Figure 1. NAPA performed on healthy donor mo-DCs incubated with native, PAD2-citrullinated, and PAD4-citrullinated fibrinogen. Alpha, beta, and gamma chains of fibrinogen are shown separately. Each colored line represents a unique peptide. Nested peptides with a common core motif are shown in the same color. Grey bar denotes peptides with identical core motif between samples.

Artificial intelligence and osteoarthritis

OP0327

EVALUATION OF THE ARTIFICIAL INTELLIGENCE SYSTEM ACCURACY IN DETERMINING THE RADIOGRAPHIC STAGE OF KNEE OSTEOARTHRITIS

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Background: Within the last decade, rapid development of artificial neural networks and machine reading programs and their introduction into medical practice is reported [1,2,3]. Recently, an innovative program, based on the artificial intelligence (AI) technologies (a neural network and machine reading) that analyses knee X-ray images for determining the radiographic stage of OA was created. It was launched on the Osteoscan.ru website and is available for use by patients and doctors.

Objectives: to validate the system ability to accurately stage OA through machine interpretation of standard knee radiographs.

Methods: Initially, 1300 x-rays of both knee joints were used to teach the neural network. Of these, 350 were presented in the form of film scans, 950 in the DICOM format.

The accuracy of the system in recognition of OA stage by knee radiographs was evaluated on a quality control sample of 130 cases (of all 1300). Independently, the radiographs were assessed by certified radiologists (considered the "gold standard") and the System.

Results: In 124 out of 130 cases the conclusion of a specialist and the System was the same, which represents 95.4% predictive power. Coincidence or discrepancy is a qualitative attribute, so, the accuracy of the estimation was calculated. Assuming a discrepancy of 0, and coincidence - of 1, $\mu = 0.954$, the standard error $s_p = 1.8\%$. It can be concluded that in 95% of cases the accuracy of the system assessment will be in the range from 91.8% to 99%.

Conclusion: Osteoscan is a program developed on the base of AI technologies, analyzes radiographic images of the knee joints for determining OA stage. It provides high accuracy in OA stage determining by assessing knee radiographs, in 95% of cases, the accuracy of the system varies from 91.8% to 99%.

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Autoimmune diseases by abnormal T cell function

OP0328

A UNIQUE PD1+CD38+ CD8+ T CELL POPULATION CHARACTERIZES CHECKPOINT INHIBITOR-ASSOCIATED INFLAMMATORY ARTHRITIS

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Background: Immune checkpoint inhibitors (CI) are monoclonal antibodies that block CTLA-4, PD-1 or PD-L1, resulting in cytotoxic T cell activation in the tumor microenvironment. They have revolutionized the management of metastatic cancer but unleash "immune related adverse events" in > 80% of treated patients, including inflammatory arthritis in ~4%. CI-associated arthritis (CI-A) often presents as a symmetrical polyarthritis, phenotypically indistinguishable from rheumatoid arthritis (RA), but whether it shares cellular and molecular features of RA has not been determined.

Objectives: To compare synovial fluid (SF) T cell populations from CI-A patients to those in patients with RA, phenotypically and functionally.

Methods: We immunophenotyped SF mononuclear cells from patients with CI-A caused by anti-PD-(L)1 therapy (n=9), seropositive RA (n=5), and psoriatic arthritis (PsA) (n=5) using a 39-marker mass cytometry (CyTOF) panel. FlowSOM was used to cluster CD4 and CD8 T cells into 15 'metaclusters' based on multidimensional phenotypes. We used Kruskal-Wallis or Mann-Whitney tests to identify significantly altered populations (p<0.05), which we confirmed by biaxial gating. Flow cytometry was used to confirm SF findings in an independent cohort, and to identify cells of interest in peripheral blood. Cytokine staining was performed on sorted T cells populations after CD3/CD28 stimulation for 72 hours, followed by 4 hour PMA/ION+BRA/MON restimulation.

Results: In CI-A patients, T cells represented 50% of SF mononuclear cells (53% CD4, 40% CD8), followed by monocytes (24%) and NK cells (8%), comparable to RA and PsA. However, FlowSOM analysis revealed expansion of a distinct population of PD-1⁺ CD38^{hi} CD127⁺ CD8 T cells (CD8 metacluster2) (Fig. 1). These cells comprised 30% of CD8⁺ SF T cells in CI-A, a 3.4-fold increase over RA/PsA, p=0.0002 (Fig. 2). Over 40% of these cells expressed Ki67 in CI-A, suggesting active proliferation. Flow cytometry on SF cells from an independent cohort of CI-A patients (n= 5) and RA/PsA comparators (n= 9) confirmed our findings. PD-1⁺ CD38^{hi} CD127⁺ CD8 T cells were also expanded in the blood of CI-A patients, where they represented 4.6% of CD8 T cells, a 2.8-fold increase over RA, p=0.0057. In addition to expressing high levels of PD-1, CD38^{hi} CD127⁺, these CD8 T cells express other immune checkpoint receptors including ICOS and TIGIT. After in vitro stimulation, CD38^{hi} CD127⁺ CD8 T cells produced granzyme B along with TNF and IFN- γ at comparable levels to other CD8 populations, suggesting that they are not functionally exhausted.

Figure 1. Mass cytometry CD8⁺ T cells (tSNE plots) with FlowSOM metaclusters.

FlowSOM analysis of SF CD4 T cells in CI-A patients revealed the expansion of a subpopulation of CD4 cells with a similar surface phenotype of PD-1⁺ CD38^{hi} CD127⁺ (metacluster2, 10% of CD4s in CI-A, a 2.4-fold increase over RA/PsA, p=0.0047). In contrast, RA patients had a significantly expanded population of PD-1⁺ ICOS⁺ CD4 T peripheral helper (Tph) cells (metacluster5, 30% of CD4s in RA, p=0.006), but these cells were not expanded in CI-A (Fig 3).

Conclusion: CyTOF analysis of SF revealed a uniquely expanded PD-1⁺ CD38^{hi} CD127⁺ CD8 T cell population in CI-A not present in RA or PsA, and a similar PD-1⁺ CD38^{hi} CD127⁺ CD4 T cell population. These cells may contribute to the amplified immune response seen in CI-A patients. Further functional and transcriptional analysis of these cells will help to elucidate their function.

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