FRI0355

MUCOSAL ASSOCIATED INVARIANT T-CELLS ARE ENRICHED AT THE HUMAN ENTHESESIS AND HAVE A RESIDENT MEMORY PHENOTYPE

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Background: Mucosal associated invariant T-cells (MAITs) are innate-like T lymphocytes that express a semi-invariant TCR repertoire. They are activated by microbial ligands or cytokines including IL-23 and secrete inflammatory cytokines, including IFN γ and IL-17A. MAIT cells are enriched at mucosal surfaces and have been implicated in the pathogenesis of spondyloarthritis (SpA) (1) and inflammatory bowel disease (IBD). Although the human enthesitis is not a mucosal surface it is the primary site of inflammation in SpA which has strong association with IBD.

Objectives: To investigate if a population of MAITs is present at the normal human enthesitis thereby establishing a potential link between gut and joint inflammation.

Methods: Healthy interspinous ligament and spinous process were harvested from patients undergoing elective surgery for the correction of mechanical spinal defects. Enthesal soft tissue (EST) and peri-enthesal bone (PEB) were separated and cells were harvested by enzymatic and mechanical digestion respectively. The proportion of cells expressing markers consistent with MAITs (CD45+, CD3+, CD161+, TCRV α 7.2+) were measured by flow cytometry in EST, PEB and matched blood. Expression of CD69 and CD45RA were examined for phenotypic analysis. Transcript analysis for IL-23/IL-17 axis and immunomodulatory genes was performed on sorted enthesal MAITs and analysed by TaqMan array.

Results: As a proportion of total T-cells, MAITs were of approximately 3 fold and 2.5 fold greater abundance in EST and PEB respectively in comparison to matched peripheral blood (both $p=0.034$). MAITs in enthesal tissue had an overwhelming resident memory phenotype (CD69+, CD45RA-) median 53.2% (range 42.4 – 78.6%) in EST and 54.9% (45.2 – 82.1%) in PEB compared to those from blood 17.7 (6.8 – 69.4). MAITs robustly expressed RORC, CCR6 and IL-23R transcript. Compared to conventional enthesal T-cells, MAITs expressed significantly less TGF β (6-fold, $p>0.001$) and significantly more IL-23R (29-fold, $p=0.004$).

Conclusion: Healthy human enthesal tissue contains an enriched population of MAITs that strongly express IL-23R transcript at a frequency comparable to that reported in the colon (2). The majority of these cells express a resident memory phenotype suggesting that they are a distinct population residing in enthesal tissue. These observations are potentially relevant to SpA pathogenesis and the observed link between SpA and IBD.

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FRI0356

DIFFERENTIAL EXPRESSION OF HUMAN ENDOGENOUS RETROVIRUSES IN PSORIATIC DISEASE

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Background: Human endogenous retroviruses (HERV) are the stably inherited remnants of ancient retroviruses that infected the ancestral germline. A growing body of research has associated the differential expression and regulation of HERVs with a number of diseases, including

systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA). HERVs are thought to contribute to the pathogenesis of autoimmune diseases by modulating the expression of host immune-related genes, molecular mimicry, or cross reactivity of host proteins with HERV encoded products.

Objectives: To compare the expression of 4 HERVs previously associated with autoimmune disorders (HERV-K, HERV-K10, HERV-W, and HERV-H) in whole blood, CD3+ T cells, and CD14+ monocytes of patients with cutaneous psoriasis without arthritis (PsC), psoriatic arthritis (PsA), and healthy controls.

Methods: PsC, PsA patients satisfying the CASPAR criteria, and healthy controls were recruited for the study. RNA was extracted from whole blood collected in Tempus tubes and HERV expression was measured by quantitative real time PCR (qRT-PCR) or droplet digital (dd)PCR with normalization to GAPDH. HERV expression in whole blood RNA from 40 PsA patients was compared to 40 age and sex matched PsC patients and 40 age and sex matched healthy controls. Subsequently, HERV expression in 55 PsC patients who progressed to develop PsA (converters) was compared to 55 age and sex matched PsC patients who did not develop PsA over the same duration of follow-up (non-converters). Finally, HERV expression in RNA isolated from CD3+ T cells and CD14+ monocytes from 19 PsA patients was compared to 13 PsC and 8 healthy controls. Expression differences between groups were determined by one-way ANOVA, Kruskal-Wallis and Mann-Whitney tests where appropriate.

Results: In whole blood, HERV-K was significantly differentially expressed between 40 PsA and 40 PsC patients (fold change [FC]=1.57, $p=0.008$). HERV-K was also significantly differentially expressed in baseline samples from 55 converters compared to 55 non-converters (FC=1.93, $p=0.03$). No other HERV genes were differentially expressed between these groups in whole blood. Significant expression differences were more evident in purified cells (Table 1).

Table 1. Differential expression of HERVs in purified T cells and monocytes.

	PsA vs. PsC		PsA vs. Controls		PsC vs. Controls	
	CD3+ T cells FC, p value	CD14+ Monocytes FC, p value	CD3+ T cells FC, p value	CD14+ Monocytes FC, p value	CD3+ T cells FC, p value	CD14+ Monocytes FC, p value
HERV-K	0.43, $p=0.02$	0.30, $p<0.01$	ns	0.17, $p<0.01$	2.18, $p=0.02$	ns
HERV-K10	2.94, $p=0.02$	ns	6.87, $p<0.01$	2.60, $p=0.04$	ns	ns
HERV-H	ns	ns	3.19, $p<0.01$	0.36, $p=0.02$	2.67, $p=0.01$	0.27, $p<0.01$
HERV-W	1.27, $p=0.04$	ns	4.12, $p<0.01$	ns	3.24, $p=0.01$	0.47, $p=0.04$

Ns, not significant.

Conclusion: In whole blood, expression of HERV-K differentiates PsA and PsC patients, and its expression is significantly elevated in PsC patients prior to the development of PsA. HERV expression differences between the groups are also evident in purified T cells and monocytes. These data suggest a role for HERVs in the pathogenesis of psoriatic disease and their potential use as prognostic markers of arthritis in patients with psoriasis.

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FRI0357

DRUG-INDUCED REMISSION AND SUBCLINICAL ACTIVITY IN PSORIATIC ARTHRITIS: TRANSCRIPTIONAL PROFILING TO CHARACTERIZE THE DISEASE STATE

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Background: Remission is an important goal of therapy in psoriatic arthritis (PsA), but data on molecular players of clinical remission and effective