

Behçet's disease: an MHC-I-opathy?

Sirs,

We read with great interest the elegant article by McGonagle *et al.* about lumping Behçet's disease with spondyloarthropathies through an abductive inference to a proposed "MHC-I-opathy" (1). To remind ourselves, an inductive inference starts with observations and experiments towards a hypothesis and a general truth. The deductive approach seeks to challenge an already formed hypothesis through data collection, experimentation and above all falsification. Finally the abductive approach seeks a pre-formed and suitable hypothesis at hand to fit with the observations made (2). While, we use the abductive approach every day when we diagnose diseases of unknown aetiology, when we try to tease out pathogeneses for such diseases, as the McGonagle *et al.* article attempts to, it will surely be desirable to add some deductive reasoning in our mental exercise.

1. As the authors point out, even in areas where the disease is endemic, only a portion of Behçet's disease patients carry the HLA B51 allele, or for that matter, any other MHC-1 allele in increased frequency. How would the proposed scheme of a barrier dysfunction operative through the HLA B51 work among the non carriers? The same query is surely present for HLA B27 – patients with AS.

2. Along the same line, the authors base many of their assumptions regarding differential immunopathology of clinical

features of Behçet's disease on a meta-analysis of the association of HLA B51/B5 with clinical characteristics of Behçet's disease. However, even with the types of lesions where a significant association was observed, the relative risks are quite low (eye involvement RR 1.13 (95% CI 1.06, 1.21), genital ulcers RR 1.07 (95% CI 1.01, 1.14) and skin involvement RR 1.10 (95% CI 1.03, 1.16)).

3. The association of certain HLA alleles with some clinical features but not with others within the same disease would more point out to the presence of disease clusters with possibly different underlying pathogenetic mechanisms, rather than the possibility of different diseases with this feature belonging to the same group.

4. The authors propose that mechanical factors might also be important in disease expression in "MHC-1-opathies". While what is said might be somewhat plausible for ankylosing spondylitis, the question of how would this mechanism extrapolate to the severe retinal pathology, very rare in ankylosing spondylitis, but a hallmark of Behçet's disease, surely needs to be readdressed.

5. We were curious not to find a reference to our group's previous work on the increased frequency of enthesitis in a subgroup of Behçet's disease patients who had acne and arthritis (3). It is worth noting that we had not observed an association with HLA B27 in this cluster of patients (4).

6. Finally the reader is told that the IL17-23 pathway is very important in the pathogenetic mechanism proposed for the MHC-1-opathies. This being the case, the reader also deserves a discussion of why

anti-IL17 treatment has singularly been unsuccessful in Behçet's disease (5).

One of us, HY, had ventured some 38 years ago that there were problems with the inclusion of Behçet's disease, which we really like to call a syndrome, among the seronegative spondyloarthritides (6). We remain to be persuaded otherwise.

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References

1. MCGONAGLE D, AYDIN SZ, GUL A, MAHR A, DIRESKENELI H: 'MHC-I-opathy'-unified concept for spondyloarthritis and Behçet's disease. *Nat Rev Rheumatol* 2015; 11: 731-40.
2. SCHICKORE J: Scientific discovery. In: ZALTA EN (Ed): The Stanford Encyclopedia of Philosophy. The Metaphysics Research Lab 2014.
3. HATEMI G, FRESKO I, TASCILAR K, YAZICI H: Increased enthesopathy among Behçet's syndrome patients with acne and arthritis: an ultrasonography study. *Arthritis Rheum* 2008; 58: 1539-45.
4. HATEMI G, FRESKO I, YURDAKUL S *et al.*: Reply to the letter by Priori *et al.* commenting on whether Behçet's syndrome patients with acne and arthritis comprise a true subset. *Arthritis Rheum* 2010; 62: 305-6.
5. DICK AD, TUGAL-TUTKUN I, FOSTER S *et al.*: Secukinumab in the treatment of noninfectious uveitis: results of three randomized, controlled clinical trials. *Ophthalmology* 2013; 120: 777-87.
6. YAZICI H: Behçet's disease. *Br Med J* 1978; 2: 952.