Pre-clinical validation of a novel immunotherapeutic treatment for endometriosis and associated chronic pain

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Introduction/Background

Endometriosis growth and associated chronic pain (CP) are highly influenced by proinflammatory and neuroangiogenic factors. Regulating both neuroangiogenesis[1] and immune cell activity[2] is netrin-1. Here, we investigate whether treatment with NP137, a clinically approved monoclonal antibody targeting netrin-1, can reduce endometriosis growth and CP in a mouse model of endometriosis.

Materials and Methods

Endometriosis (Endo) was surgically induced in ovariectomized/estradiol treated mice, together with sham counterparts, as previously described[3]. Between 4-9 weeks of development, mice were treated with either NP137 or control antibody NP001 (10mg/kg intraperitoneally). Endometriosis growth and CP was then assessed by quantifying: i) lesion size, ii) vaginal and colonic pain (visceromotor response to distension), iii) thermal and mechanical sensitivity (hot plate and von Frey hair), iv) bladder function (voiding patterns), and v) overall well-being (nesting).

Results

NP137 treatment significantly reduced the growth of lesions developed in Endo mice (32.2% reduction in size compared to lesions in Endo mice treated with NP001). Moreover, NP137 reduced endometriosis-induced vaginal and colonic pain sensitivity to low (<40mmHg) distension pressures (56% and 78.5% reduction, respectively), as well as sensitivity to mechanical (35.4% reduction) and thermal stimuli (17.5% reduction). NP137 treatment also reduced endometriosis-altered spontaneous behaviors, including improved bladder function (26.9% normalization in voiding patterns, specifically small size urine spots) and an increase in overall wellbeing (13.4% improvement of nest building capacity). Importantly, all evoked and spontaneous pain-like responses measured in Endo mice treated with NP137 were normalized to levels comparable to those measured in Sham mice treated with NP001.

Conclusion

Treatment with NP137 significantly reduced both endometriosis growth, and the enhanced widespread pain-like responses developed by mice with endometriosis. This study strongly supports NP137 as a feasible, non-invasive therapeutic strategy and an effective treatment for endometriosis growth and associated CP. Ongoing studies aim to elucidate mechanisms underlying our findings.

Key words

Monoclonal antibody, endometriosis growth, chronic pain.

References

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