standard:0, No swelling;1, Slight redness and swelling;2, Moderate redness and swelling of ankle; 3, Severe redness and swelling of the entire paw;4, Maximally inflamed limb with involvement of multiple joints [3]). Day 28–42, hind foot redness and swelling of the mouse continued to develop and extended to the forefoot. Compared with the normal group, incidence of CIA model group reached 100%. Day 49, compared with the model group by joint scores, medium-dose group, high-dose group and leflunomide group have Significant differences on CIA model ($p<0.01$). Compared with the Leflunomide group, low-dose group, medium-dose group and high-dose group have no obvious difference ($p>0.05$). Compared with the low-dose group, medium-dose group and high-dose group have no difference ($p>0.05$).

Table 1. Joint scores (mean ± SD)

groups	28d	35d	42d	49d
a	o	o	o	o
b	8.05±1.62	12.40±2.10	14.68±1.77	12.33±1.68
c	8.66±0.14	11.99±0.23	12.10±0.23**	11.30±0.22**
d	7.90±0.34	11.40±0.18	12.80±0.20**	12.00±0.13
e	7.40±0.23	10.90±0.13*	10.40±0.44**	10.60±0.36**
f	8.80±0.24	10.60±0.30*	11.30±0.22**	8.80±0.55**

a. Blank group. b. Model group. c. Leflunomide group. d. Low-dose group. e. Medium-dose group. f. High-dose group. Compared with the model group, *$p<0.05$, **$p<0.01$.

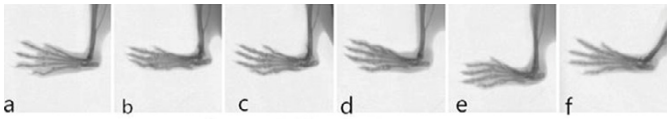

figure 1. Ankle Joint X-ray

a.blank group b.model group c.leflunomide group d.low-dose group e.medium-dose group f.high-dose group

Conclusions: CIA model has a high morbidity, long duration, macroscopic pathological manifestation and irreversible ankle joint deformation, which is consistent with the progress of human RA disease and pathological damage. Medium-dose of ChuanTengTongBi decoction, high-dose and leflunomide group had inhibitory effect on the progress of arthritis, and the effect of high-dose was better than that of leflunomide group.

References:

[1] Brand, D.D. Rodent models of rheumatoid arthritis. Comp. Med. 55, 114–122(2005).

[2] Shen S, Yang Z, Yiyang H U, et al. The Effect of Tripterygium Wilfordii glycoside on the Expression of CD_4+CD_(25)~(high) Regulatory T cells,Th1 and Th2 with IgA Nephropathy[J]. Chinese Journal of Integrated Traditional & Western Nephrology, 2013.

[3] David D Brand, Kary A Latham, & Edward F Rosloniec. Collagen-induced arthritis. Nature Protocol.5.1270–1274(2007).

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3396

AB0111 CADMIUM NANOPARTICLES CITRULLINATE INTRACELLULAR CYTOKERATINS: CADMIUM POTENTIALLY LINKS RHEUMATOID ARTHRITIS TO SMOKING AND NUMEROUS WORKING CLASS OCCUPATIONS

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Background: Smoking has emerged as a consistent risk factor for ACPA positive RA, although the specific constituents of cigarette smoke that induce citrullination are unknown. It has been hypothesised that cadmium triggers RA as its inhalation links various well established risk factors for RA such as smoking (the most important environmental source of cadmium) and numerous working class occupations [1].

Objectives: To determine whether the cadmium-derived materials induce intracellular citrullination.

Methods: Human A549 lung epithelial cells were exposed to cadmium in ionic and particulate form represented by cadmium chloride and cadmium oxide, respectively, and their combinations with ultrafine carbon black (ufCB) nanoparticles produced following high temperature combustion, imitating cigarette burning. Protein citrullination in cell lysates was analysed by SDS-PAGE electrophoresis with western blotting and verified by immunofluorescence staining and confocal microscopy. Target citrullinated proteins were identified by proteomic analysis.

Results: Cytotoxicity studies demonstrated that cadmium compounds were toxic to the cells. Based on the results of cytotoxicity measurements, all the materials utilised in the experiments were subsequently applied to the cells in sub-toxic concentrations. Cadmium oxide, ufCB and its combination with cadmium chloride and cadmium oxide after high temperature combustion induced citrullination of multiple proteins in cultured human lung epithelial cells of A549 cell line, as demonstrated by SDS-SDS-PAGE electrophoresis and western blotting. This phenomenon develops via a peptidylargininedeiminase-dependent mechanism, as demonstrated in our previous studies [2]. The majority of citrullinated proteins were represented by the bands corresponding to the molecular weights between 55 and 72 kDa, and several less abundant bands at the level of ~25kDa and over 130 kDa. Acidic cytokeratins of type I (9, 10) and basic/neutral cytokeratins type II (1, 2, 5, 6A, 6B and 77) were identified as major intracellular citrullination targets. Immunofluorescent staining demonstrated that the citrullinated proteins were localised both in the cytoplasm and nuclei of cells exposed to cadmium particles, similar to the distribution patterns observed in cells exposed to ufCB.

Conclusions: Cadmium nanoparticle exposure facilitates post-translational citrullination of proteins.

References:

[1] Hutchinson D. Cadmium, one of the villains behind the curtain:has exposure to cadmium helped to pull the strings of seropositive rheumatoid arthritis pathogenesis all along? International journal of rheumatic diseases 2015;18:570–3.

[2] Mohamed BM, Verma NK, Davies AM, McGowan A, Crosbie-staunton K, Prina-Mello A, et al. Citrullination of proteins:a common post-translational modification pathway induced by different nanoparticles in vitro and in vivo. Nanomedicine 2012;7:1181–95.

Acknowledgements: This work has been supported by the Higher Education Authority of Ireland, Science Foundation of Ireland through the Advanced Materials and BioEngineering Research (AMBER) project (Grant #SFI/12/RC/2278) and the Cornwall Arthritis Trust.

Disclosure of Interest: None declared

DOI: 10.1136/annrheumdis-2017-eular.3620

Spondyloarthritis - etiology, pathogenesis and animal models

AB0112 INTERFERON-REGULATED GENES (IRG) SIGNATURES DIFFERENTIATE GROUPS OF AS PATIENTS AND ARE ASSOCIATED WITH ANTI-TNF RESPONSE: PILOT DATA

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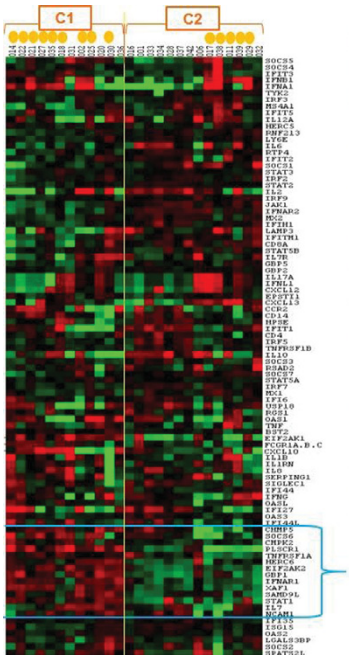
Background: Ankylosing Spondylitis (AS) is a chronic inflammatory arthritis characterised by sacroiliac/ lumbar spinal inflammation and extra-articular manifestations. Currently, TNF inhibitors (TNFi) are licensed for treatment-refractory AS; however, many patients do not respond to treatment and there is no way to predict Response/Non-Response (R/NR). The expression of several Interferon (IFN) signalling related genes (IRG) are associated with inflammatory diseases, including AS. Furthermore, an IRG expression signature has been used to predict treatment response in phase-Ia trials in systemic lupus erythematosus (1), demonstrating the feasibility of the use of IRG signatures as biomarkers in routine clinical practice.

Objectives: To explore whether IRG signatures differentiate groups of AS patients, and can be associated with response to TNFi in AS.

Methods: Twenty-six week-0 peripheral blood mononuclear cell (PBMC) samples



Unsupervised Hierarchical Clustering of IRG in AS patients

Red represents higher levels of gene expression and green represents lower levels of gene expression of the corresponding gene following normalisation to the housekeeping gene, GAPDH. Clustering defined two groups (C1 and C2), driven by expression of the 14 IRG (blue box). Patient study numbers are listed at the top of the cluster. An orange dot adjacent to a particular patient indicates that they were an ASDAS NR.