**Deregulated DNA damage response-repair network in Behcet’s disease**

Nikolaos I. Vlachogiannis¹, Panagiotis A. Ntouros¹, Maria Pappa¹, Kleo-Maria Verrou¹², Aikaterini Arida¹, Vassilis L. Soulitis¹³, Petros P. Sfikakis¹²

1. Joint Rheumatology Program, National and Kapodistrian University of Athens Medical School, Athens, Greece
2. Center of New Biotechnologies & Precision Medicine, National and Kapodistrian University of Athens Medical School, Athens, Greece
3. Institute of Chemical Biology, National Hellenic Research Foundation, Athens, Greece

**Background**

**AIM:** To search for potential aberrations in DNA damage response and repair network in BD

**RESULTS-1:** Increased endogenous DNA damage levels

Using single-cell gel electrophoresis (alkaline comet assay) we found that patient-derived PBMCs displayed higher levels of single-/double-strand DNA breaks.

**RESULTS-2:** Excessive DNA damage formation and increased oxidative stress

BD-derived PBMCs showed 2-fold lower GSH/GSSG indicative of increased oxidative stress levels, as well as 3-fold increased abasic sites, resulting to excessive formation of DNA damage.

**RESULTS-3:** Defective nucleotide excision repair (NER) and DNA double-strand break repair (DSBR) in BD

Functional analysis after ex vivo treatment of PBMCs with UVC-irradiation or melphalan revealed defects in 2 central DNA repair mechanisms, namely NER and DSBR, in BD patients.

**RESULTS-4:** Increased DNA damage correlates with decreased mRNA expression of DNA repair enzymes

Expression of central DNA repair enzymes as shown by RNA-sequencing, including ATM and NEIL1, was decreased in BD. Individual DNA damage levels in PBMCs showed a negative correlation with gene expression of both ATM and NEIL1.

**RESULTS-5:** Increased DNA damage correlates with elevated expression of senescence markers

Expression of the senescence gene p21/CDKN1A was increased in BD showing a positive correlation with endogenous DNA damage levels.

**Conclusion**

Inflammation in BD is associated with a) increased oxidative stress, resulting in excessive DNA damage formation, and b) defective DNA repair in PBMCs.

The latter may be partly mediated by transcriptional downregulation of central DNA repair enzymes.

Whether the subsequent DNA damage accumulation fuels the inflammatory cascade warrants further study.

No conflicts of interest

Correspondence: nivlachogiannis@gmail.com; psfikakis@med.uoa.gr