***Supplementary Materials***

***Juzentaihoto Exerts Anti-allergic Effect by Inhibiting Effector T Cell Activation and Inducing and/or Activating Regulatory T Cells in a Murine Model of Contact Hypersensitivity***

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Short Title: Juzentaihoto exerts anti-allergic effects by regulating effector and regulatory T cells

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**Figure S1.** Three-dimensional HPLC profile of juzentaihoto (JTT)

**Figure S2.** Effect of juzentaihoto (JTT) on the induction and/or activation of regulatory T cells without antigen sensitization of donor mice

**(a)** Experimental protocol. **(b)** Ear swelling 24 h after the topical application of 1% TNCB on the ear. In donor mice, JTT (1.5 g/kg, 10 times the human dose) was administered orally once daily to the treated group and distilled water was administered to the control (CTRL) group. After 7 days, lymphocytes were obtained from the dLNs and injected into naïve recipient mice. The lymphocytes obtained from the control donor mice were injected intravenously into the CTRL group, while the lymphocytes obtained from the JTT-treated donor mice were injected intravenously into the JTT group. HBSS alone was injected intravenously in the vehicle mice. All mice, except those in the normal (N) group were sensitized on shaved abdomens with 5% TNCB 24 h after cell transfer and then challenged on their right ears with 1% TNCB after 7 days. Ear swelling was measured 24 h after the challenge. Each column represents the mean ± S.E.M. of 6 to 7 mice. \*\*\* *p* < 0.001 *vs.* the control group using ANOVA with Bonferroni correction for multiple comparisons.

**Figure S3.** Antigen specificity of regulatory T cells induced and/or activated by oral administration of juzentaihoto (JTT)

**(a)** Experimental protocol. **(b)** Ear swelling 48 h after the topical application of 0.5% oxazolone (OXZ) on the ear. In donor mice, JTT (1.5 g/kg, 10 times the human dose) was administered orally once daily to the treated group and distilled water was administered to the control (CTRL) group. After 7 days, lymphocytes were obtained from the dLNs and injected into naïve recipient mice. The lymphocytes obtained from the control donor mice were injected intravenously into the CTRL group, while the lymphocytes obtained from the JTT-treated donor mice were injected intravenously into the JTT group. HBSS alone was injected intravenously in the vehicle mice. All mice, except those in the normal (N) group were sensitized on shaved abdomens with 0.5% OXZ 24 h after cell transfer and then challenged on their right ears with 0.5% OXZ after 7 days. Ear swelling was measured 24 h after the challenge. Each column represents the mean ± S.E.M. of 6 to 7 mice. \*\*\* *p* < 0.001 *vs.* the control group using ANOVA with Bonferroni correction for multiple comparisons. †† *p* < 0.01 *vs.* the control group using ANOVA with Bonferroni correction for the selected two group comparisons.