

Targeted Inhibition of Pro-Inflammatory S1a+ Monocytes Using WGA-Functionalized Nanoparticles Encapsulating Itacitinib: A Novel Therapeutic Approach

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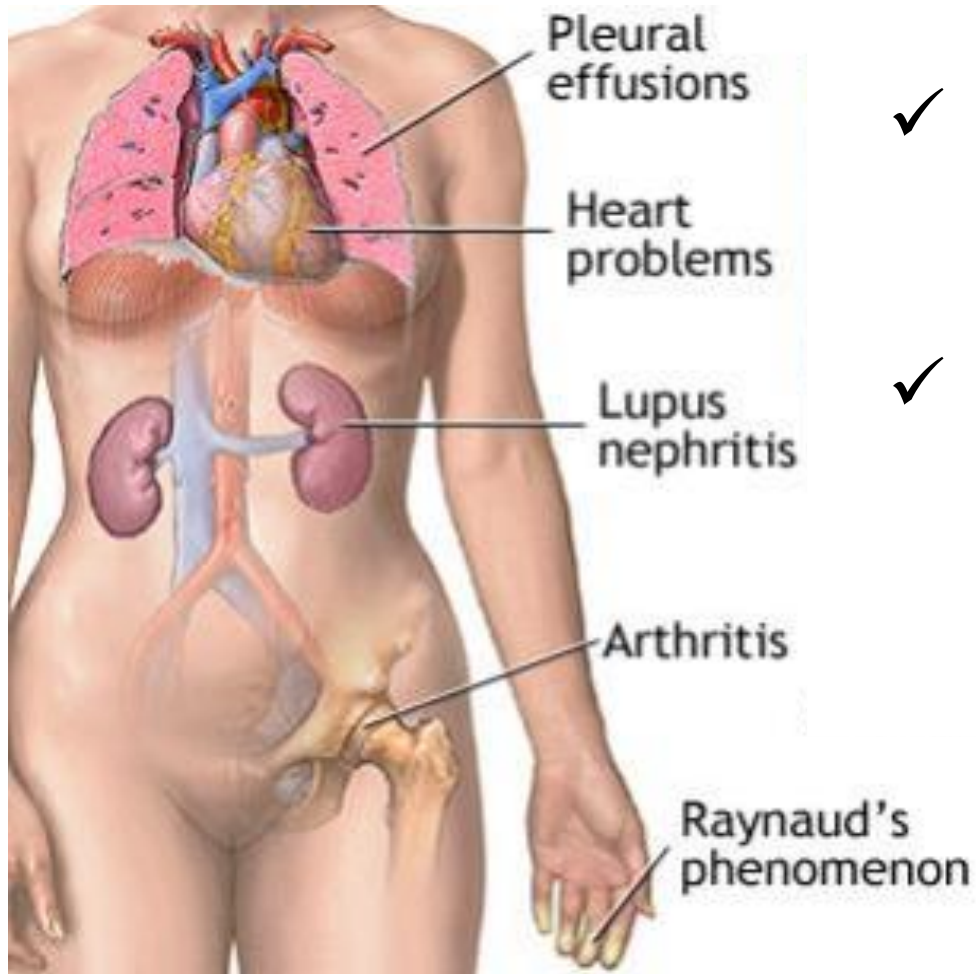
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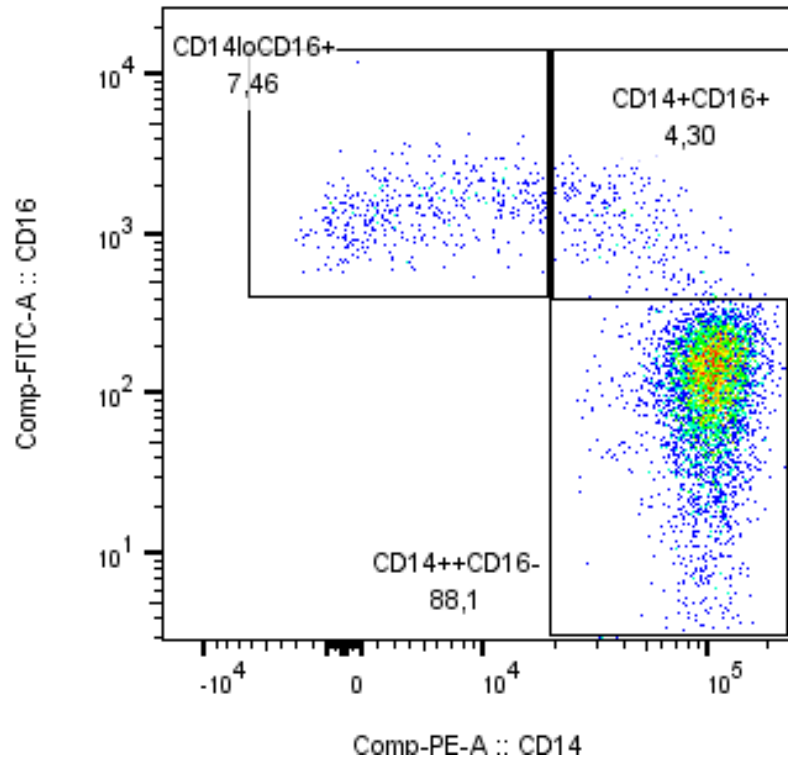


— Systemic lupus erythematosus (SLE) —

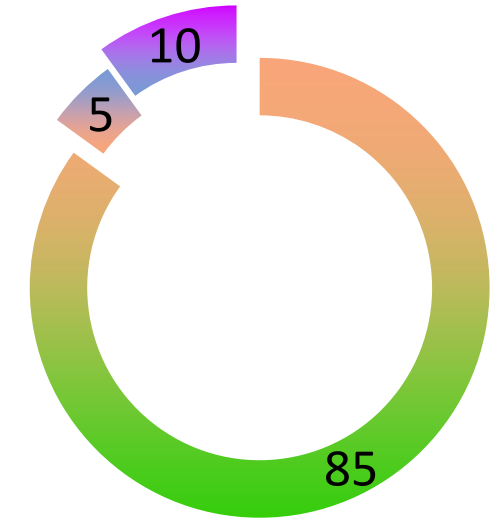


- ✓ **Progressive systemic inflammatory disease resulting in major organ system failure.**
- ✓ **Lupus patients have alterations in innate and adaptive immune cells, including MONOCYTES.**

— Monocytes subpopulations —

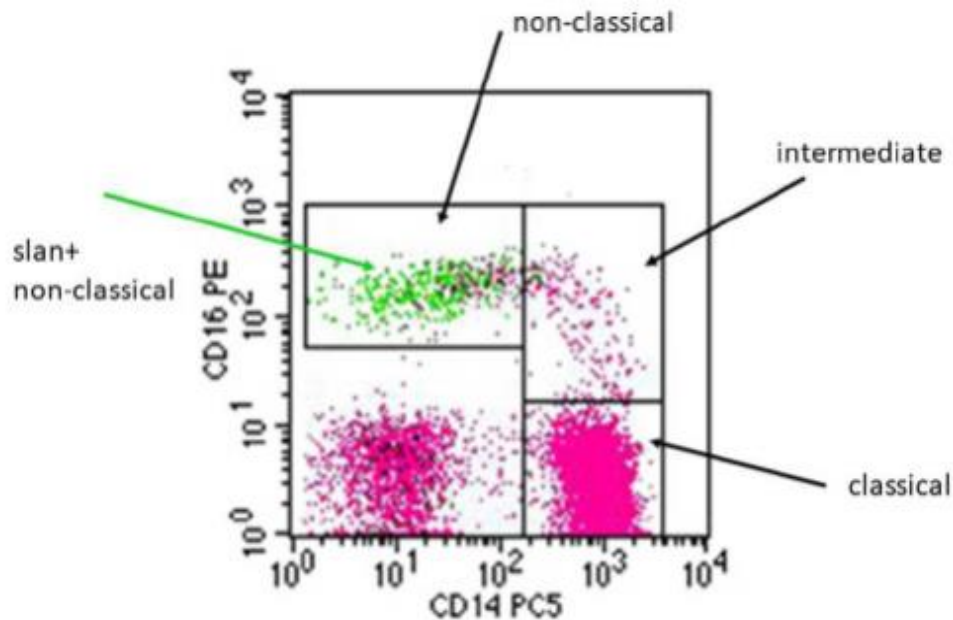


- Classical
- Intermediate
- Non-classical



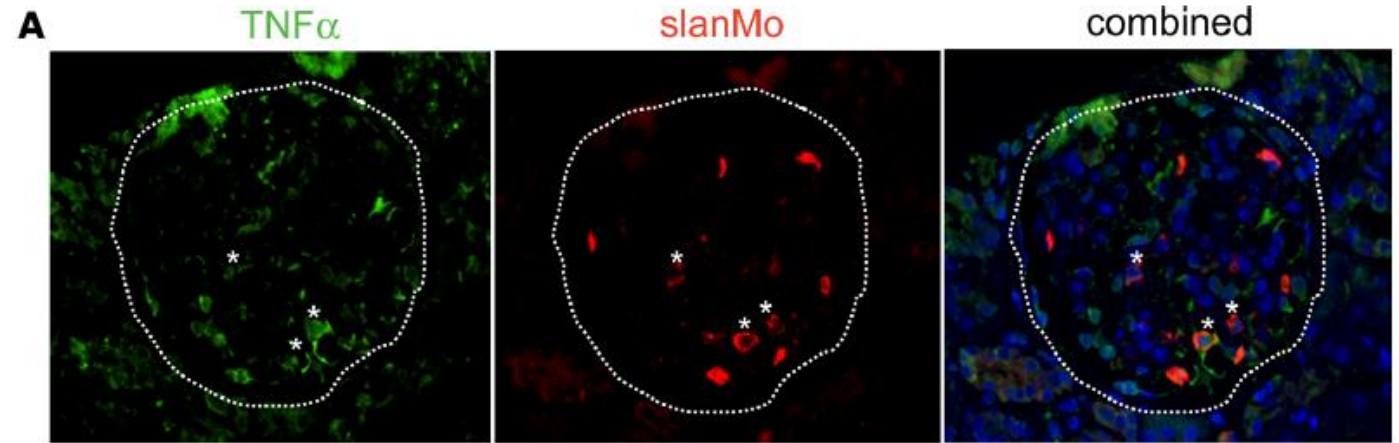
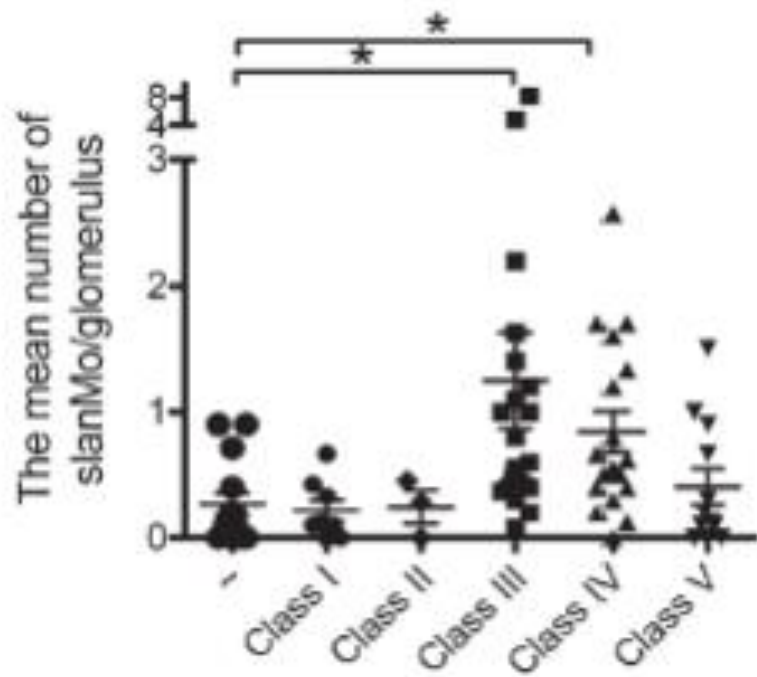
- ✓ Monocytes play a significant role in the pathogenesis of SLE
- ✓ The proportion and numbers of monocyte subsets are altered in lupus patients.

— slan+ monocytes



6-sulfo LacNAc+ (slan) monocytes (slanMo) are a subset of nonclassical monocytes, which have been considered as one of the principal pro-inflammatory cells in different diseases, including the autoimmune ones, such as systemic lupus erythematosus (SLE).

— Slan+ monocytes —



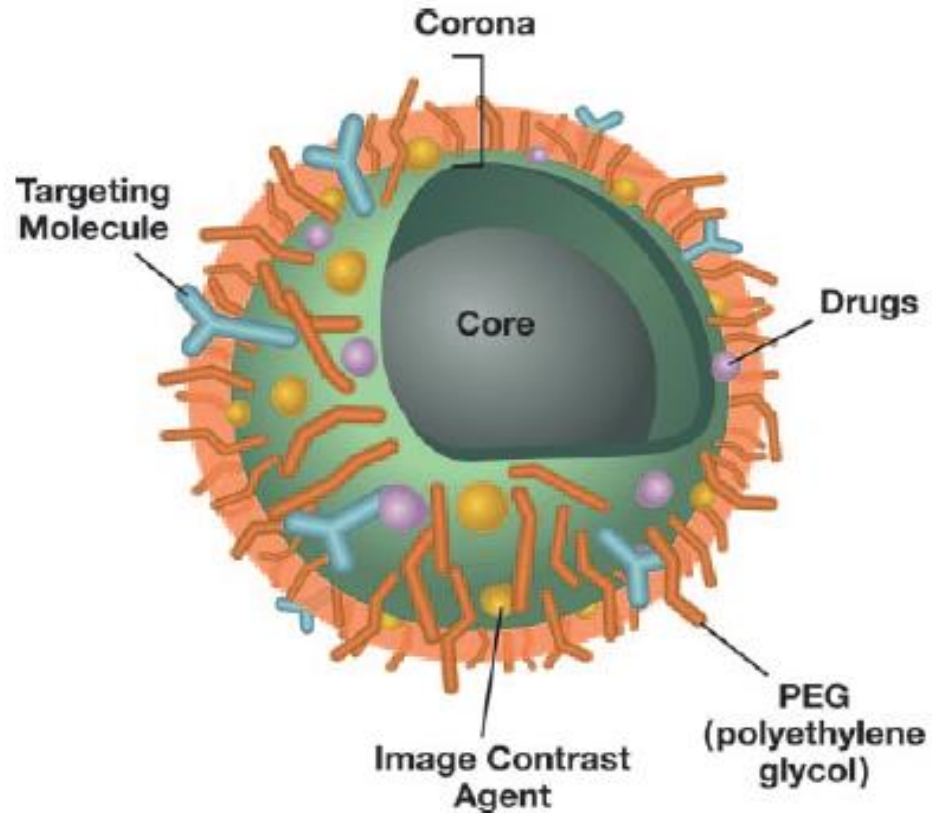
Slan+ Monocytes were increased within glomeruli of human lupus nephritis samples, which locally expressed TNF- α .

— JAK-STAT pathway and SLE —

- ✓ Increased levels of total STAT1 protein and its activated/phosphorylated form were detected in kidney samples from MRL/lpr mice with LN as compared to those from control mice (***Dong et al. Lupus. 2007***)
- ✓ Lupus patients have polymorphisms in JAK2, TYK2 y STAT4 (***Bolin et al. Plos one. 2013***)
- ✓ The mRNA expression level of SOCS1 was significantly decreased in SLE patients in comparison with healthy controls (***Qiu et al. Clin Exp Med. 2015***)

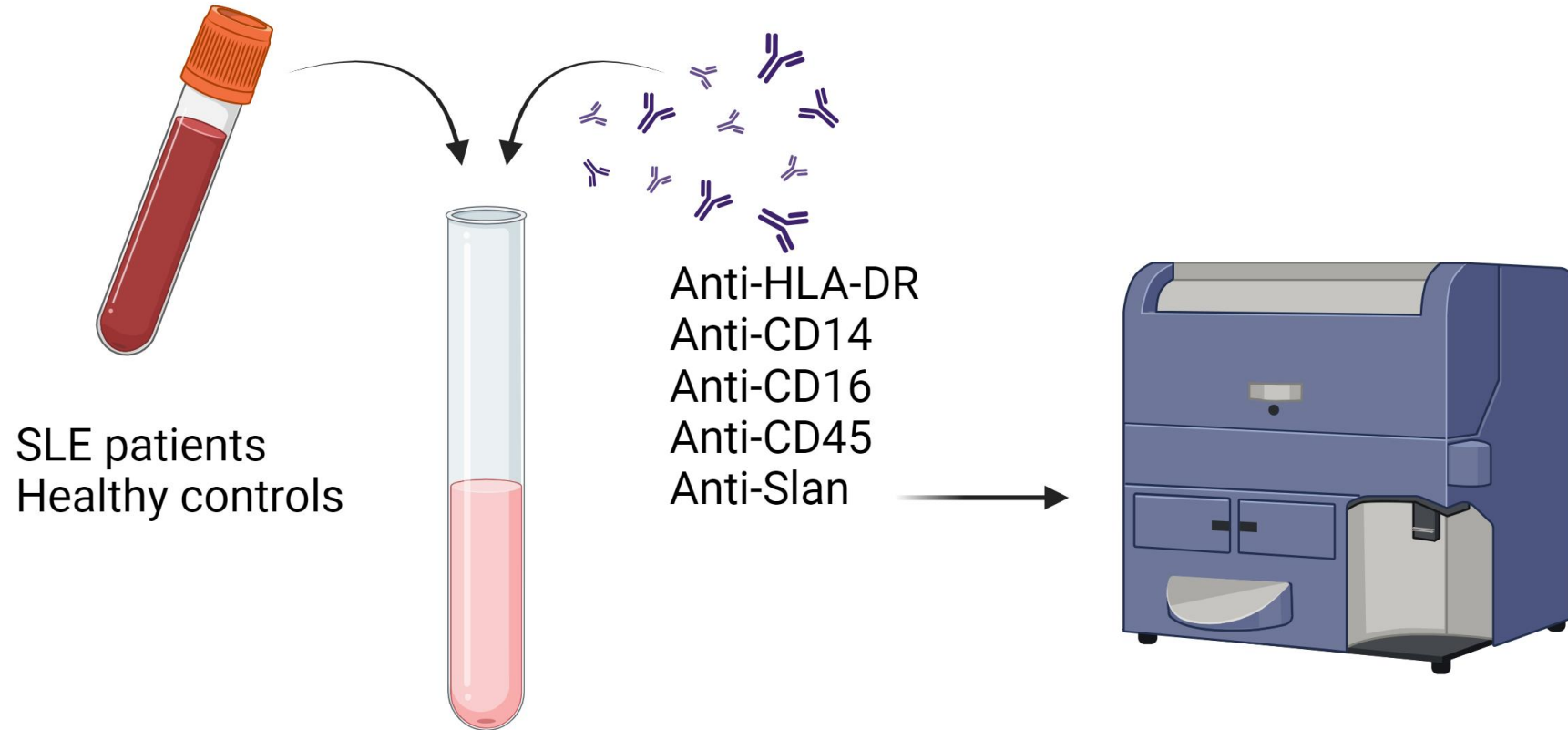
Jak inhibitors (Jak inhibitors) could be used in the treatment of SLE. However, the use of these Jak inhibitors have been associated with different side effects.

— Nanoparticles —

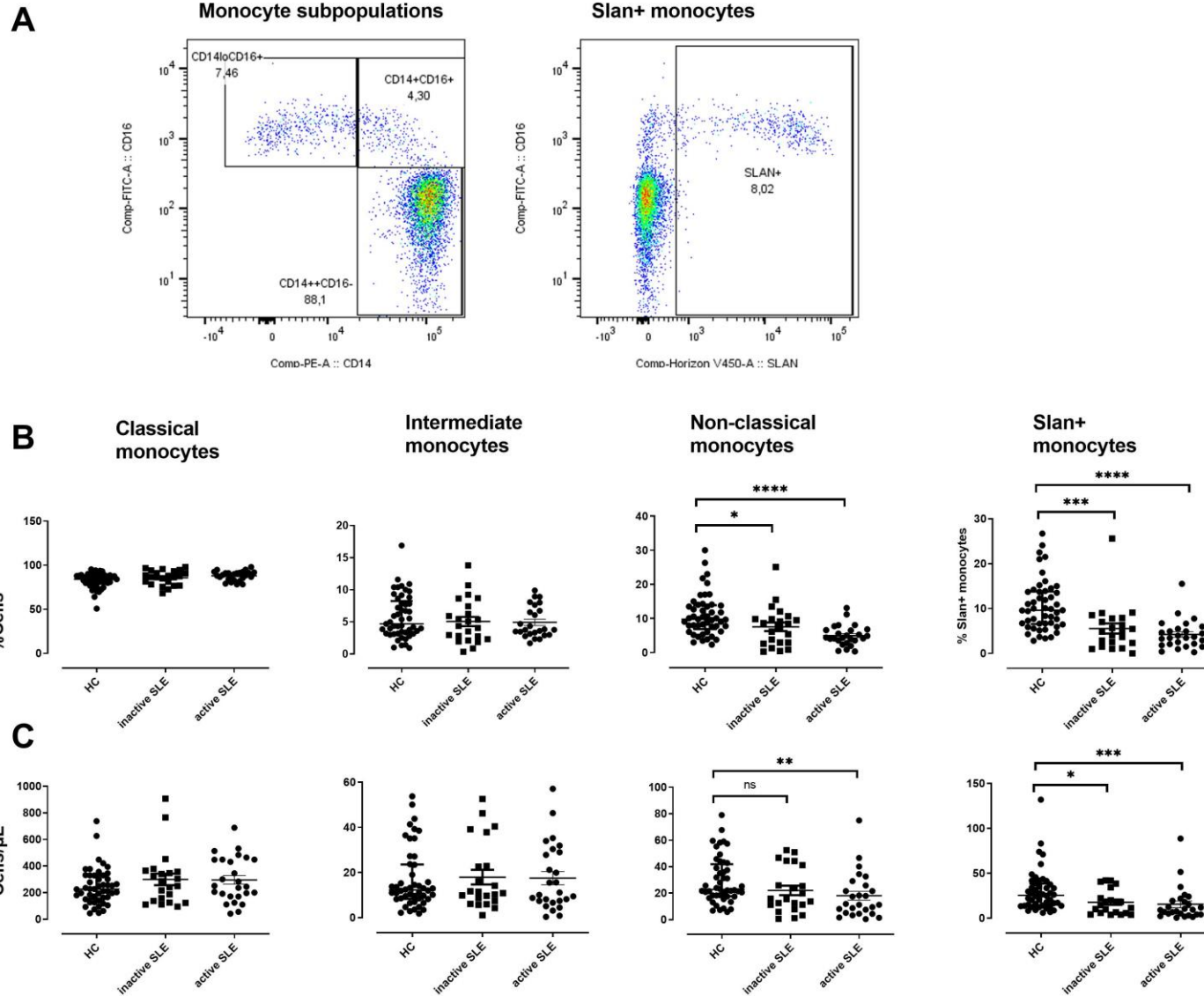


The encapsulation of itacitinib (ITA) —a JAK1 inhibitor— into WGA-functionalized F127-emulsified polylactic-co-glycolic acid (PLGA) nanoparticles could specifically interact with slan⁺ monocytes and modulate the activation and function of these cells without affect other immune cells.

— Monocyte subpopulations —

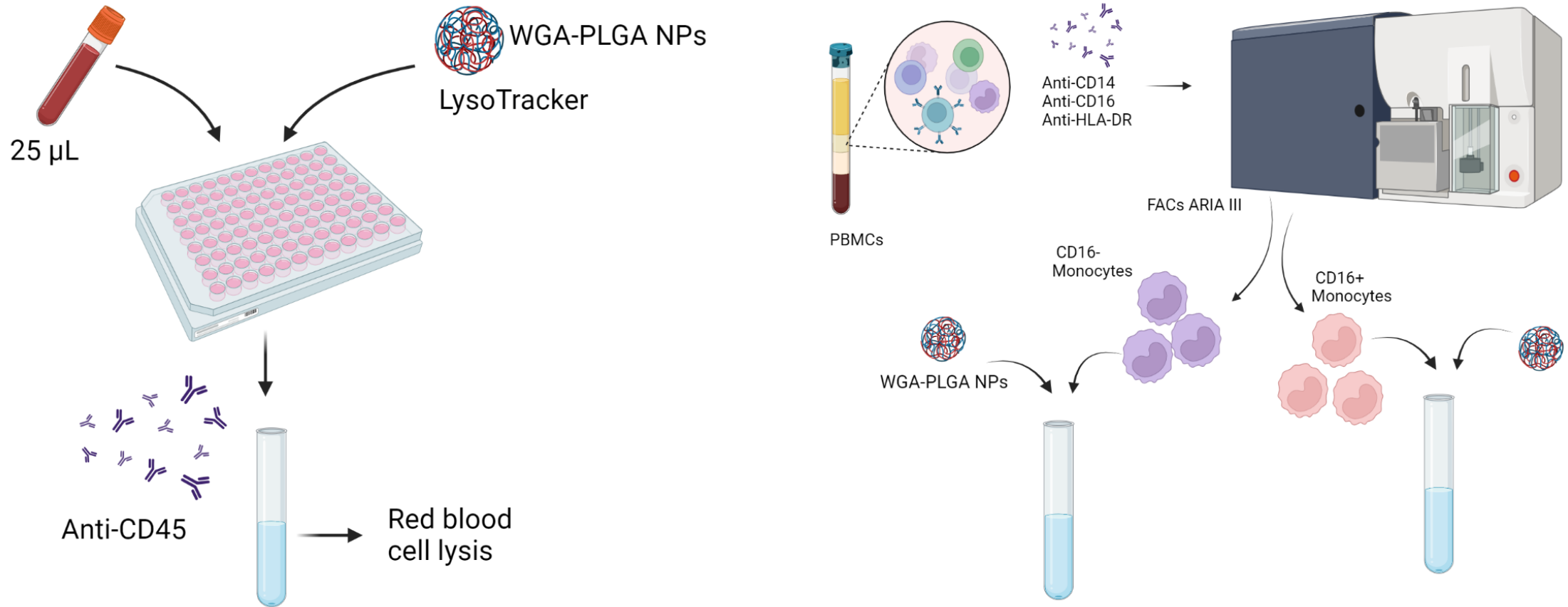


Monocytes subpopulations

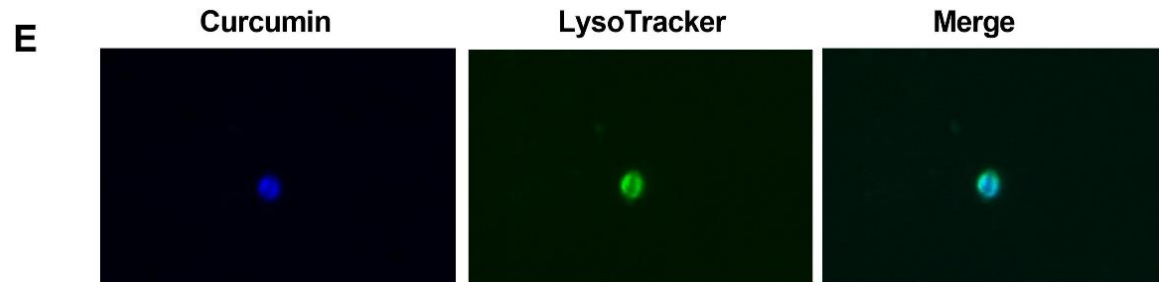
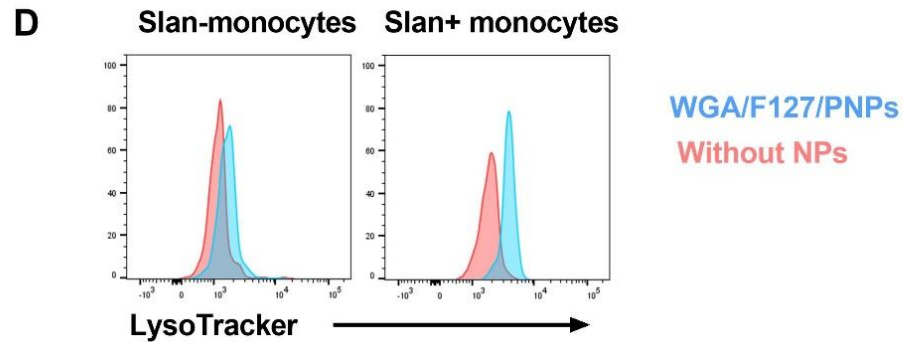
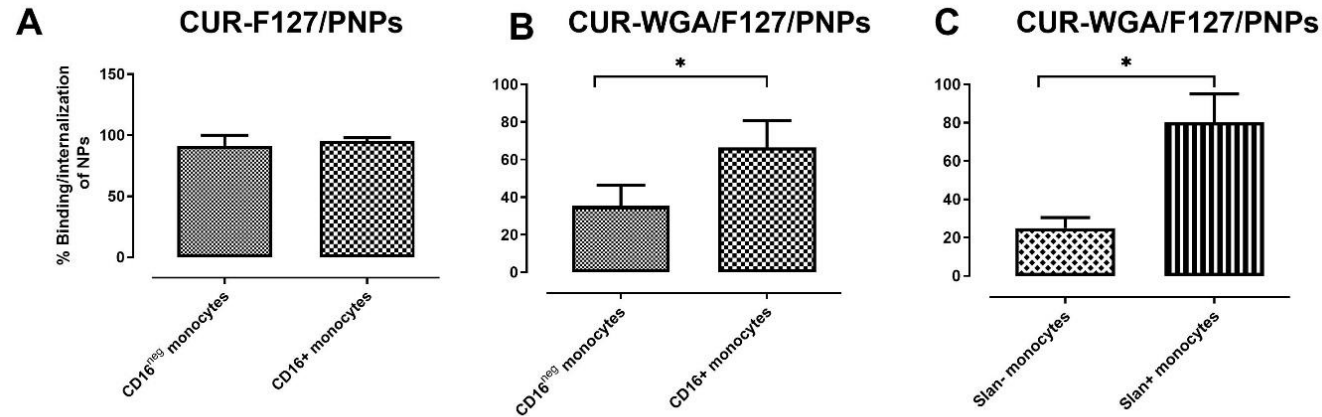


Relative and absolute counts of circulating non-classical and slan+ monocytes were significantly reduced in patients with SLE compared to healthy controls. This reduction was even more significant in patients with active SLE.

— Binding/Internalization assay —

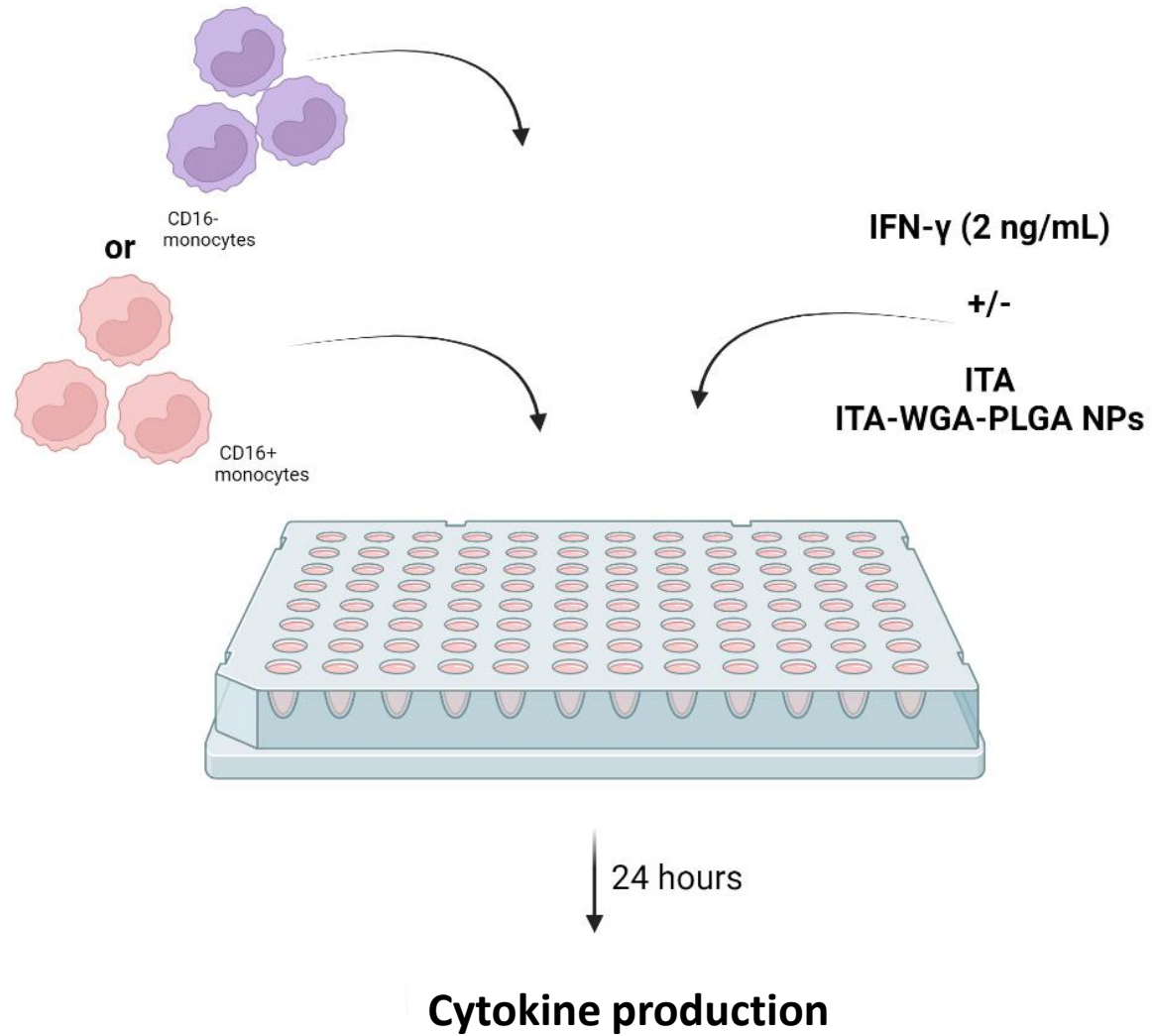


— Binding/Internalization of NP —

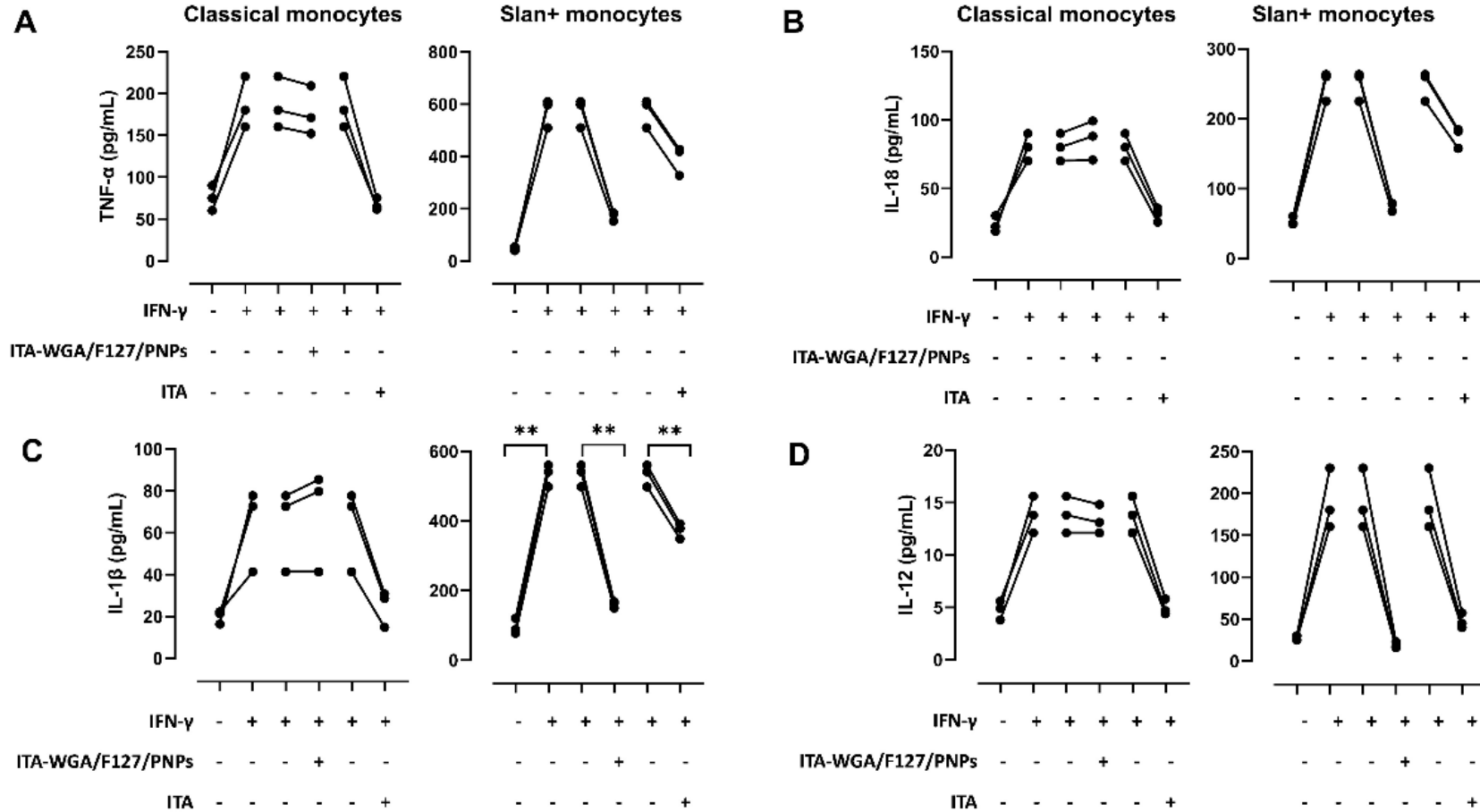


WGA-functionalization of curcumin-F127/PNPs increased their binding and internalization by the non-classical slan⁺ monocyte subsets

Cytokine production



Cytokine production



Bcytokine production

