# Interleukin-17A causes osteoarthritis-like transcriptional changes in human osteoarthritis-derived chondrocytes and synovial fibroblasts in vitro

# What is the Manuscript Microscope Sentence Audit?

The Manuscript Microscope Sentence Audit is a research paper introspection system that parses the text of your manuscript into minimal sentence components for faster, more accurate, enhanced proofreading.

# Why use a Sentence Audit to proofread your manuscript?

- Accelerated Proofreading: Examine long technical texts in a fraction of the usual time.
- Superior Proofreading: Detect subtle errors that are invisible to traditional methods.
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- Reliable Proofreading: Ensure every single word of your manuscript is correct.
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Bonus 1: Improved Productivity: Rapidly refine rough drafts to polished papers.
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### **Features of the Sentence Audit:**

The Sentence Audit combines two complementary proofreading approaches:

- 1. Each sentence of your text is parsed and displayed in isolation for focused inspection.
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The Minimal Sentence Components shown are the smallest coherent elements of each sentence of your text as derived from it's conjunctions, prepositions and selected punctuation symbols (i.e. commas, semicolons, round and square brackets).

The combined approaches ensure easier, faster, more effective proofreading.

### **Comments and Caveats:**

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- Depending on the source of the input text, the Sentence Audit may contain occasional html artefacts that are parsed as sentences (E.g. "Download figure. Open in new tab").
- Always consult the original research paper as the true reference source for the text.

### **Contact Information:**

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All queries, feedback or suggestions are also very welcome.

# **Research Paper Sections:**

The sections of the research paper input text parsed in this audit.

Section No.	Headings	Sentences
Section: 1	Abstract	12
Section: 2	1 Introduction	15
N/A		0

Interleukin-17A causes osteoarthritis-like transcriptional changes in human osteoarthritis-derived chondrocytes and synovial fibroblasts in vitro

# S1 [001] Abstract

**S1 [002]** Increased interleukin (IL)-17A has been identified in joints affected by osteoarthritis (OA), but it is unclear how IL-17A, and its family members IL-17AF and IL-17F, can contribute to human OA pathophysiology.

```
Increased interleukin ...
... (IL)-17A has been identified ...
... in joints affected ...
... by osteoarthritis ...
... (OA), ...
... but it is unclear how IL-17A, ...
... and its family members IL-17AF ...
... and IL-17F, ...
... can contribute ...
... to human OA pathophysiology.
```

**S1 [003]** Therefore, we aimed to evaluate the gene expression and signalling pathway activation effects of the different IL-17 family members in fibroblasts derived from cartilage and synovium of patients with end-stage knee OA.

```
Therefore, ...
... we aimed ...
... to evaluate the gene expression ...
... and signalling pathway activation effects ...
... of the different IL-17 family members ...
... in fibroblasts derived ...
... from cartilage ...
... and synovium ...
... of patients ...
... with end-stage knee OA.
```

**S1 [004]** Immunohistochemistry staining confirmed that IL-17 receptors A (IL-17RA) and IL-17RC are expressed in end-stage OA-derived cartilage and synovium.

```
Immunohistochemistry staining confirmed ...
... that IL-17 receptors A ...
... (IL-17RA) ...
... and IL-17RC are expressed ...
... in end-stage OA-derived cartilage ...
... and synovium.
```

**S1 [005]** Chondrocytes and synovial fibroblasts derived from end-stage OA patients were treated with IL-17A, IL-17AF, or IL-17F, and gene expression was assessed with bulk RNA-Seq.

```
Chondrocytes ...
... and synovial fibroblasts derived ...
... from end-stage OA patients were treated ...
... with IL-17A, ...
... IL-17AF, ...
... or IL-17F, ...
... and gene expression was assessed ...
... with bulk RNA-Seq.
```

**S1 [006]** Hallmark pathway analysis showed that IL-17 cytokines regulated several OA pathophysiology-related pathways including immune-, angiogenesis-, and complement-pathways in both chondrocytes and synovial fibroblasts derived from end-stage OA patients.

```
Hallmark pathway analysis showed ...
... that IL-17 cytokines regulated several OA pathophysiology-related pathways including immune-, ...
... angiogenesis-, ...
... and complement-pathways ...
... in both chondrocytes ...
... and synovial fibroblasts derived ...
... from end-stage OA patients.
```

**S1 [007]** While overall IL-17A induced the strongest transcriptional response, followed by IL-17AF and IL-17F, not all genes followed this pattern.

```
While overall IL-17A induced the strongest transcriptional response, ...
... followed by IL-17AF ...
... and IL-17F, ...
... not all genes followed this pattern.
```

**S1 [008]** Disease-Gene Network analysis revealed that IL-17A-related changes in gene expression in these cells are associated with experimental arthritis, knee arthritis, and musculoskeletal disease gene-sets.

Disease-Gene Network analysis revealed ...
... that IL-17A-related changes ...
... in gene expression ...
... in these cells are associated ...
... with experimental arthritis, ...
... knee arthritis, ...
... and musculoskeletal disease gene-sets.

**S1 [009]** Western blot analysis confirmed that IL-17A significantly activates p38 and p65 NF-κB.

```
Western blot analysis confirmed ... ... that IL-17A significantly activates p38 ... ... and p65 NF-κB.
```

**S1 [010]** Incubation of chondrocytes and synovial fibroblasts with IL-17A antibody secukinumab significantly inhibited IL-17A-induced gene expression.

```
Incubation ...
... of chondrocytes ...
... and synovial fibroblasts ...
```

**S1 [011]** In conclusion, the association of IL-17-induced transcriptional changes with arthritic gene-sets supports a role for IL-17A in OA pathophysiology.

```
In conclusion, ...
... the association ...
... of IL-17-induced transcriptional changes ...
... with arthritic gene-sets supports a role ...
... for IL-17A ...
... in OA pathophysiology.
```

**S1 [012]** Therefore, secukinumab could be investigated as a potential therapeutic option in OA patients.

```
Therefore, ...
... secukinumab could be investigated ...
... as a potential therapeutic option ...
... in OA patients.
```

## S2 [013] 1 Introduction

**S2 [014]** Osteoarthritis (OA) is the most common musculoskeletal disease, affecting 8.75 million people in the UK alone.

```
Osteoarthritis ...
... (OA) ...
... is the most common musculoskeletal disease, ...
... affecting 8.75 million people ...
... in the UK alone.
```

**S2 [015]** Characterised by the loss of articular cartilage, it causes pain, disability, a reduced quality of life, and has a significant socioeconomic impact[1].

```
Characterised ...
... by the loss ...
... of articular cartilage, ...
... it causes pain, ...
... disability, ...
... a reduced quality ...
... of life, ...
... and has a significant socioeconomic impact[1].
```

**S2 [016]** There are currently no disease-modifying treatments for OA and treatment is limited to joint replacement surgery with its associated costs and morbidity.

```
There are currently no disease-modifying treatments ...
... for OA ...
... and treatment is limited ...
... to joint replacement surgery ...
```

```
... with its associated costs ... ... and morbidity.
```

**S2** [017] OA is a multifactorial disease with a complex pathophysiology[1, 2].

```
OA is a multifactorial disease ...
... with a complex pathophysiology[1, 2]...
...
```

**S2 [018]** Newly gained knowledge on the pathophysiology of osteoarthritis (OA) has shifted the traditional dogma of OA as a degenerative "wear-and-tear" disease of the articular cartilage to a hypothesis that OA is a whole joint disease with a significant inflammatory component.

```
Newly gained knowledge ...
... on the pathophysiology ...
... of osteoarthritis ...
... (OA) ...
... has shifted the traditional dogma ...
... of OA ...
... as a degenerative "wear-and-tear" ...
... disease ...
... of the articular cartilage ...
... to a hypothesis ...
... that OA is a whole joint disease ...
... with a significant inflammatory component.
```

**S2 [019]** Despite the loss of articular cartilage being hallmark feature of OA, the mechanisms underlying this OA-related cartilage degradation are poorly understood.

```
Despite the loss ...
... of articular cartilage being hallmark feature ...
... of OA, ...
... the mechanisms underlying this OA-related cartilage degradation are poorly understood.
```

**S2** [020] Histological analyses have shown a clear infiltration of inflammatory cells into the synovium.

```
Histological analyses have shown a clear infiltration ... ... of inflammatory cells ... ... into the synovium.
```

**S2 [021]** Molecular interrogation has shown complement pathway activation in cartilage, synovium, and synovial fluid, and an increase in inflammatory mediators in synovium and synovial fluid[3–5].

```
Molecular interrogation has shown complement pathway activation ...
... in cartilage, ...
... synovium, ...
... and synovial fluid, ...
... and an increase ...
... in inflammatory mediators ...
... in synovium ...
... and synovial fluid[3–5].
```

# **End of Sample Audit**

This is a truncated Manuscript Microscope Sample Audit.

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