
Figures and figure supplements

An herbal drug combination identified by knowledge graph alleviates the clinical symptoms of plasma cell mastitis patients: A nonrandomized controlled trial

Caigang Liu et al.

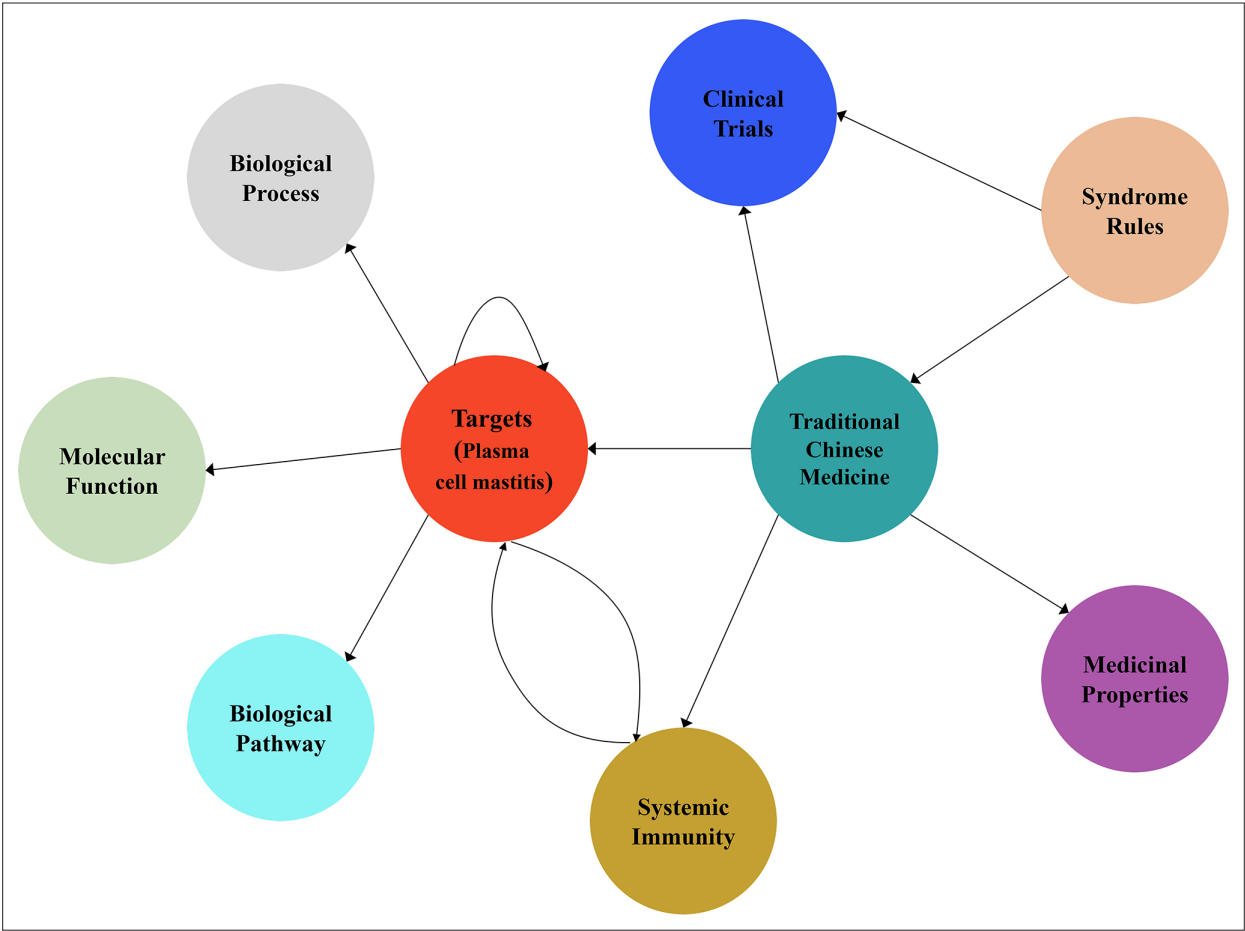


Figure 1. Schematic diagram of the knowledge graph for the drug discovery of plasma cell mastitis in the present work.

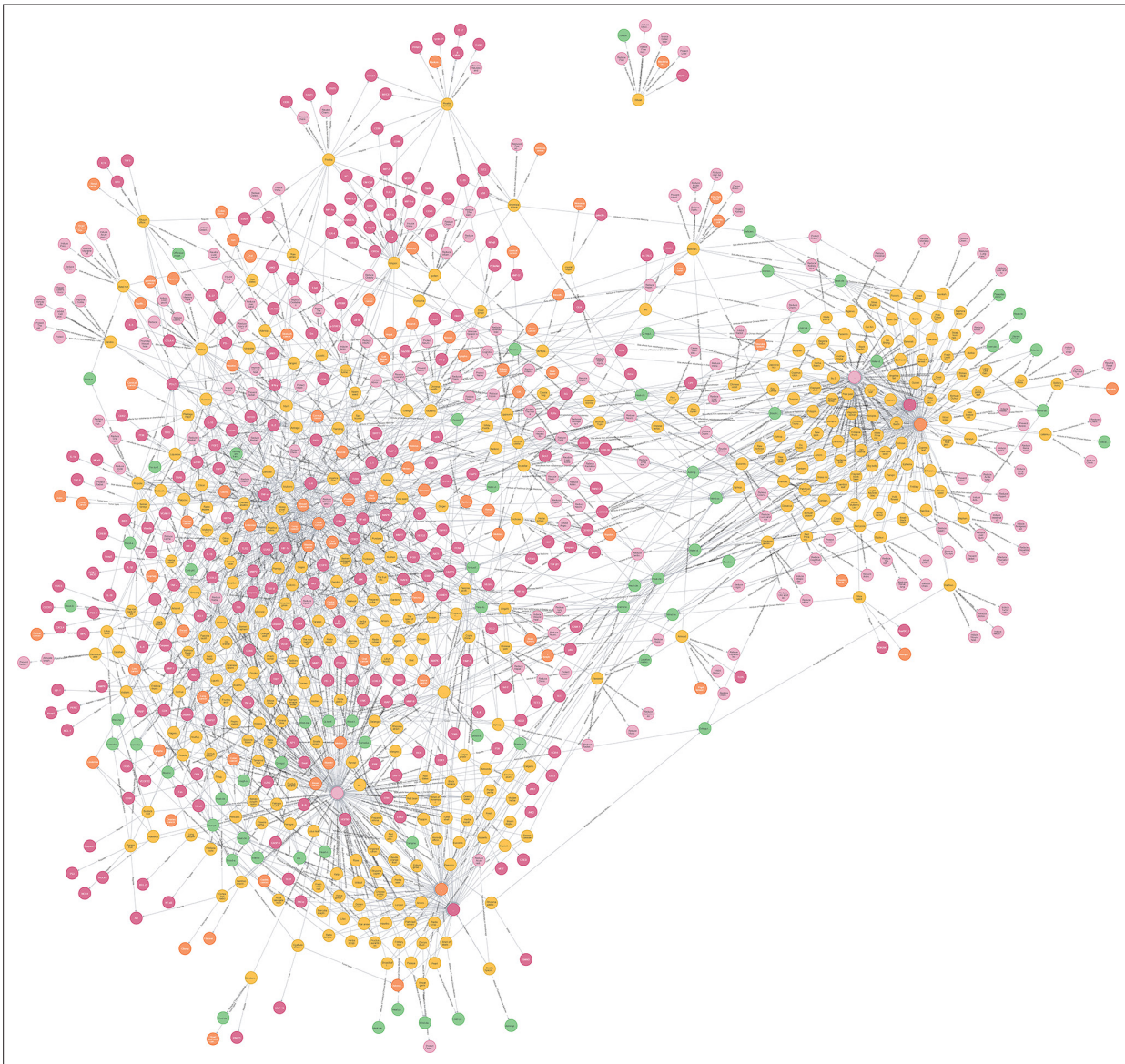


Figure 1—figure supplement 1. Snapshot of the medical knowledge graph toward immunotherapy. The knowledge graph was constructed using Neo4j and Python tools (<http://www.ikgg.org/kghti>). The yellow color represents the herbal drug entity, the pink color represents the cellular targets, and the green color represents the attributes of herb drugs.

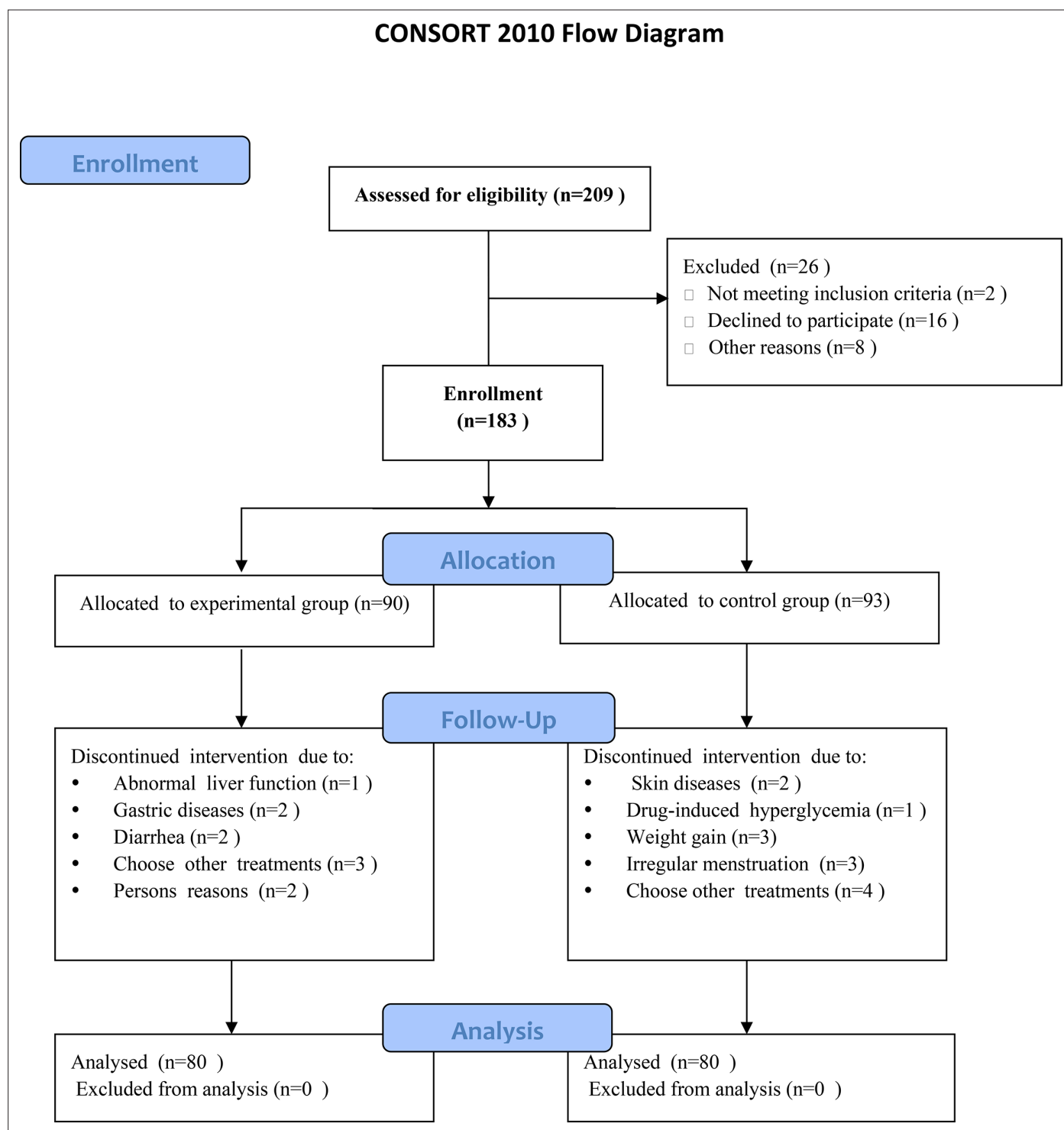


Figure 1—figure supplement 2. CONSORT flowchart diagram of the clinical trial for the herbal drug combination.

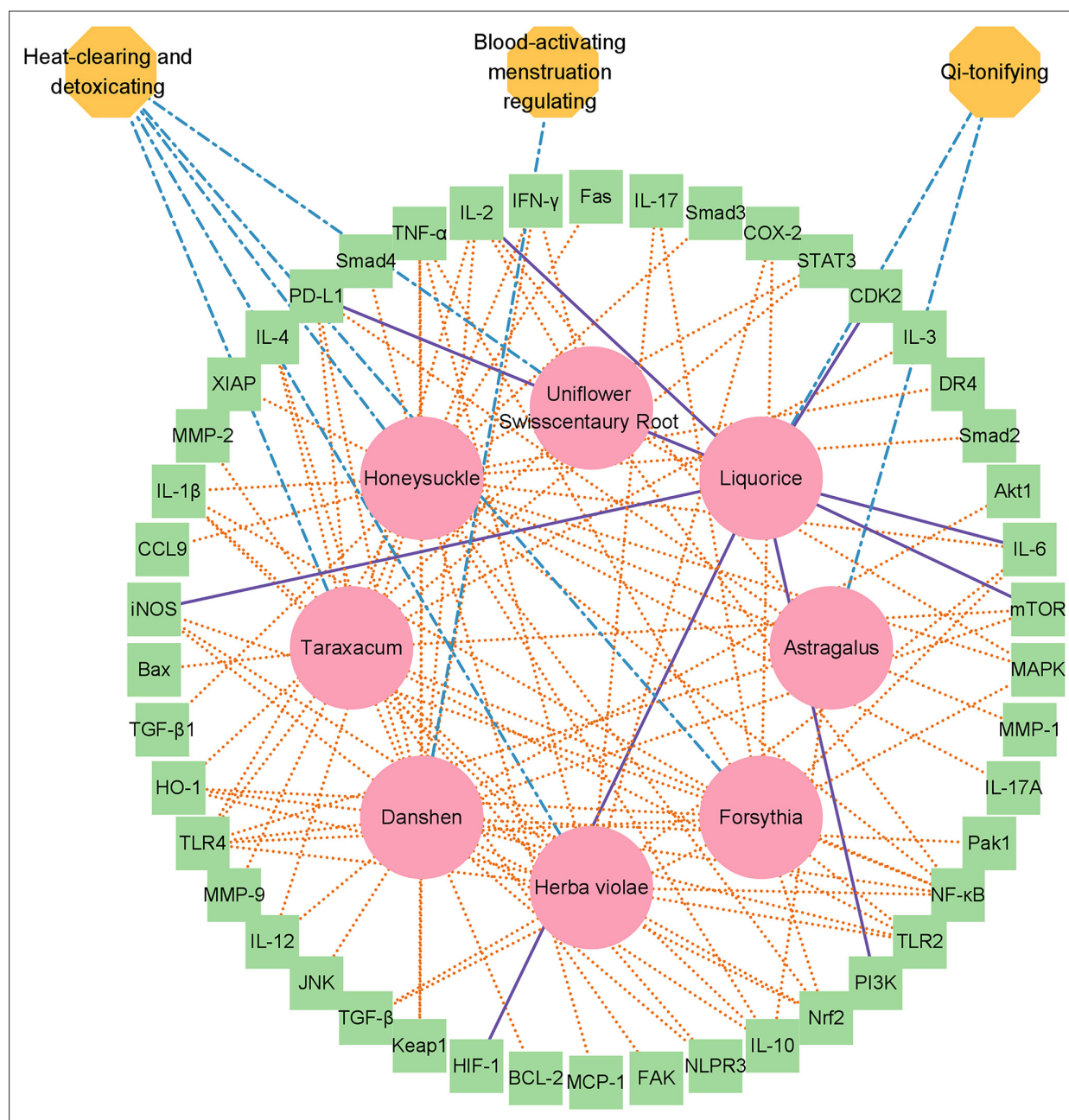


Figure 2. Network diagram of the herbal drug combination consisting of eight entities, including 'Honeysuckle,' 'Taraxacum,' 'Astragalus,' 'Danshen,' 'Forsythia,' 'Herba violae,' 'Liquorice,' and 'Uniflower swisscentaury root,' displayed in red circles. In total, 46 cellular targets related to systemic immunity were hit by the drug combination such as NLPR3, IL-17, TLR4, STAT3, IL-6, iNOS, and TLR2, which are displayed in the green box model. Three major medicinal attributes (properties) were identified for these herbal drug entities, including 'heat-clearing and detoxicating,' 'Qi-tonifying,' and 'blood-activating menstruation regulation'.

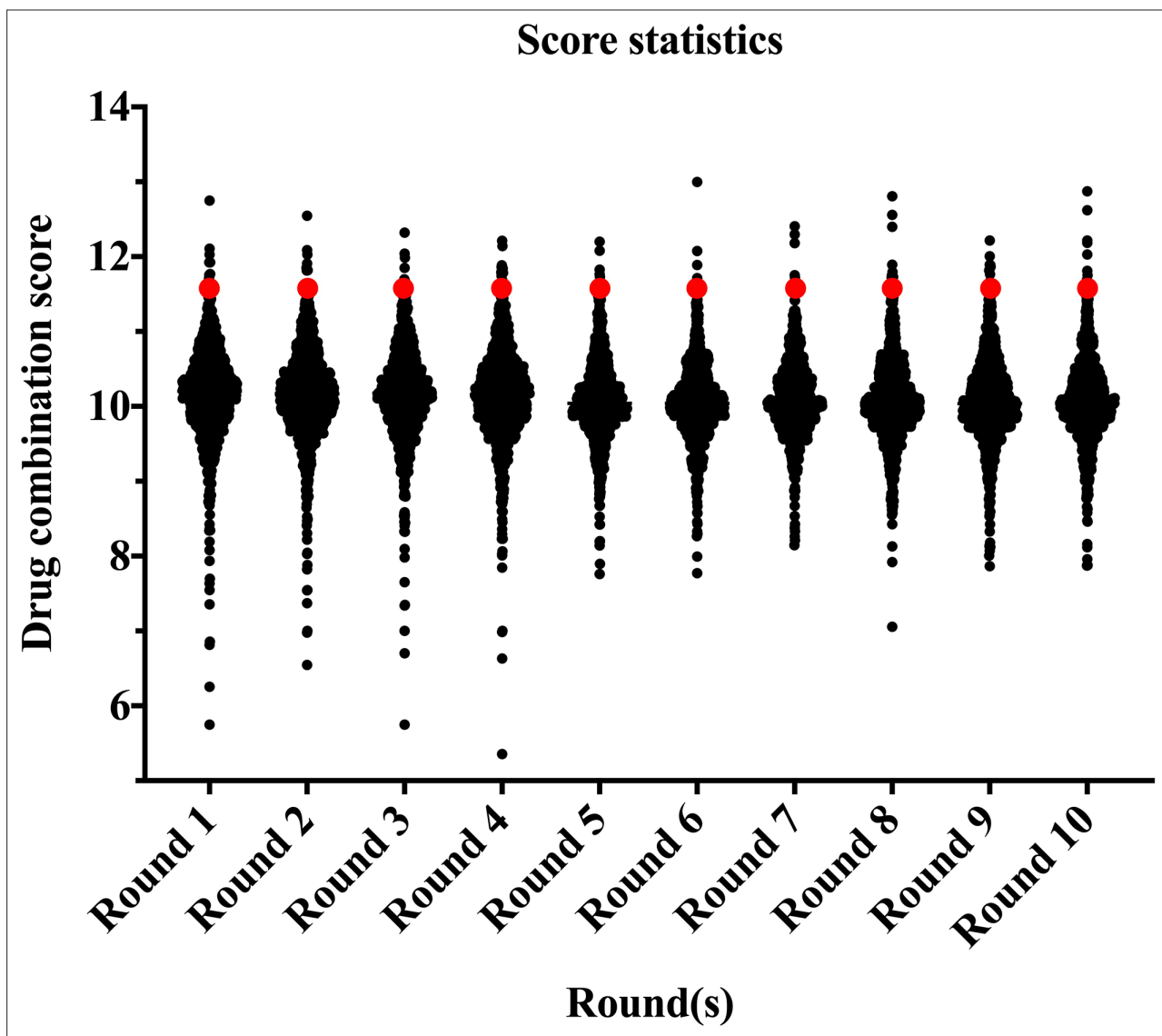


Figure 2—figure supplement 1. The score statistics of 10 rounds of random herbal drug combinations (1000 random combination from each round) for the treatment of plasma cell mastitis. It is noteworthy that the scoring results of the 10 rounds are presented as normal distributions. The herbal drug combination identified for the clinical trial was among the top 20 choices in all the 10 rounds and is marked with red dots.

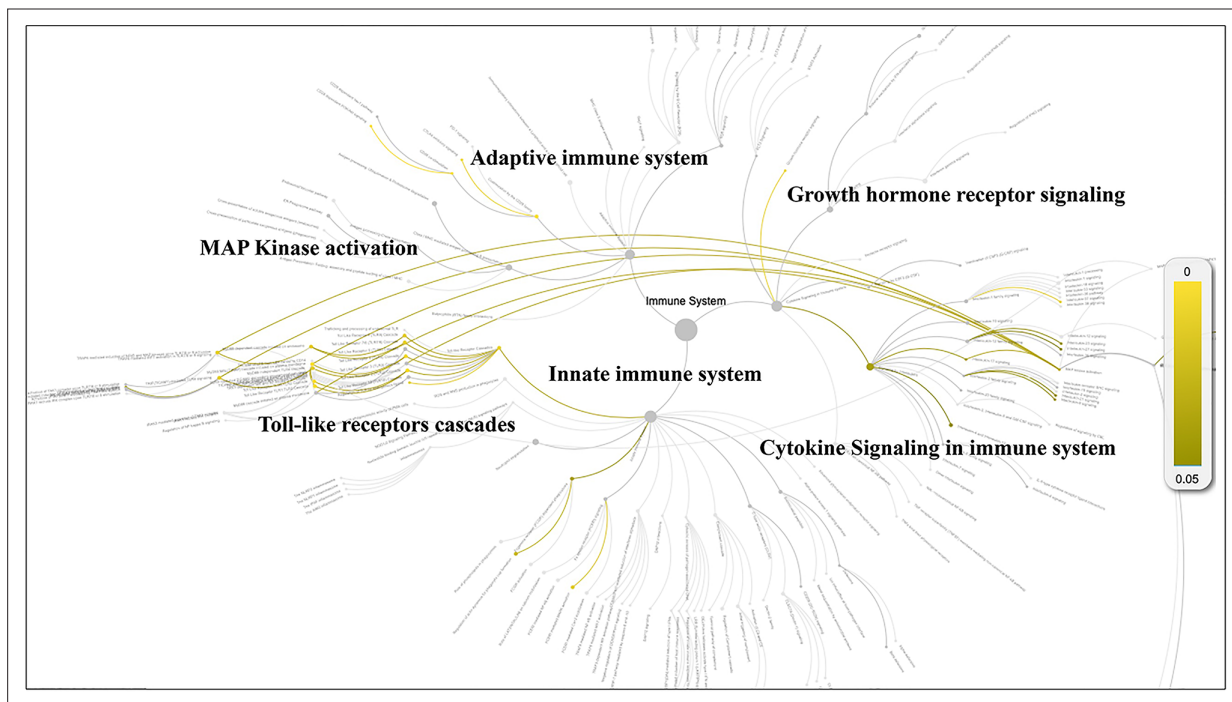


Figure 3. Pathway analysis for the potential cellular targets of the herbal drug combination via Reactome Knowledgebase. The statistically significant pathways are highlighted and displayed in yellow color ($p < 0.05$).

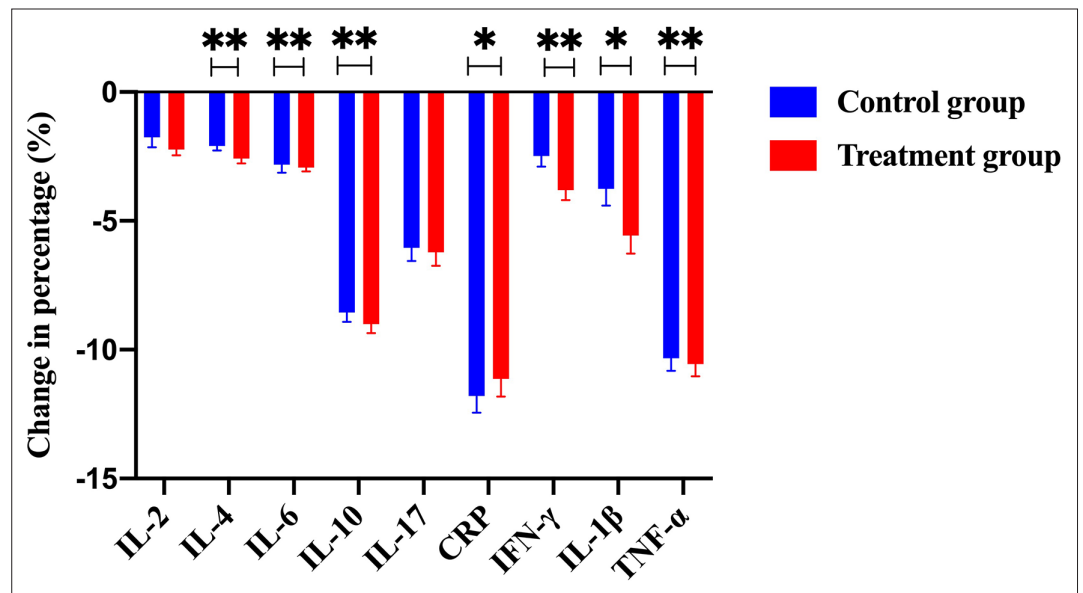


Figure 4. The change of percentage for numerous immunological cytokines, including IL-2, IL-4, IL-6, IL-10, IL-17, CRP, IFN- γ , IL-1 β , and TNF- α , from the control group and the treatment group (with Traditional Chinese Medicine [TCM] treatment). Notably, a few key cytokines such as IL-2, IL-4, IFN- γ , IL-1 β , and TNF- α were significantly downregulated in the treatment group compared to the control group.

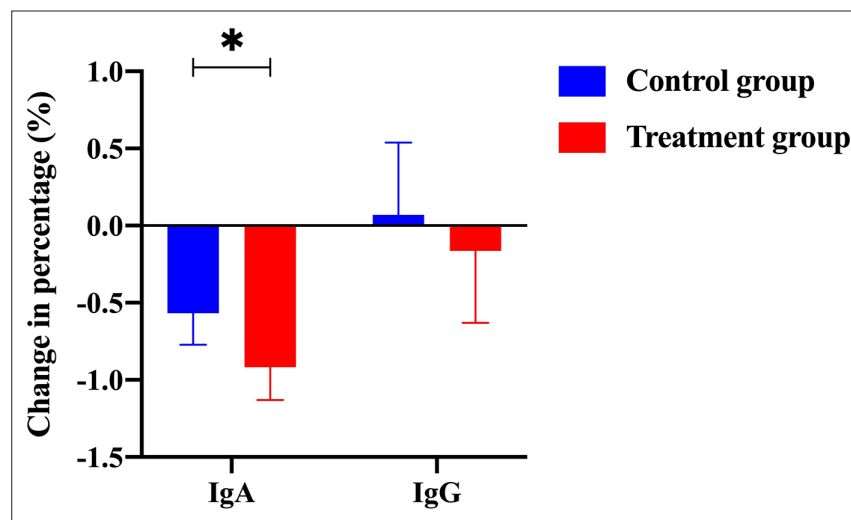


Figure 5. The change of percentage for IgA level and IgG level from the control group and the treatment group (with Traditional Chinese Medicine [TCM] treatment).

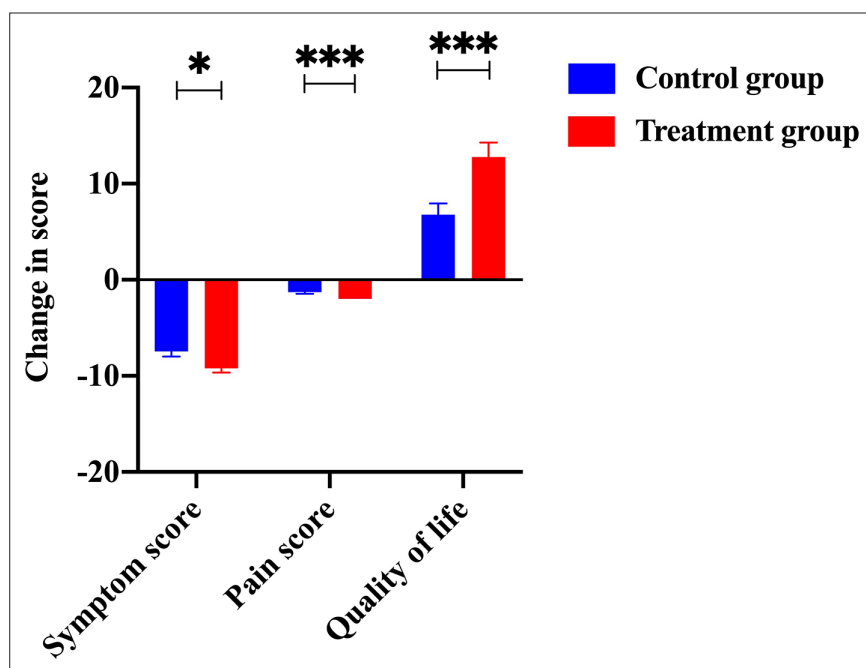


Figure 6. The change of scores from items, including symptom, pain, and living quality. The scores of symptoms, pain, and living quality from the treatment group were significantly improved compared to the control group.

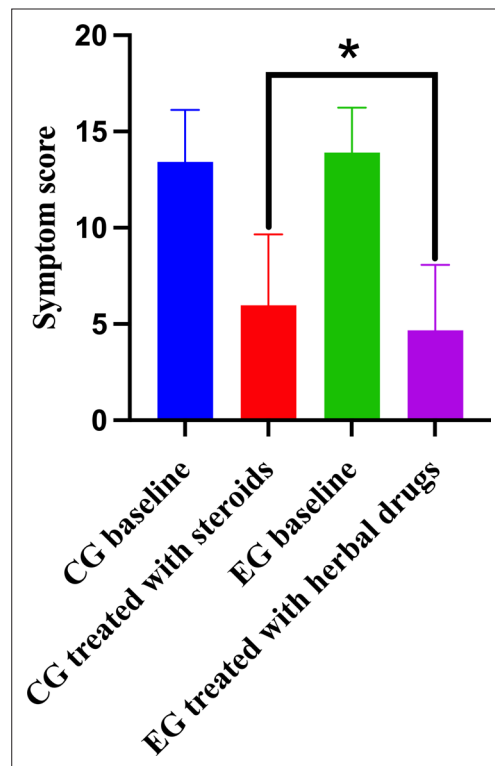


Figure 6—figure supplement 1. The comparison of symptom score between different groups. Control group (CG) baseline, experimental group (EG) baseline, CG treated with methylprednisolone, and EG treated with herbal drug combinations.

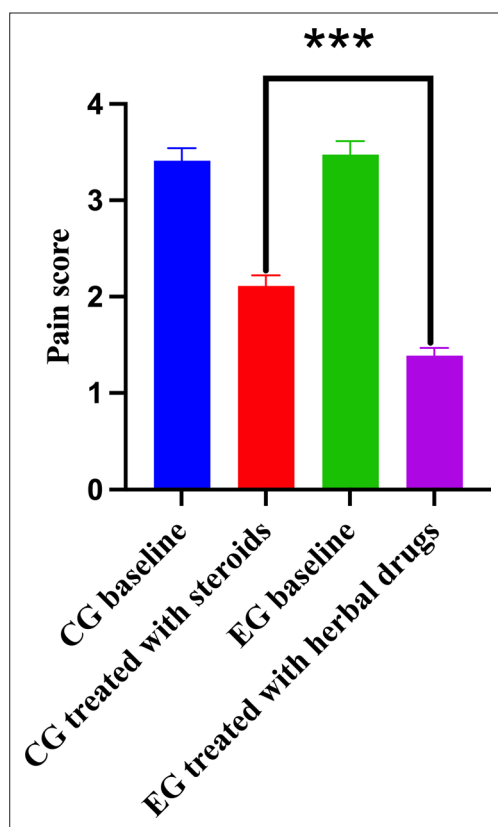


Figure 6—figure supplement 2. The comparison of pain score between different groups. Control group (CG) baseline, experimental group (EG) baseline, CG treated with methylprednisolone, and EG treated with herbal drug combinations.

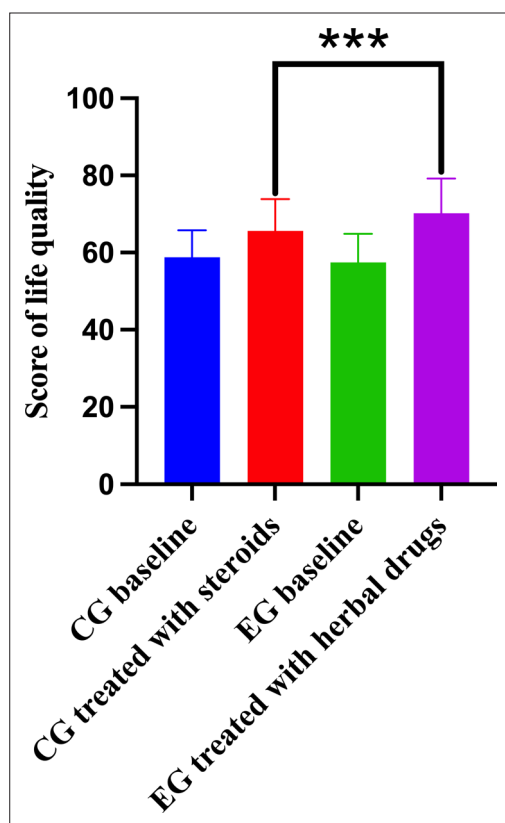


Figure 6—figure supplement 3. The comparison of score of life quality between different groups. Control group (CG) baseline, experimental group (EG) baseline, CG treated with methylprednisolone, and EG treated with herbal drug combinations.

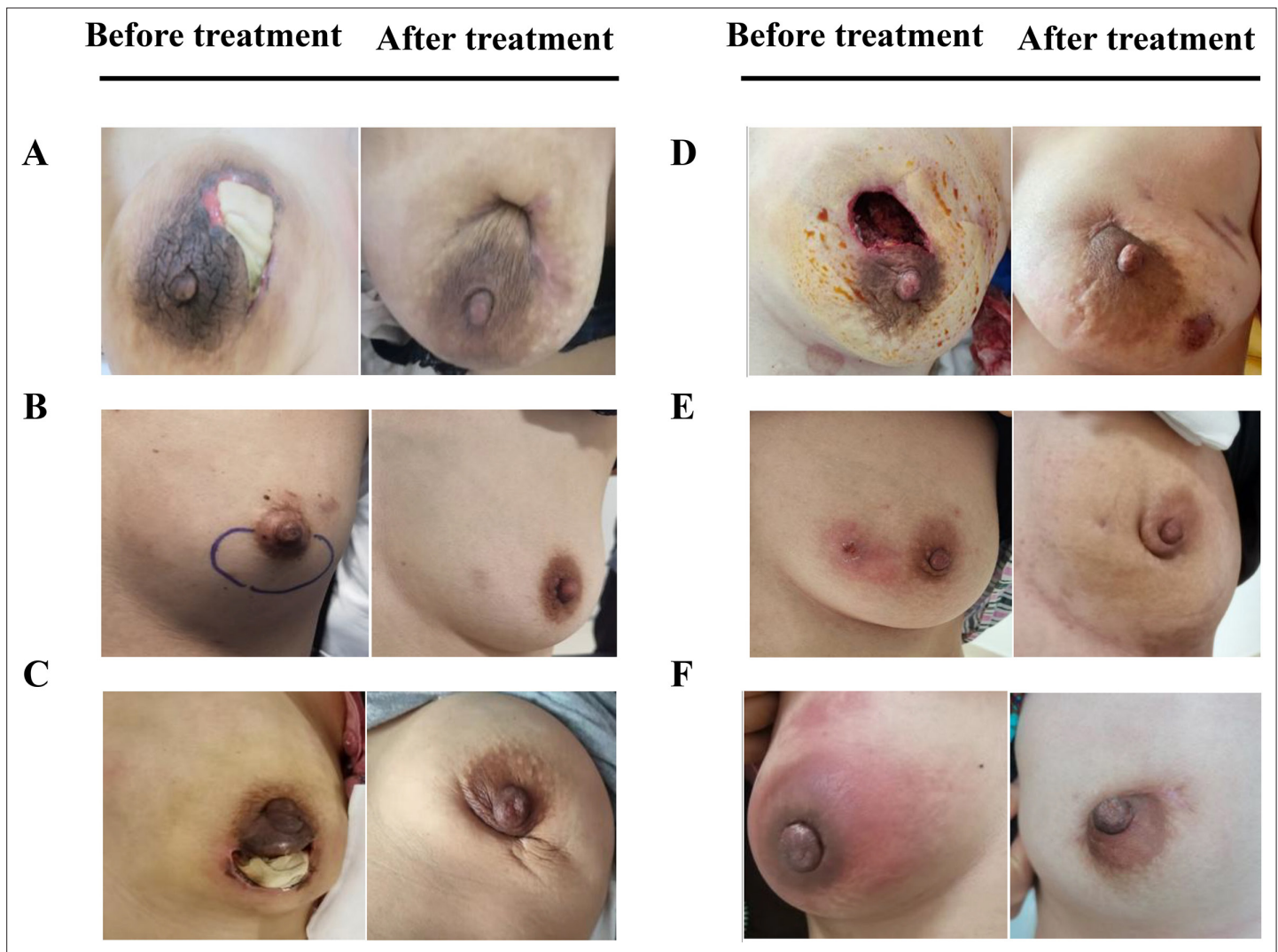


Figure 7. The comparison of whole breast for six representative plasma cell mastitis (PCM) patients in the experimental group (EG) before treatment and after treatment. **(A-F)**, Six selected PCM patients in the clinical trial to reveal the effects of herbal drug combination. Written informed consents have been provided by all the patients (including written informed consent for the publication of the images in this figure), and detailed patient information is provided in **Supplementary file 3**.