Correspondence on “Isolation of HLA-DR-naturally presented peptides identifies T-cell epitopes for rheumatoid arthritis” by Maggi et al

The article titled ‘Isolation of HLA-DR naturally presented peptides identifies T cell epitopes for rheumatoid arthritis’ reports the elution and characterisation by mass spectrometry of ‘naturally processed’ peptides from the synovial fluid and synovium of patients with rheumatoid arthritis.1

It uses state of the art technology to produce monocyte-derived dendritic cells and analyse the peptides associated with their Human Leucocyte Antigen DR molecules by mass spectrometry. However, the whole project is based on the a priori hypothesis that RA develops in the synovium and that only synovium-derived antigens are relevant. Thus, dendritic cells are pulsed with IgG-depleted, albumin-depleted synovial fluid or synovial tissue (This eliminates any antigen contained in an immune complex.). Later, among the analysed proteins/peptides, sequences from skin-specific proteins are discarded (this would eliminate filaggrin) and citrullinated proteins are specifically selected. This way of constructing a study makes sure that nothing new will be found: RA ‘relevant’ autoantigens will be found in synovial extracts, some of them citrullinated...so what?

Besides this conception bias, the study ignores a peculiarity of HLA-DR processing in the context of RA. Indeed, the severe RA-associated HLA-DRB1*0401 allele has super efficient processing properties due to original intracellular route2 and the results should consider whether the DC donor expresses HLA-DRB1*0401 or not. Finally, data critical to understand the article are presented in table 1, under a highly confusing format: column 2, titled ‘HLA-DRB1 alleles’, presents HLA-DRB1 genotypes but fails to explain whether they belong to dendritic cells or to synovium. It is my understanding that they actually indicate the DC donor’s genotypes in the upper 14 lines and the synovium donor’s genotypes in the lower three lines, but if this is correct, then it is highly confusing.

Where RA starts, which antigen(s), citrullinated or not, trigger(s) the initial event(s) by activating (helper?) T cells is unknown and this high tech, high bias study will not help clarifying these issues.

Jean Roudier

1Autoimmune arthritis, INSERM UMRs1097, Aix Marseilles University, Marseille, France
2Rheumatology, APHM/IML, Marseilles, France

Correspondence to Professor Jean Roudier, Immunogenetics of RA, INSERM UMRs 1097, 13288 Marseille cedex 9, France; jean.roudier@insERM.fr

Handling editor Josef S Smolen

Contributors This letter is a short criticism of a recently published article.

Funding This study was funded by Institut National de la Santé et de la Recherche Médicale (UMRs1097).

Competing interests None declared.

Patient and public involvement Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Patient consent for publication Not applicable.

Ethics approval Not applicable.

Provenance and peer review Commissioned; internally peer reviewed.

Data availability statement Data sharing not applicable as no datasets generated and/or analysed for this study.

© Author(s) (or their employer(s)) 2022. No commercial re-use. See rights and permissions. Published by BMJ.

To cite Roudier J. Ann Rheum Dis Epub ahead of print: [please include Day Month Year]. doi:10.1136/annrheumdis-2022-222750

Received 4 May 2022
Accepted 5 May 2022

Linked

http://dx.doi.org/10.1136/annrheumdis-2022-222758


ORCID ID
Jean Roudier http://orcid.org/0000-0001-5435-8567

REFERENCES