SUPPLEMENTARY MATERIAL

# Supplementary Material

**Table i.** Search string for systematic review on the role of metabolic profiling in human synovial fluid.

| Search term |
|---|
| metabo#omic*; metabolome*; metabolic adj profil*; metabolite*; biomarker*; biologic* adj marker*; exp Metabolomics/; exp Metabolome/ |
| **AND** |
| synovia*; joint fluid*; articular fluid*; synovium |
| **NOT** |
| exp animals/ not humans.sh; exp child/ not (exp adult/ or exp aged/); exp review/ |

**Table ii.** List of all identified metabolites by article in human synovial fluid.

| Underlying pathology | Metabolite | Change | Joint | Author and year |
|---|---|---|---|---|
| PTAA | Glutamate | Increased | Ankle | Adams et al, 2014[1] |
| | DSGEGDFXAEGGGVR | | | |
| | 2-hydroxypalmitate | | | |
| | Arachidonate | | | |
| | Palmitoyl-sphingomyelin | | | |
| | 2-hydroxystearate | | | |
| | 1-stearoylglycerophosphoinositol | | | |
| | 1-oleoylglycerophosphoethanolamine | | | |
| | Tryptophan | | | |
| | 1-arachidonoylglycerophosphoinositol | | | |
| | Kynurenine | | | |
| | Dihomo-linoleate-20-2n6 | | | |
| | Androsterone sulfate | | | |
| | 1-stearoylglycerophosphoethanolamine | | | |
| | 4-androsten-3beta-17beta-diol-disulfate-1-bilirubin E-E | | | |
| | Mannose | | | |
| | Cis-4-decenoyl-carnitine | | | |
| | Lactate | | | |
| | Pseudouridine | | | |
| | Urate | | | |
| | Alpha-tocopherol | | | |
| | 5-dodecenoate (12:1n7) | | | |
| | 1-arachidonoylglycerophosphoethanolamine | | | |
| | Cortisol | | | |
| | 3-indoxyl-sulfate | | | |
| | Uridine | | | |
| | Carnitine | | | |
| | ADSGEGDFXAEGGGVR | | | |
| | Cystine | | | |
| Behcet's disease | Glutamate | Increased in BD with arthritis compared to SNA | N/A | Ahn et al, 2015[2] |
| | Citramalate | | | |
| | Valine | | | |
| | Leucine | | | |
| | Methionine sulfoxide | | | |
| | Glycerate | | | |
| | Phosphate | | | |
| | Lysine | | | |
| | Isoleucine | | | |
| | Urea | | | |
| | Citrulline | | | |
| OA or RA | Citrate | Increased in OA compared to RA | Knee | Anderson et al, 2018[3] |
| | Creatine | | | |
| | Glucose | | | |
| | Glutamine | | | |
| | Glycerol | | | |
| | Pyruvate | | | |
| | Taurine | | | |
| | 3-hydroxybutarate | Increased in RA compared to OA | | |
| | Acetate | | | |
| | Isoleucine | | | |

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**Supplementary Table ii** (Continued)

| Underlying pathology | Metabolite | Change | Joint | Author and year |
|---|---|---|---|---|
| | Leucine | | | |
| | Sarcosine | | | |
| | Threonine | | | |
| OA or RA | Citric acid | Decreased in OA and RA compared to controls | N/A | Carlson et al, 2018[4] |
| | D-lactic acid methyl ester | | | |
| | hydroxyl-L-proline | | | |
| | L-isoleucine | | | |
| | L-methionine | | | |
| | L-citrulline | Increased in OA compared to RA and controls | N/A | |
| OA | 4-hydroxy-L-proline (Hyp) | Increased in OA | Knee | Chen et al, 2018[5] |
| | Alanine | | | |
| | Arginine | | | |
| | Creatine | | | |
| | Isoleucine | | | |
| | Leucine | | | |
| | Lysine | | | |
| | Tryptophan | | | |
| | Tyrosine | | | |
| | Valine | | | |
| | Acetyl-carnitine | Decreased in OA | | |
| | Aminobutyric acid | | | |
| | Asparagine | | | |
| | Citrulline | | | |
| | Creatinine | | | |
| | Dimethylglycine | | | |
| | Glutamine | | | |
| | Phenylalanine | | | |
| | Proline | | | |
| | Serine | | | |
| | Taurine | | | |
| | γ-aminobutyric acid (GABA) | | | |
| Inflammatory arthropathies | 3-hydroxybutyrate | Increased in SSA and RA | Knee | Dubey et al, 2019[6] |
| | Citrulline | | | |
| | Glucose | | | |
| | Glutamate | | | |
| | Glycine | | | |
| | Histidine | | | |
| | Isoleucine | | | |
| | Leucine | | | |
| | LDL | Decreased in SSA and RA | | |
| | VLDL | | | |
| | Choline | | | |
| | PUFA | | | |
| | Valine | Increased in SSA | | |
| | Lysine | | | |
| | Arginine | | | |
| | Acetate | | | |
| | Acetoacetate | | | |
| | Creatinine | | | |
| | Phenylalanine | | | |
| Acute fracture | Sphingomyelin | Increased with acute fracture | Knee | Furman et al, 2017[7] |
| | 2-hydroxy-fatty acids | | | |
| RA or OA | Maltose | Increased in RA compared to OA | N/A | Hwang et al, 2013[8] |
| | Lignoceric acid | | | |
| | Uracil | | | |
| | Mannitol | | | |
| | Pyrophosphate | | | |
| | Phosphoric acid | | | |
| | Lysine | Increased in OA compared to RA | | |
| | Tyrosine | | | |
| | Valine | | | |
| | Glyceric acid | | | |
| | Alanine | | | |

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**Supplementary Table ii** (Continued)

| Underlying pathology | Metabolite | Change | Joint | Author and year |
|---|---|---|---|---|
| | Asparagine | | | |
| | Hydroxylamine | | | |
| | Tryptophan | | | |
| | Glycerol | | | |
| | Glutamine | | | |
| | Citrulline | | | |
| Inflammatory arthropathies | Succinic acid | Increased in RA compared to other inflammatory arthropathies (AS, BD, gout) | N/A | Hwang et al, 2013[9] |
| | Octadecanol | | | |
| | Asparagine | | | |
| | Terephthalic acid | | | |
| | Salicylaldehyde | | | |
| | Glutamine | | | |
| | Citrulline | | | |
| | Tyrosine | | | |
| | Uracil | | | |
| | Lysine | | | |
| | Phenylalanine | | | |
| | Ribitol | | | |
| | Tryptophan | | | |
| | Xylose | | | |
| | Pyrophosphate | | | |
| | Isopalmitic acid | Decreased in RA compared to other inflammatory arthropathies (AS, BD, gout) | | |
| | Glycerol | | | |
| | Myristic acid | | | |
| | Palmitoleic acid | | | |
| | Hydroxylamine | | | |
| | Ethanolamine | | | |
| | Alanine | | | |
| | Serine | | | |
| OA or RA | N6,N6,N6-Trimethyl-L-lysine | Increased in OA compared to RA | Knee | Kang et al, 2015[10] |
| | L-Carnitine | | | |
| | 3-Hydroxymandelic acid | | | |
| | Kynurenine | | | |
| | Indolelactic acid | | | |
| | Indoleacetaldehyde | | | |
| | N′-Formylkynurenine | | | |
| | Phenylacetic acid | | | |
| | Trihydroxyeicosatrienoic acid/13,14-Dihydrolipoxin A4 | | | |
| | 12,20-Dioxoleukotriene B4 | | | |
| | 11b-Hydroxy-3,20-dioxopregn4-en-21-oic acid | | | |
| | LysoPC(18:1) | | | |
| | 5-L-Glutamyltaurine | Decreased in OA compared to RA | | |
| | Taurine | | | |
| | (S)-Ureidoglycolic acid | | | |
| | Methylguanine | | | |
| | CE[24:1(15Z)] | | | |
| | Trimethyltridecanoic acid | | | |
| | Docosapentaenoic acid | | | |
| | Galactosylceramide (d18:1/16:0) | | | |
| ACL deficient knee (trauma) | Alanine | Increased following pivot shift test in ACL deficient knee | Knee | Khatib et al, 2018[11] |
| | Choline | | | |
| Early vs late OA | Squalene | Increased in late OA compared to early OA | Knee | Kim et al, 2017[12] |
| | Palmitoleic acid | | | |
| | Pentadecanoic acid | | | |
| | Glycerol | | | |
| | Myristic acid | | | |
| | Lignoceric acid | | | |
| | α-tocopherol | | | |
| | Heptadecanoic acid | | | |
| | Oleic acid | | | |
| | Linolenic acid | | | |

*(Continued)*

**Supplementary Table ii** (Continued)

| Underlying pathology | Metabolite | Change | Joint | Author and year |
|---|---|---|---|---|
| | Threose | | | |
| | 3-hydroxypropionate | | | |
| | Lanosterol | | | |
| | Ethanolamine | | | |
| | Putrescine | | | |
| | N-carbamoylaspartate | | | |
| | Capric acid | | | |
| | Malate | | | |
| | Asparagine | | | |
| | Arachidonic acid | | | |
| | Pelargonic acid | | | |
| | Benzoate | | | |
| | Palmitic acid | | | |
| | 1-monostearin | | | |
| | Salicylaldehyde | | | |
| | Stearic acid | | | |
| | Adipate | | | |
| | Phenylalanine | | | |
| Inflammatory arthropathies | Succinate | Increased in RA compared to other inflammatory arthropathies (AS, BD, gout) | N/A | Kim et al, 2014[13] |
| | Octadecanol | | | |
| | Asparagine | | | |
| | Terephthalate | | | |
| | Salicylaldehyde | | | |
| | Glutamine | | | |
| | Citrulline | | | |
| | Tyrosine | | | |
| | Uracil | | | |
| | Lysine | | | |
| | Ribitol | | | |
| | Tryptophan | | | |
| | Xylose | | | |
| | Ribose | | | |
| | Isopalmitic acid | Decreased in RA compared to other inflammatory arthropathies (AS, BD, gout) | | |
| | Glycerol | | | |
| | Myristic acid | | | |
| | Palmitoleic acid | | | |
| | Hydroxylamine | | | |
| | Ethanolamine | | | |
| Acute fracture vs control | Oleate | Increased following intra-articular ankle fracture and decreased six months post-surgery | Ankle | Leimer et al, 2017[14] |
| | Eicosenoate | | | |
| | 10-heptadecenoate | | | |
| | Myristoleate | | | |
| | Palmitoleate | | | |
| | Linoleate | | | |
| | Dihomo-linoleate | | | |
| | Arachidonate | | | |
| | Linolenate | | | |
| | Dihomo-linolenate | | | |
| | Stearoyl sphingomyelin | | | |
| | Palmitoly sphingomyelin | | | |
| | Octadecanedioate | | | |
| | 5-dodecenoate | | | |
| | Oleoylcarnitine | | | |
| | Cis-4-decenoyl carnitine | | | |
| OA vs cadaveric controls | Fructose | Increased in OA compared to cadaveric controls | Knee | Mickiewicz et al, 2015[15] |
| | Citrate | | | |
| | Malate | Decreased in OA compared to cadaveric controls | | |
| | Methionine | | | |
| | N-Phenylacetylglycine | | | |
| | O-Acetylcarnitine | | | |

*(Continued)*

**Supplementary Table ii** (Continued)

| Underlying pathology | Metabolite | Change | Joint | Author and year |
|---|---|---|---|---|
| | Hexanoylcarnitine | | | |
| | Creatine | | | |
| | Ethanol | | | |
| | Ethanolamine | | | |
| | 3-hydroxybutyrate | | | |
| RA vs healthy controls | LDL | Increased in RA comparted with control samples | Knee | Naughton et al, 1993[16] |
| RA vs controls | beta-Mannosylglycerate | Increased in RA comparted with control samples | Knee | Yang et al, 2015[17] |
| | Carnitine | | | |
| | Diglycerol | | | |
| | Lactic acid | | | |
| | Pipecolinic acid | | | |
| | 5-Methoxytryptamine | Decreased in RA comparted with control samples | | |
| | Citric acid | | | |
| | Gluconic lactone | | | |
| | D-glucose | | | |
| | Glucose-1-phosphate | | | |
| | Mannose | | | |
| | Ribitol | | | |
| | L-valine | | | |
| OA vs controls | 1,5-Anhydroglucitol | Increased in OA compared to healthy controls | Knee | Zheng et al, 2017[18] |
| | Gluconic lactone | | | |
| | Threonine | | | |
| | 8-Aminocaprylic acid | Decreased in OA compared to healthy controls | | |
| | Glutamine | | | |
| | Tyramine | | | |

ACL, anterior cruciate ligament; AS, ankylosing spondylitis; BD, Behçet's disease; LDL, low-density lipoprotein; N/A, not available; OA, osteoarthritis; PTAA, post-traumatic ankle arthritis; PUFA, polyunsaturated fatty acid; RA, rheumatoid arthritis; SNA, seronegative arthritis; SSA, seronegative spondyloarthropathy; VLDL, very low-density lipoprotein.

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