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CD209+/CD14+ Dendritic Cells Characterization In Rheumatoid Versus Psoriasis Arthritis patients

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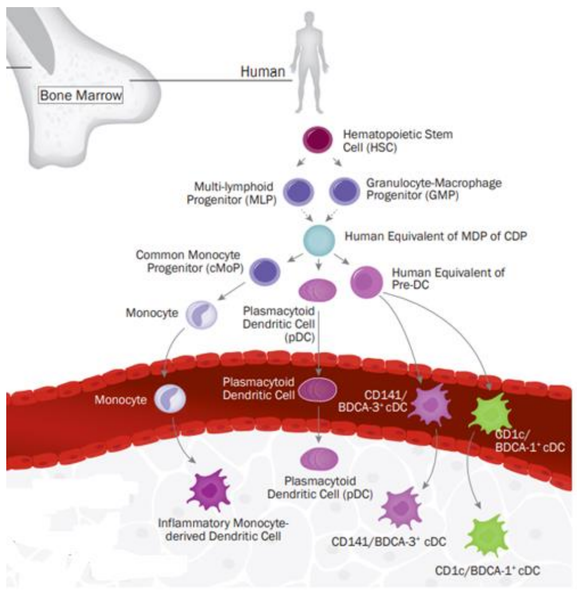
Introduction

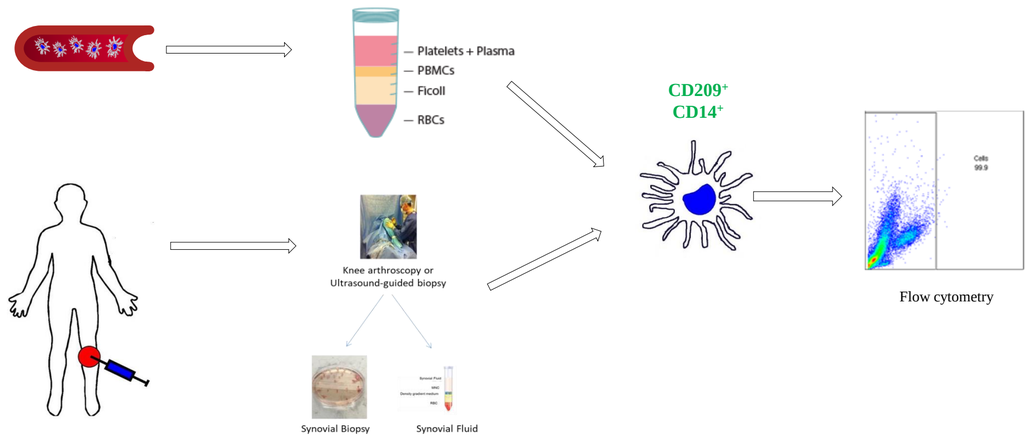
Dendritic cells (DCs) are a heterogeneous population of professional antigen-presenting cells which are at the interface between innate and adaptive immunity. There are different DC subsets which are classified according to their tissue location and function. A specific subset of DCs is known to derive from monocytes and have a key role in inflammation and infection.



Objective

This study firstly aimed to identify and characterize a specific subset of dendritic cells derived from monocytes ($CD209^+CD14^+$) and to evaluate their characteristics at the periphery of inflammatory arthritic patients: psoriatic (PsA) and rheumatic (RA) arthritis. In addition, it aimed to evaluate the enrichment and activation state of the specific DC subset at the site of inflammation, the joint of PsA and RA patients.

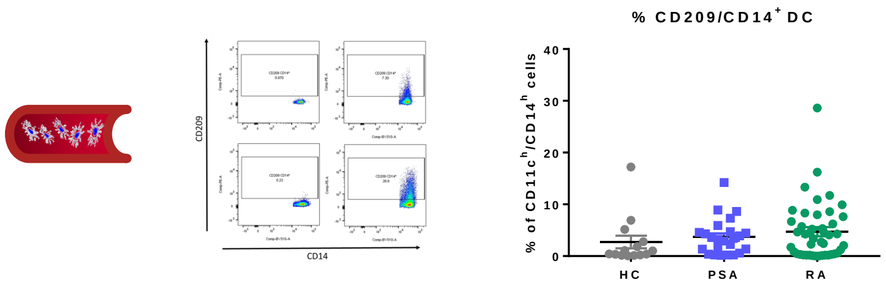
Experimental design



Results

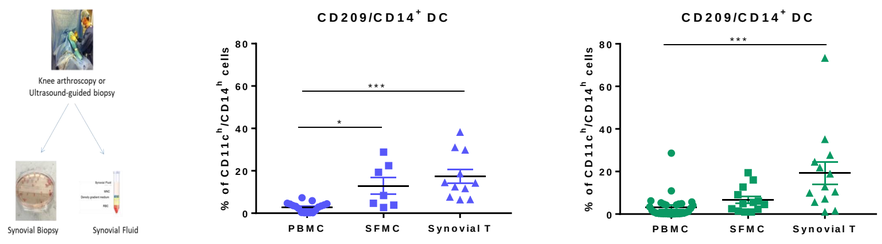
1. $CD209^+/CD14^+$ DC population in blood

The $CD209^+CD14^+$ DC population in the blood of healthy subject (HC), rheumatoid (RA) and psoriatic arthritic (PsA) patients was identified by flow cytometric analysis. The percentage of $CD209^+/CD14^+$ DC was not significantly different among the three groups.



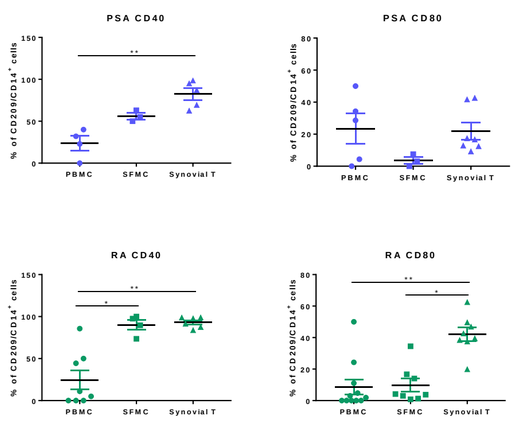
2. $CD209^+CD14^+$ DC population is enriched in the joint of RA and PsA patients

The $CD209^+CD14^+$ DC population was enriched in the synovial fluid mononuclear cells (SFMC) of both PsA ($p<0.05$), suggesting this population is recruited to the site of inflammation. In addition, we observed a further increase of the $CD209^+CD14^+$ DC population in the synovial tissue cell suspension (biopsy) of RA and PsA patients ($p<0.001$).



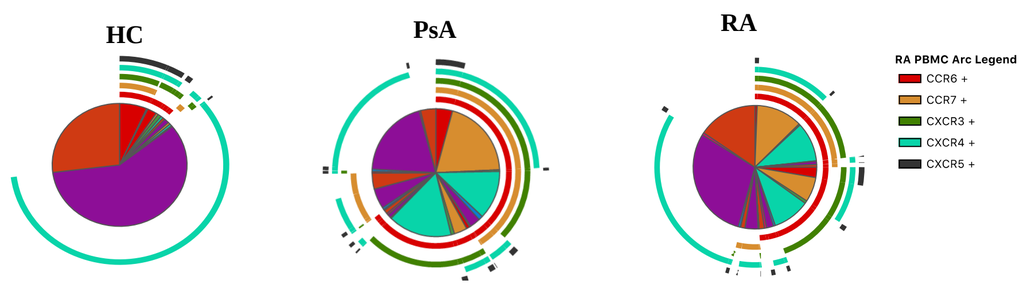
3. $CD209^+CD14^+$ DC population express DC maturation markers at the site of inflammation

The $CD209^+CD14^+$ DC population express higher percentages of the maturation marker CD40, and CD80 in SFMC and synovial tissue suspension RA patients, and at lesser extent PsA patients. This suggests that this DC population is in a semi-mature state in the joint and can be further activated



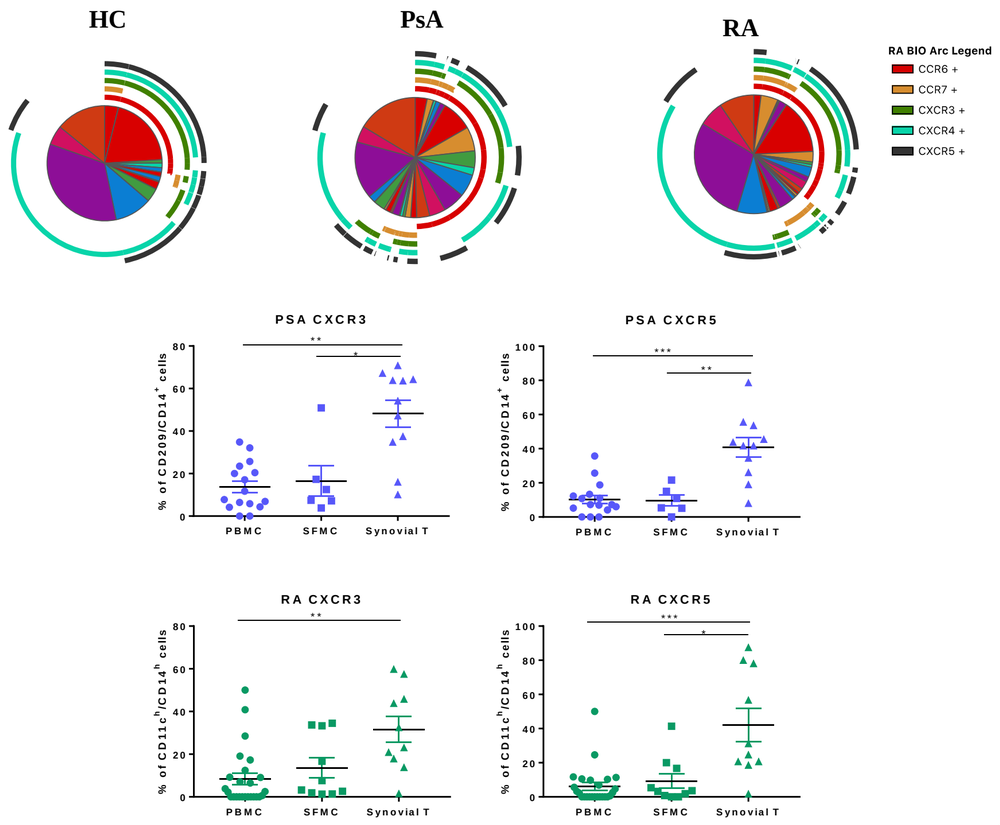
4. $CD209^+CD14^+$ DC population present a unique chemokine receptor expression profile in the periphery of PsA and RA patients

SPICE algorithm flow cytometric analysis identified a differential expression and co-expression of chemokine receptors at the periphery of RA and PsA patients, when compared to the HC, with higher percentage of CCR7, necessary for the trafficking of DC into the T cell-reach areas of lymph nodes for antigen presentation.



5. $CD209^+CD14^+$ DC population present a unique chemokine receptor expression profile at the site of inflammation

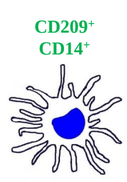
The chemokine receptor expression was further evaluated in the $CD209^+/CD14^+$ DC population at the site of inflammation, the synovial tissue cell suspension of both PsA and RA patients. A distinct profile of chemokine receptor was observed at the site of inflammation with increased percentage of CXCR3 and CXCR5, which may be involved in the recruitment and activation of DC cells.



Summary

- We identified for the first time, the $CD209^+CD14^+$ DC population in the periphery of HC, PsA and RA patients.
- The $CD209^+CD14^+$ DC population is enriched at the site of inflammation in both PsA and RA patients.
- The $CD209^+CD14^+$ DC population is in a semi-mature state in the joint, where it is further activated, as shown by higher expression of CD40 and CD80.
- The $CD209^+CD14^+$ DC population exhibit a unique chemokine receptor profile in the peripheral blood of PsA and RA patients, which is further defined at the site of inflammation.

Conclusions



The $CD209^+CD14^+$ DC population is recruited to the site of inflammation in both PsA and RA patients where it is further activated, suggesting a pathological role for the DC in the inflamed synovium of PsA and RA patients.

Chemokine receptor inhibition may be a new therapeutic approach to prevent the synovial accumulation of the pathogenic DC subset.

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