for targeted and therapeutic manipulation of the microbiota in chronic inflammatory diseases.

Methods We have developed high-resolution microbiota flow cytometry which allows us to analyze the microbiota on a single cell level. This provides a non-invasive, fast and efficient diagnostic tool to visualize dramatic changes of microbiota composition in inflammatory diseases, fast and efficiently, and isolate distinct bacteria for functional and molecular analyses.

Results We have identified bacteria belonging to the genus *Anaeroplasm*, which enhances the levels of mucosal IgA. Adoptive transfer of *Anaeroplasm* increases the numbers of IgA+ germinal center B cells in the Peyer's patches and of IgA-secreting plasma cells in the lamina propria of the small intestine leading to significantly enhanced mucosal IgA levels. *Anaeroplasm* controls IgA expression presumably its ability to induce expression of the regulatory cytokine TGF- β in T cells, as we show here.

Conclusions The anti-inflammatory properties of *Anaeroplasm* to induce the anti-inflammatory cytokine TGF- β , thereby also strengthening the intestinal barrier by enhancing mucosal IgA, qualify *Anaeroplasm* as potent probiotic for the prevention and treatment of chronic inflammation.

Disclosure of Interest None declared.

P105

IDENTIFICATION OF RARE CODING VARIANTS IN IL-1-RELATED PATHWAYS IN PATIENTS WITH ADULT-ONSET STILL'S DISEASE

^{1,2}G Cavalli*, ²R van Deuren, ^{2,3}P Arts, ³M Steehouwer, ⁴P Sfriso, ⁵S Colafrancesco, ⁵R Priori, ⁶L Cantarini, ¹E Baldissera, ²F van de Veerdonk, ¹L Dagna, ³A Hoischen, ^{2,7}CA Dinarello. ¹Unit of Immunology, Rheumatology, Allergy and Rare Diseases (UnIRAR), Vita-Salute San Raffaele University, Milan, Italy; ²Radboud Institute of Molecular Life Sciences; ³Department of Human Genetics, Radboud University Medical Center, Nijmegen, Netherlands; ⁴Rheumatology, University of Padua, Padua; ⁵Rheumatology, Sapienza University, Rome; ⁶Rheumatology, University of Siena, Siena, Italy; ⁷Department of Medicine, University of Colorado Denver, Aurora, CO, USA

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Career situation of first and presenting author Assistant.

Introduction Adult-onset Still's disease (AOSD) is a rare auto-inflammatory disease characterized by fever, arthritis, and multi-organ involvement. Inflammation in AOSD is mediated by interleukin (IL)-1 β , as confirmed by the clinical efficacy of selective blockers. The genetic predisposition to this IL-1-driven inflammation remains nevertheless elusive. Previous studies failed to identify associations between polymorphisms in the IL-1 genes and AOSD, thus pointing at more complex genetic mechanisms. These cannot be investigated with traditional techniques for genetic partitioning, such as GWAS, which only assess common variants and polymorphisms. Studies focusing on highly penetrant rare variants or different types of mutations (i.e. small copy-number variations; insertions/deletions) are warranted.

Objectives We hypothesized that genetically determined changes in IL-1-related pathways resulting in excessive IL-1 β activity lead to the development of autoinflammation in AOSD. Scope of this study was to unravel the combined mutational variation of a network of IL-1-related receptors, pathways, counter-regulators, and cellular processes possibly involved in the pathogenesis of IL-1-mediated inflammation.

Methods We collected clinical and genetic data from a large cohort of 76 AOSD patients and developed an innovative platform based on molecular inversion probes technology, which enables highly multiplexed targeted-resequencing of the coding sequence of 48 genes related to the IL-1-pathway, and allows studying rare and common variants in one assay. We have also screened 500 healthy controls, and 1000s of samples with other disorders using the same assay.

Results We identified rare and unique (i.e. private variants) in the IL-1 pathway in several individuals with AOSD. Whether any of these are involved in a strong predisposition to AOSD is currently followed-up. Rare genetic variants have been identified in six IL-1-pathway 'clusters':

1. Inflammasomes;
2. IL-1 pathway;
3. IL-1 family;
4. IL-18 pathway;
5. Autophagy;
6. ROS production.

Conclusions Unraveling the genetic bases of inflammation in AOSD deepens our understanding of the human innate immunome. This study platform may now serve for the genetic analysis of other IL-1-mediated conditions (i.e. gout and other autoinflammatory diseases), whose genetic predisposition remains elusive. Equally important, the identification of pathways amenable to targeting with small molecules or biologics may translate into remarkable clinical implications.

Disclosure of Interest None declared.

P106/O25

DNA METHYLATION IN LYMPHOCYTE SUBSETS AS A MEDIATOR OF GENETIC RISK IN EARLY RHEUMATOID ARTHRITIS

¹AD Clark*, ²N Nair, ¹AJ Skelton, ¹AE Anderson, ¹N Thalayasingam, ¹N Naamane, ¹J Diboll, ²J Massey, ²S Eyre, ²A Barton, ¹JD Isaacs, ³LN Reynard, ¹AG Pratt. ¹Institute of Cellular Medicine and NIHR Newcastle Biomedical Research Centre, Newcastle University and Newcastle upon Tyne Hospitals NHS Foundation Trust, Newcastle Upon Tyne; ²ARUK Centre for Genetics and Genomics, Centre for Epidemiology and NIHR Manchester Musculoskeletal Biomedical Research Centre, Manchester University and Manchester University NHS Foundation Trust, Manchester; ³Institute of Genetic Medicine, Newcastle University, Newcastle upon Tyne, UK

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Career situation of first and presenting author Student for a master or a PhD.

Introduction Genome-wide association studies (GWAS) have identified over 100 RA-associated risk loci, whose enrichment for lymphocyte-specific enhancer elements is consistent with a regulatory function of many causal variants in these cells. Epigenetic modifications have also been strongly implicated in RA pathogenesis.

Objectives To investigate the role of DNA methylation as a mediator of RA genetic risk.

Methods CD4+ T lymphocyte-specific DNA and RNA were extracted from freshly isolated blood of 43 RA and 60 disease control patients, along with equivalent material from B-lymphocytes of 46 RA and 73 controls. Comparator groups were drug-naïve and matched for age, sex, and acute phase response. Genotyping, gene expression and methylation