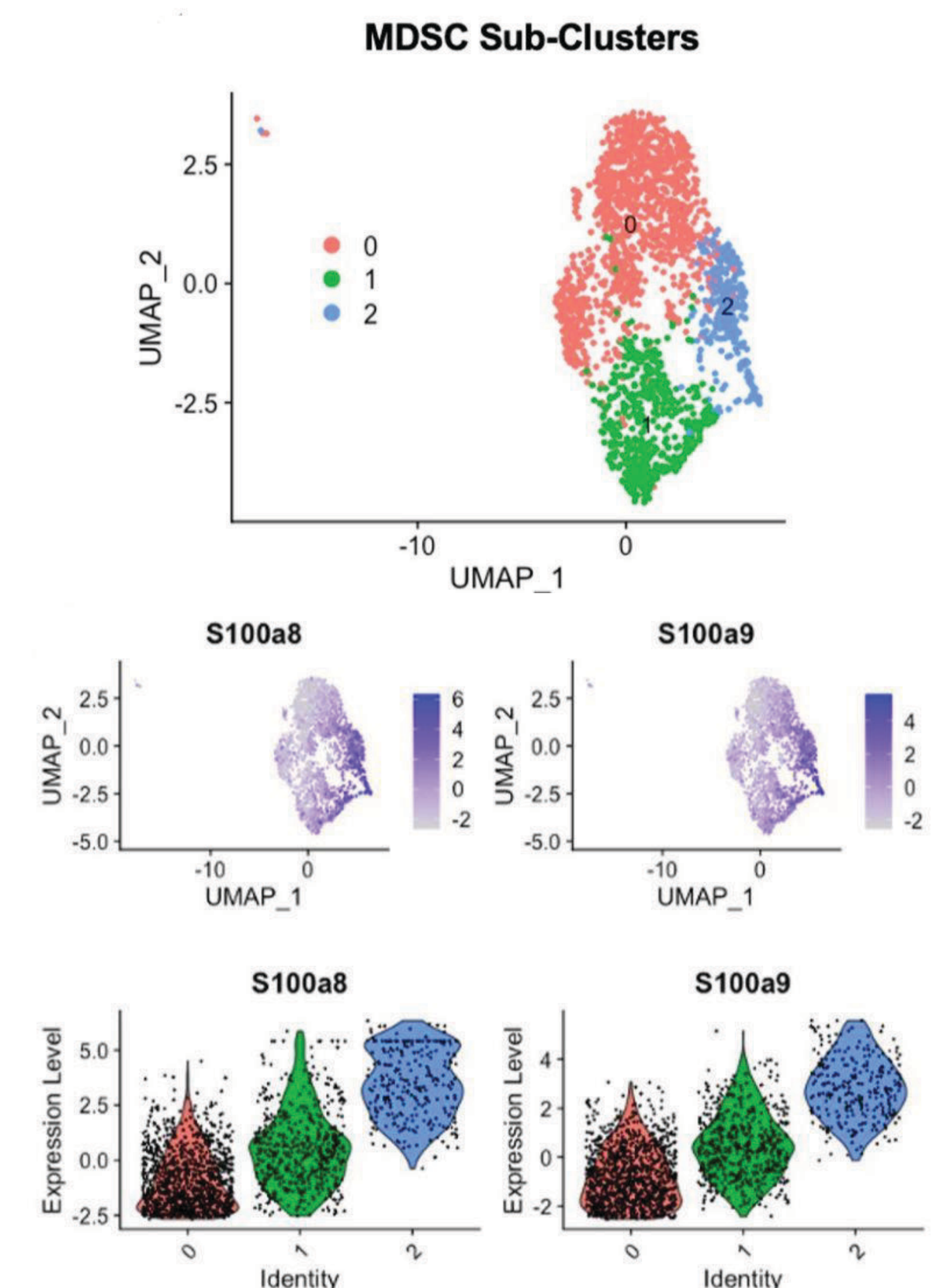
- 1 SNAB treatment led to an increase in total MDSCs and worse bone healing.



- 2 In SNAB rats, high sidescatter MDSCs were significantly depleted, while low sidescatter MDSCs significantly expanded.



- 3 MDSC sub-populations exhibit different expression of the S100A8/A9 protein.



References: [1] Cheng, A. and Vantucci, C. et al., PNAS, 2021, 118. [2] Vantucci, C. and Guyer, T. et al., Frontiers in Surgery, 2022, 9.