A Novel *In Vitro* Cell Culture Model for Juvenile Idiopathic Arthritis

Background

- Juvenile idiopathic arthritis (JIA) is the most common rheumatic disease in children, affecting around 1 in 1,000 and posing a risk of lifelong disability.
- Gaps in understanding disease mechanisms have hindered development of targeted therapies.

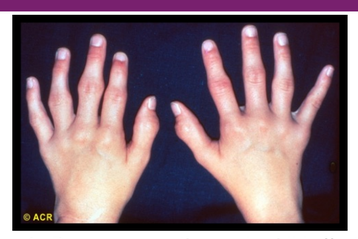

Figure 1: Bony overgrowth seen in child affected by JIA. From About Juvenile Idiopathic Arthritis [Image], n.d., American College of Rheumatology: Rheumatology for Primary Care (https://rheumforprimarycare.org/jia/)

- **Fibroblast-like synoviocytes (FLS),** found within the joint synovium, are cells that drive JIA disease progression (Figure 2).
- JIA FLS adopt inflammatory and proliferative states and have a **unique chondrocyte-like characteristic**. Chondrocytes are also known to contribute to bone formation.

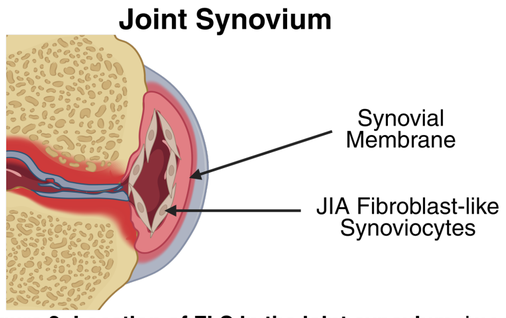

Figure 2: Location of FLS in the joint synovium. Image adapted from BioRender template and edited by Finalist, 2025.

Problem: The study of JIA lacks an *in vitro* cell culture model (lab model) and relies mainly on primary cells, limiting investigation of disease.

- The **growth factor BMP4** has been found to drive cell types other than FLS toward displaying a chondrocyte-like phenotype, making it a strong candidate for inducing JIA FLS–like properties.
- Rheumatoid arthritis (RA) is frequently used as a reference for JIA
  - RA FLS studies are supported by the use of a well-characterized *in vitro* cell culture model, the synovial sarcoma cell line **SW982.**

Research Questions: Can BMP4-treated SW982 cells serve as an *in vitro* model of JIA FLS? Does BMP4 treatment induce proliferation, inflammation, and a chondrocyte-like phenotype comparable JIA FLS? (Figure 3)

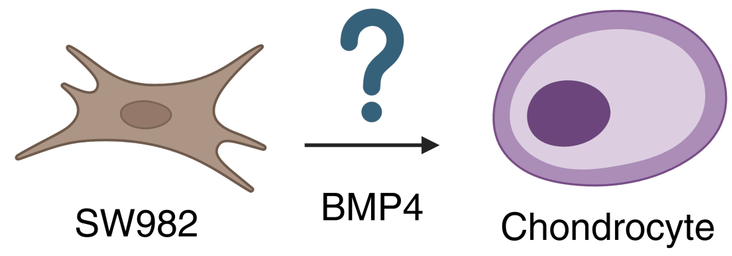

Figure 3: Whether BMP4-treated SW982 cells can model the chondrocyte-like behavior of JIA FLS remains to be elucidated. Image created by Finalist using BioRender, 2025.

Methods

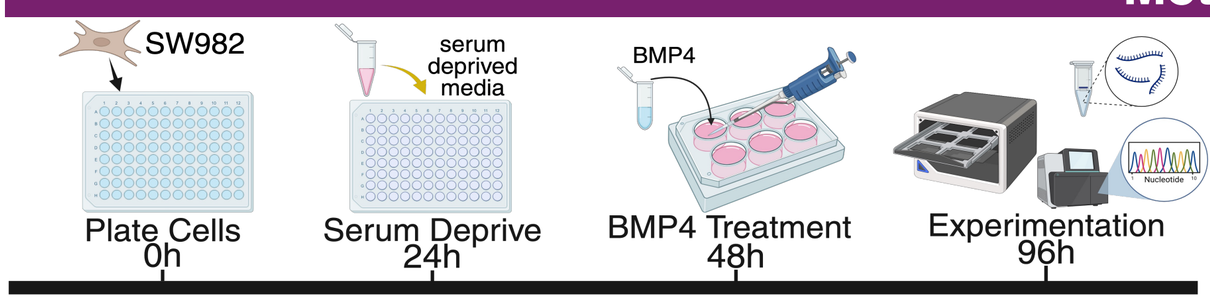

Figure 4: Experimental timeline with serum deprivation (0.2% FBS) after 48 hours of treatment. Image created by Finalist in BioRender, 2026.

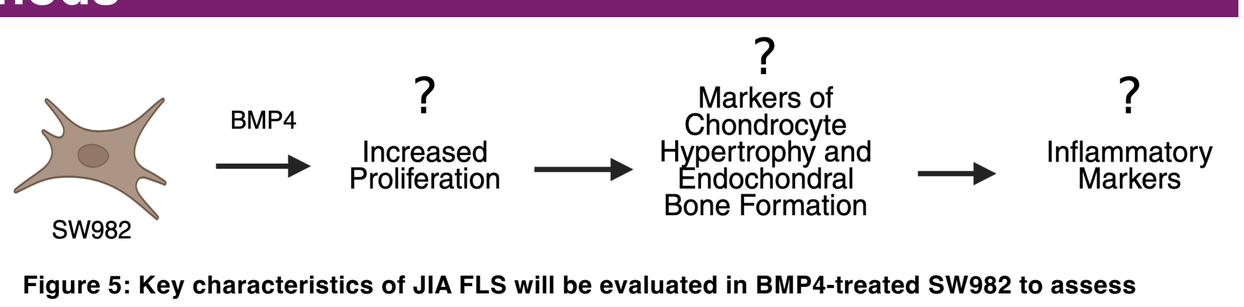

Figure 5: Key characteristics of JIA FLS will be evaluated in BMP4-treated SW982 to assess suitability as an *in vitro* model. Three characteristics will be analyzed: proliferation, chondrocyte-like phenotype, and inflammatory markers. Image created by Finalist in BioRender, 2025.

Creating The Novel Model: Model Exhibits JIA FLS Proliferative Phenotype

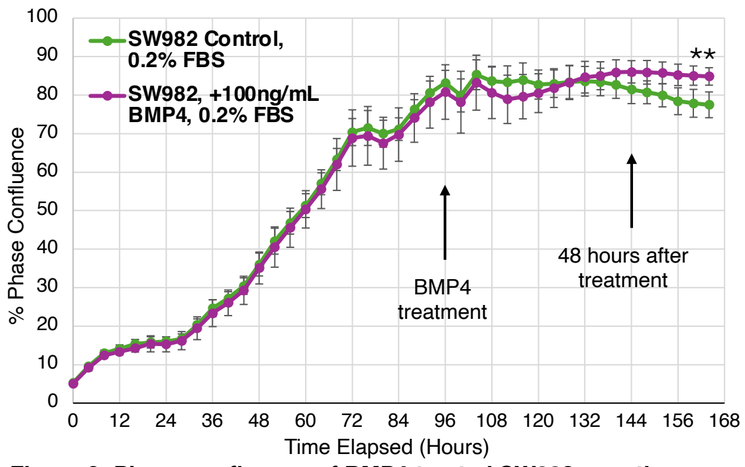

Figure 6: Phase confluence of BMP4-treated SW982 over time, showing proliferative phenotype of model. (* = p<0.05) (n=3). Image created by Finalist in Excel, 2025.

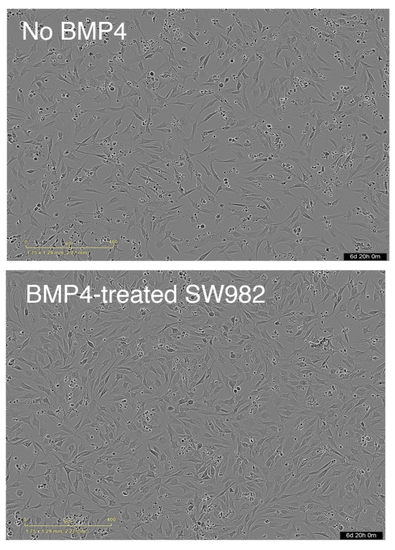

Figure 7: Effect of BMP4 on SW982 proliferation. Evidence of cell proliferation after 48 hours of treatment of 100 ng/mL BMP4 in 0.2% FBS compared to vehicle control. Taken on IncuCyte S3 at 10x. Images taken by Finalist and formatting in BioRender, 2025.

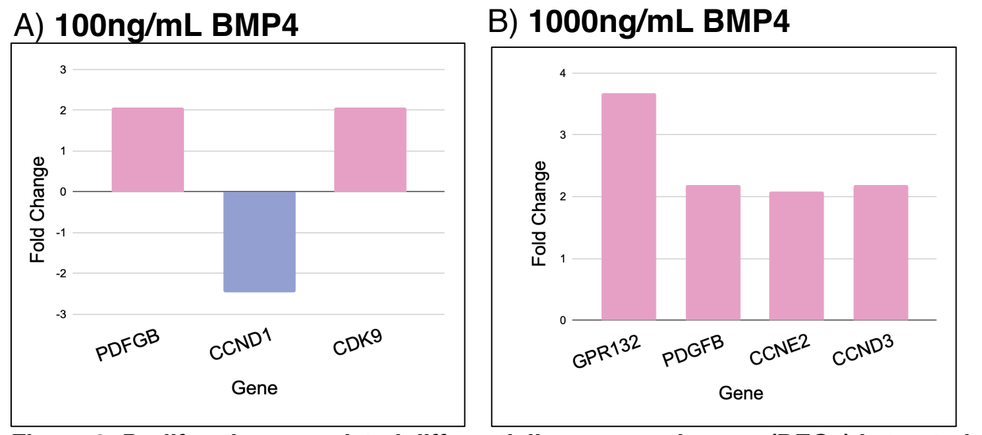

Figure 8: Proliferation associated differentially expressed genes (DEGs) in treated SW982 (48h). A) DEGs in model (100ng/mL BMP4). **B)** DEGs in model (1000ng/mL BMP4) (IFCI>2). Blue indicates downregulated genes. Pink indicates upregulated genes. Image created in Google Sheets by Finalist, 2025.

Model Exhibits JIA FLS Chondrocyte-like Phenotype

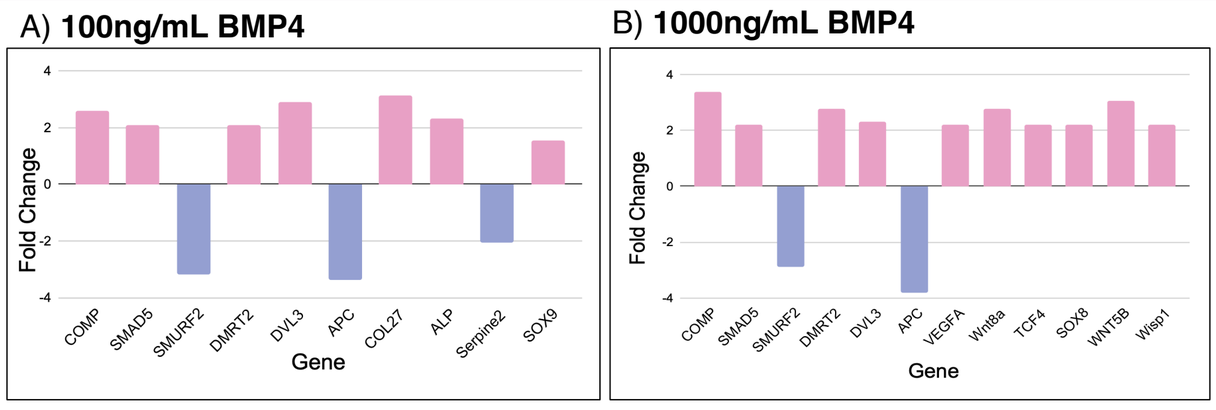

Figure 9: Chondrocyte associated DEGs in BMP4 treated SW982 (48h). A) DEGs in model (100ng/mL BMP4). **B)** DEGs in model (1000ng/mL BMP4) (IFCI>1.5). Blue indicates downregulated genes. Pink indicates upregulated genes. Image created in Google Sheets by Finalist, 2025.

Model Exhibits JIA FLS Inflammatory Phenotype

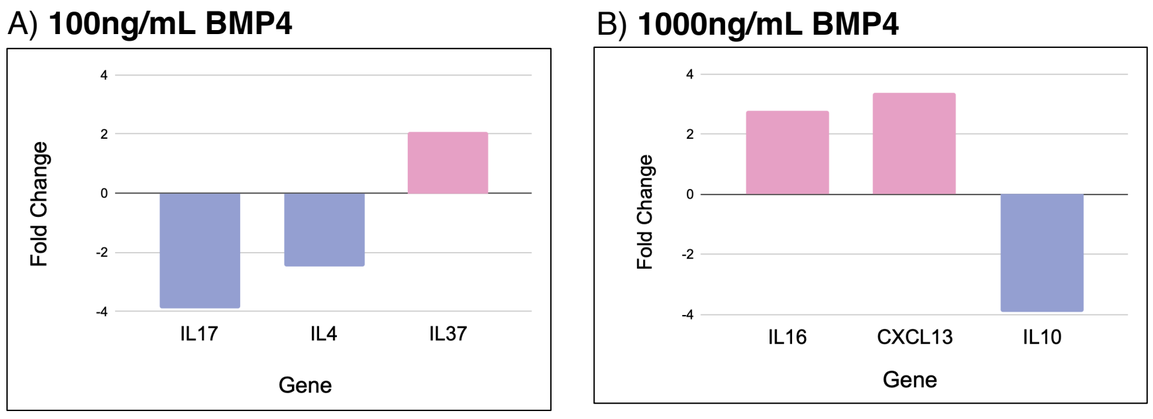

Figure 10: Inflammation associated DEGs in BMP4 treated SW982 (48h). A) DEGs in model (100ng/mL BMP4). **B)** DEGs in model (1000ng/mL BMP4) (IFCI>2). Blue indicates downregulated genes. Pink indicates upregulated genes. Image created in Google Sheets by Finalist, 2025.

Conclusions/Applications

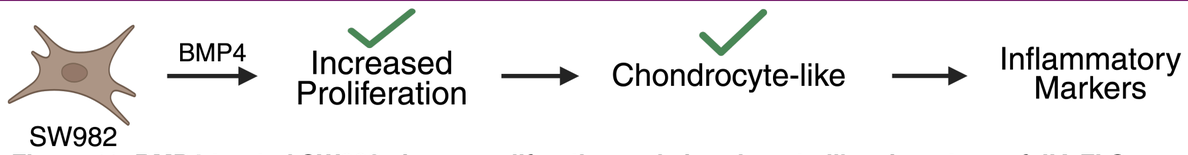

Figure 11: BMP4-treated SW982 shows proliferative and chondrocyte-like phenotype of JIA FLS, suggesting a novel *in vitro* model for JIA FLS. Image created in BioRender by Finalist, 2026.

Findings: For the first time, This study suggests a BMP4-treated SW982 *in vitro* JIA FLS model, moving research towards improved therapies for children.

- Model shows characteristics of JIA FLS proliferative and chondrocyte-like phenotype.
- Study proposed the canonical BMP4 and Wnt pathway are involved in JIA disease progression.
  - Reveals novel pathways to explore for treatment
  - Noggin and chordin, BMP4 inhibitors, can be investigated as potential treatments

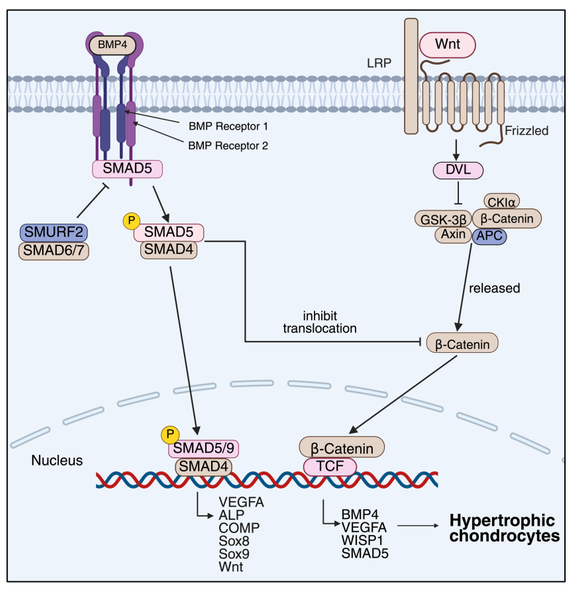

Figure 12: Model shows similar gene profile to BMP4 and Wnt pathway. Image made in BioRender by Finalist, 2026.

Future Works

- Noggin and chordin, inhibitors of BMP4, will be used to verify that observed changes in SW982 are driven by BMP4 signaling.
- Effects of methotrexate (MTX), a first line treatment for JIA, on model will be explored.
- In JIA FLS, MTX has been shown to inhibit the chondrocyte-like phenotype (Simonds et al., 2024).

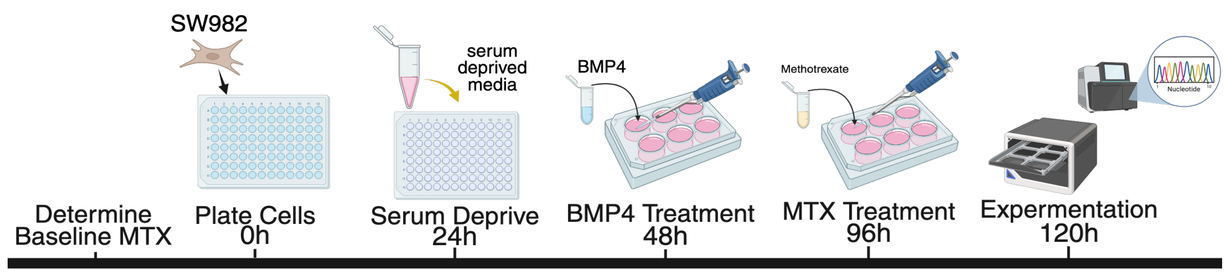

Figure 13: Treatment of novel model with methotrexate to determine JIA FLS–like responses and investigate mechanisms of disease pathogenesis. Image created in BioRender by Finalist, 2026.

Key References

1. Brescia, A. C., Simonds, M. M., McCahan, S. M., Fawcett, P. T., & Rose, C. D. (2014). The role of transforming growth factor β signaling in fibroblast-like synoviocytes from patients with oligoarticular juvenile idiopathic arthritis. *Arthritis & Rheumatology, 66*(5), 1352–1362. https://doi.org/10.1002/art.38336
2. Simonds, M. M., Freer, S. T., & Brescia, A. M. C. (2024). Methotrexate inhibits BMP4 and abrogates the hypertrophic chondrocyte phenotype of synovial fibroblasts in juvenile idiopathic arthritis. *Pediatric rheumatology online journal*, *22*(1), 6. https://doi.org/10.1186/s12969-023-00940-6
3. Simonds, M. M., Schlefman, A. R., McCahan, S., et al. (2020). Juvenile idiopathic arthritis fibroblast-like synoviocytes influence chondrocytes to alter BMP antagonist expression (2020). *Pediatric Rheumatology, 18*, 89. https://doi.org/10.1186/s12969-020-00483-0)