Disclosure of Interests: Wendy Gerhart Grant/research support from: The Canadian Spondylitis Association received funding from multiple pharmaceutical companies for the comorbidity awareness campaign., Employee of: I was employed by Janssen Canada until October 2016. I have been working with the Canadian Spondylitis Association since March 1, 2017. Janssen did not provide support for the awareness campaign., Gerald Major: None declared, Austin Gerhart: None declared, Marilyn Walsh: None declared
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OP0219-PARE LUPUS EUROPE YOUTH PANEL – WHAT WE LEARNED FROM YOUNG PEOPLE LIVING WITH LUPUS

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Background: Since 2014, Lupus Europe conducts patient panels, where 10 to 12 persons from all over Europe living with lupus discuss the selected topic guided by facilitators living with lupus themselves. This allows to capture qualitative feedback of relevance, without the obstacle of the "white blouse". In 2018, 10 Young (18-27) European Lupus patients (8 female, 2 male) with diverse Lupus types met to discuss "Lupus and youth".

Objectives: Understand specificity of being young with lupus to better include young patients in Lupus groups action plans

Methods: 11 young patients, mostly with little or no involvement in patient groups were recruited through Lupus Europe's network. They were asked to send ahead of time their top challenges/issues living with lupus as well as their key questions for the panel. This input was used to build the 2 days program itself. Mid May, 10 of the 11 met face-to-face in Brussels, and explored multiple aspects of their input through 7 specifically designed interactive workshops

Results: While they considered taking pills every day as a key problem, they preferred to focus on the collective issues of being understood by friends and family and having to live with limitations.

A big "Wow" was the feeling of guilt expressed by several female participants (guilt of imposing limits to their partners, guilt of not being able to do as much as others, ...), a very important underlying dimension of their social and affective life, which is likely much misunderstood by doctors and patient organizations; young people with lupus remain fundamentally more positive on their life with lupus than the average patients. While they perceive lupus as being "all over their lives", they refuse to be ruled by it...

They view the future of a LUPUS EUROPE youth group as a "virtual group" on social media, with minimal commitment required, but bringing together "friends" around highly visual messages, short stories and the exchange of ideas that could lead to small group gatherings.

On the medical front, when we probed what would drive them to consider joining a clinical trial, clear first media is their lupus doctor, second are national lupus groups and LUPUS EUROPE. Other medias have a very limited impact.

Conclusion: Young patients needs must be addressed in a more aspirational way and using more virtual tools than average patients (more focused on health issues and geographic proximity).

The feeling of guilt of young women with regards to their affective life must be further explored to give them confidence and reassurance.

REFERENCE:

- [1] Lupus Europe Patient panel 3 project report, available on request at secretariat@lupus-europe.org

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Fighting and fixing: from initiation to resolution of inflammation

OP0220

SINGLE-CELL TRANSCRIPTOMIC AND FUNCTIONAL ANALYSES REVEAL NOVEL HETEROGENEITY IN PATHOGENIC PATHWAYS MEDIATED BY HUMAN SYNOVIAL TISSUE MACROPHAGES

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Background: We hypothesise that synovial tissue macrophages (STM) are heterogeneous and mediate discrete pathogenic pathways that may underlie partial or absent therapeutic responses in RA patients. Better understanding of STMs will provide novel targets for re-instating synovial homeostasis. We have shown that the human synovium contains at least two major populations of STMs (CD206/MerTK^{neg} and CD206/MerTK^{pos}) with transcriptomes suggesting different function.

Objectives: To dissect the phenotypic and functional heterogeneity of STMs using single-cell transcriptomics and associated functional assays.

Methods: The relative proportions of the two major populations of STMs were quantified in 64 RA synovial biopsies (including 26 from RA patients in sustained remission), and in 8 healthy synovial tissues by flow cytometry. To uncover STM phenotypes, single-cell RNA sequencing of STMs from healthy donors (n=4), active RA (n=7; DAS28 ≥5.1) and RA in remission (n=4; DAS28 ≤2.6) was performed with 10X Genomics. 21,000 STMs were sequenced and analysed (Seurat). For functional analysis, CD206/MerTK^{neg} and CD206/MerTK^{pos} STMs were sorted from biopsies of active RA (n=15) and RA in remission (n=8). These were stimulated *in vitro* with LPS (to mimic activation by joint damage) or with LPS plus the MerTK agonist GAS6 to activate MerTK^{pos} STMs; or co-cultured with FLS.

Results: The synovium of healthy subjects and RA patients in remission contain predominantly CD206/MerTK^{pos} STMs, whereas RA patients with any disease activity additionally contain substantial proportions of CD206/MerTK^{neg} STMs. In active RA, the CD206/MerTK^{neg} STMs produce TNF while CD206/MerTK^{pos} STMs produce type I interferon following TLR4 activation. Interestingly, CD206/MerTK^{pos} STMs from RA patients in remission showed a limited response to TLR stimulation, and their cytokine production was further inhibited by GAS6. This regulatory function of GAS6/MerTK was confirmed in macrophage-fibroblast co-culture assays: inhibition of MerTK in macrophages increased macrophage-induced cytokine production by FLS. STM single-cell transcriptomic analysis uncovered further STM heterogeneity in healthy, active RA and RA in remission (5 distinct subpopulations). These included three subpopulations that were not present in healthy and remission RA. These inflammatory subpopulations differ in their expression of surface receptors, spectrum of activated pathways and in their frequency in the synovium of patients with similar high DAS28. One of the subpopulations, characterised by increased metabolism, pro-inflammatory cytokines (e.g. IL-1β, BAFF) and chemokines, dominated in 3 out of 7 RA patients with active RA analysed; the second, characterised by high levels of MHC II and GPR receptors in 2 out of 7 patients while the third one characterised by high levels of alarmins (e.g. S100A8, 9 and 12) dominated in the remaining 2 inflamed RA synovia.

Conclusion: Pathogenic diversity of inflammatory synovial tissue macrophage subpopulations may partially account for unpredictable clinical responses in RA. Identifying and targeting the predominant STM subpopulation may facilitate novel therapeutic development and eventually patient stratification.

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