Loss of SENP3 Mediated the Formation of Nasal Polyps in Chronic Sinusitis by Increasing Macrophage Alternative Activation

Ximing Bao[1], Bin Liu[1], Tingting Feng[1], Wanxin Cao[1], Jiali Shi[2], Chun Zhang[2], Yiming Jiang[1], Jun Liu[1], Yi Zhang[1], Hua Zhang[1], Xiaorui Chen[3], Jie Yang[4], Jiping Li[1], and Zheng Zhou[1]

[1]Shanghai Jiao Tong University School of Medicine Affiliated Renji Hospital
[2]Shanghai Jiaotong University
[3]Shanghai Xuhui Central Hospital
[4]Shanghai Jiao Tong University School of Medicine

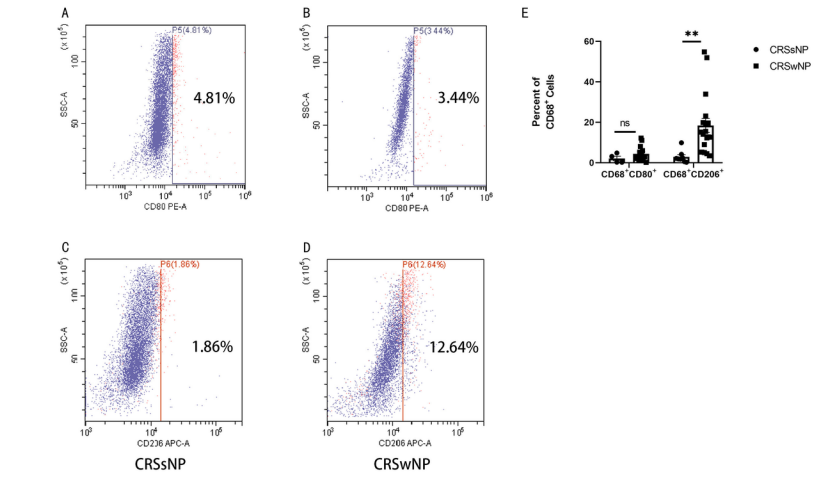
June 30, 2020

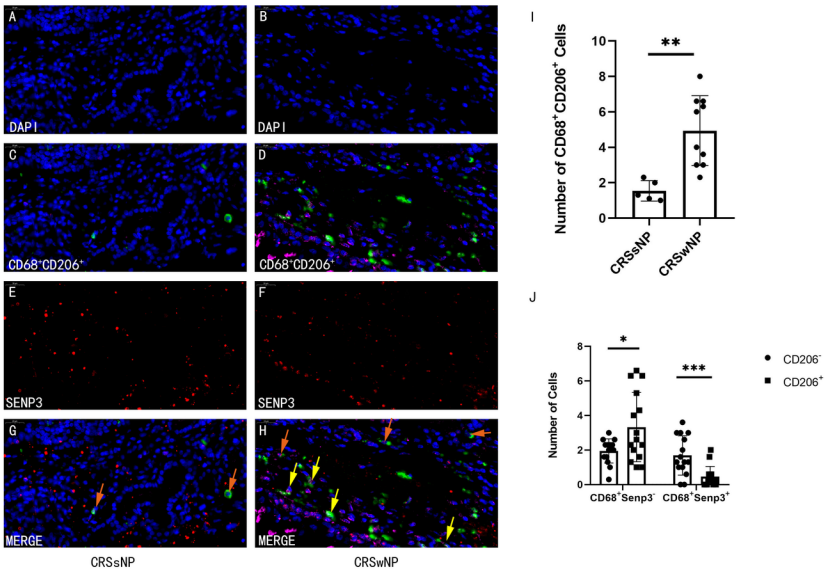
Abstract

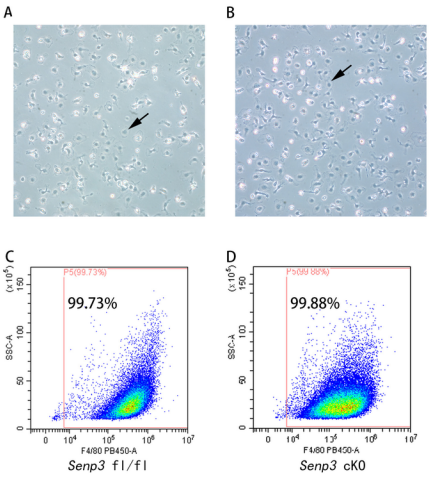
Background and aim: Small ubiquitin–like modifier (SUMO)-specific protease (SENP)3 is a protease molecule that responds to reactive oxygen species (ROS) with high sensitivity. However, the role of ROS and SENP3 in the formation of nasal polyps (NPs) remains unclear. This study aimed to explore how SENP3 influenced the outcome of chronic rhinosinusitis (CRS) by altering macrophage function, that is, the formation of NPs. Methods: The alternative activation of macrophage (M2) was detected with CD68+CD206+ in humans and CD206+ in mice. The nasal mucosa of patients with CRS was tested using flow cytometry (CD68, CD80, and CD206) and triple-color immunofluorescence staining (CD68, CD206, and SENP3). The bone marrow–derived macrophages from SENP3 knockout and control mice were stimulated with interleukin (IL)-4 and IL-13 to analyze alternative macrophage polarization in vitro. An animal model of allergic rhinitis was constructed using SENP3 knockout mice. CD206 was detected by immunofluorescence staining. The thickening of eosinophil-infiltrated mucosa was detected by Luna staining. Results: The number of CD68+ CD206+ M2 increased in the nasal mucosa of patients with CRS with NP (CRSwNP) compared with patients with CRS without NP (CRSsNP), but with no significant difference between the groups. SENP3 knockout increased the polarization of F4/80+CD206+M2. Meanwhile, the number of CD206+M2 significantly increased in the allergic rhinitis model constructed using SENP3 knockout mice and controls, with a more obvious proliferation of the nasal mucosa. Conclusion: The downregulation of the expression of macrophage SENP3 in the nasal mucosa in chronic sinusitis promoted the formation of NPs.

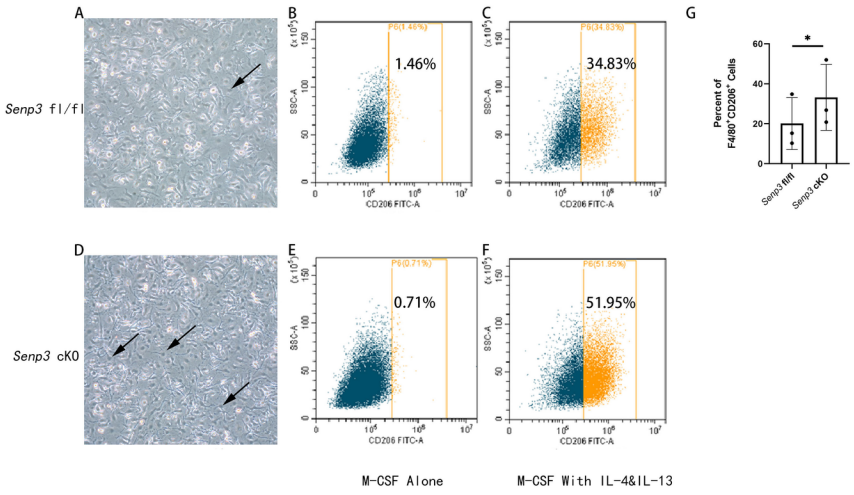
Hosted file

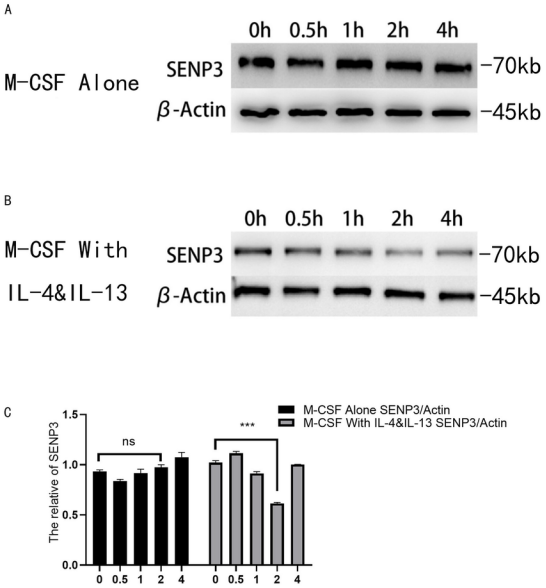
Manuscript--Loss-of-SENP3-Mediated-the-Formation-of-Nasal-Polyps-in-Chronic-Sinusitis-by-Increasing-Mac
available at https://authorea.com/users/338155/articles/464173-loss-of-senp3-mediated-the-formation-of-nasal-polyps-in-chronic-sinusitis-by-increasing-macrophage-alternative-activation

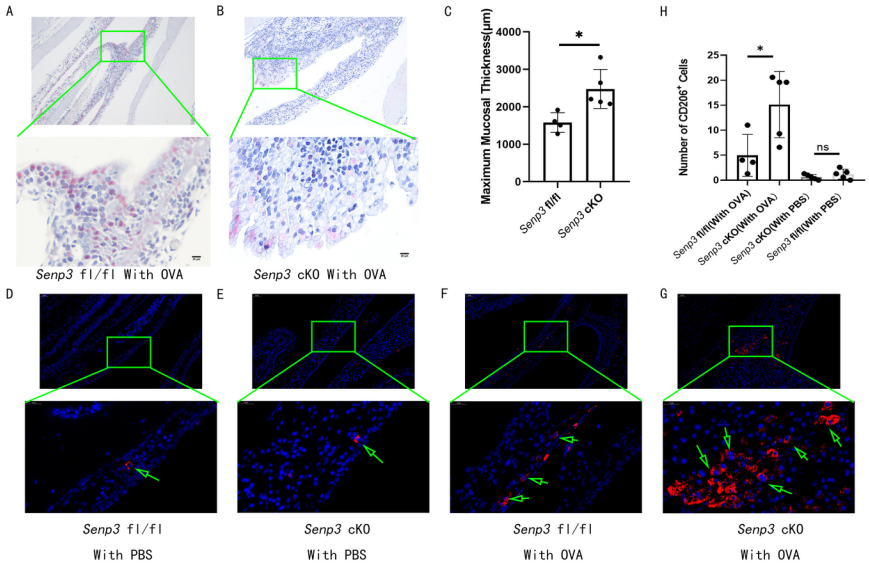












CRSwNP（N=28）			CRSsNP（N=13）		
Gender		Age（Mean±SD）	Gender		Age（Mean±SD）
F（N=6）	M（N=22）	49.607±17.240	F（N=6）	M（N=7）	49.077±14.483