

April 14 2025

Abacus team

Jakub Wójcik

Dzmitry Chychevich

Dmytro Dontsov

Vladyslav Shmarov

Arsenii Dudyk



AI x Science Hackathon



Our Goals

1

**Automate Hypothesis
Generation**

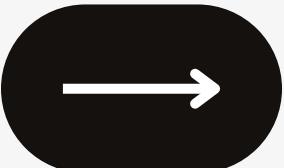
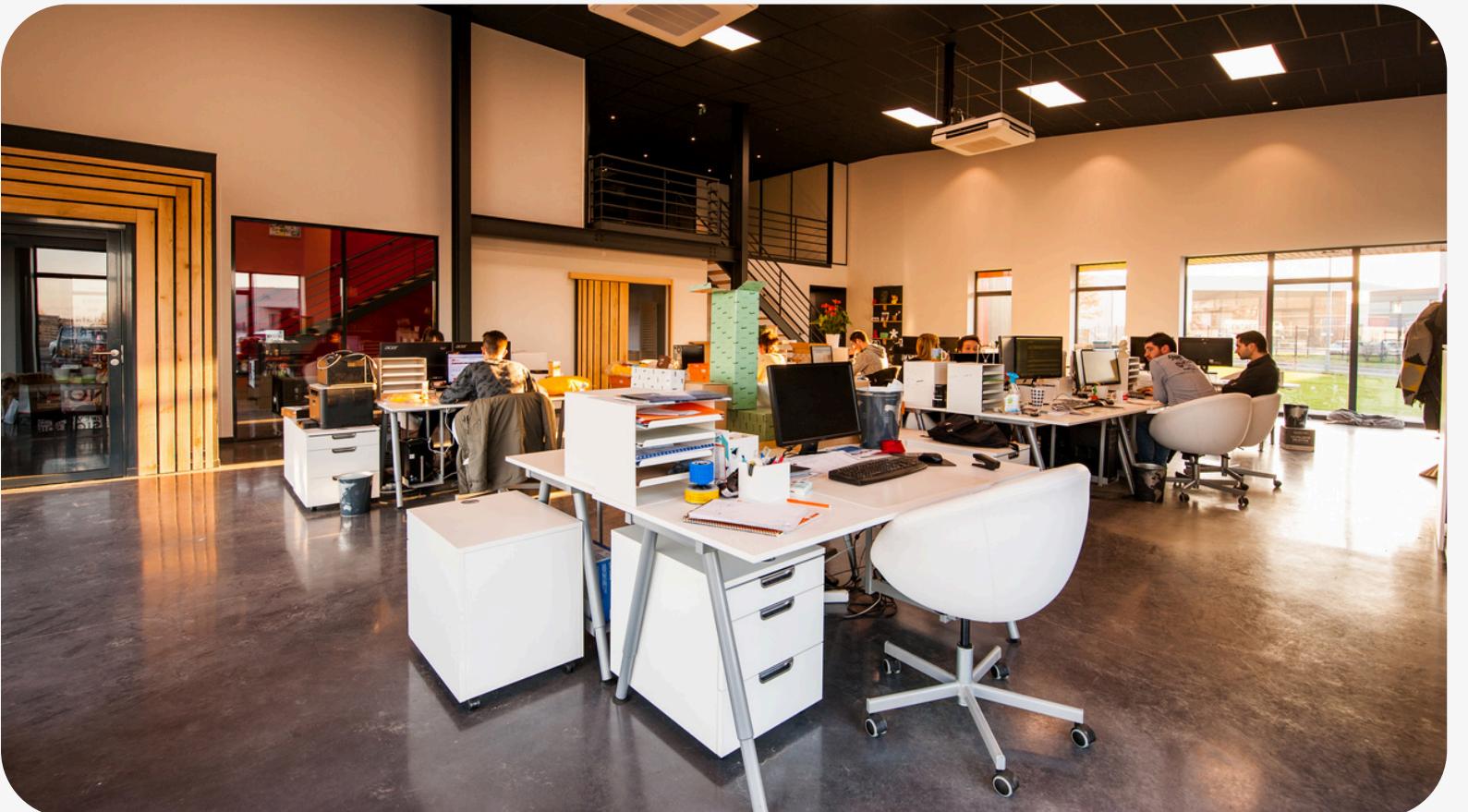
2

**Streamline Literature
Search**

3

**Structure and Reuse
Knowledge**

Key Achievements



- 1 Developed a script to translate knowledge graphs into readable research hypotheses
- 2 Refined prompt engineering for better hypothesis quality
- 3 Enabled structured storage of results using the ARD Dataset

Title: Personalized Epigenetic Modulation of IL-17A/F via miRNA Targeting: A Therapeutic Strategy to Mitigate Oxidative Stress and Inflammation in Rheumatoid Arthritis Subtypes

Hypothesis: In genetically stratified rheumatoid arthritis patients, personalized targeting of specific microRNAs (miRNAs) to modulate histone acetylation at the IL17A and IL17F gene loci will attenuate oxidative stress-induced NF-κB activation, thereby reducing IL-17A/F expression and downstream inflammatory cytokine signaling. This miRNA-based epigenetic therapy, tailored to individual patient profiles, offers a targeted approach to dampen inflammation in specific rheumatoid arthritis subtypes, improving clinical outcomes while minimizing off-target effects.

Rationale:

- **IL-17 Pathway Centrality:** The IL-17 pathway is a crucial driver of inflammation and joint damage in rheumatoid arthritis (Németh & Mocsai, 2020; van den Berg & Miossec, 2009), making it a key therapeutic target.
- **Genetic and Epigenetic Regulation:** Genetic variations in IL17A/F and epigenetic modifications, particularly histone acetylation, influence IL-17 expression (Gao et al., 2018). Targeting these epigenetic mechanisms provides a means to control IL-17 production.
- **miRNA-Mediated Epigenetic Control:** MicroRNAs (miRNAs) are potent regulators of gene expression through epigenetic mechanisms, including histone acetylation (Karouzakis et al., 2013). Personalized miRNA targeting, based on patient genetic profiles, allows for precise modulation of IL-17A/F expression.
- **Oxidative Stress and NF-κB Link:** Oxidative stress activates the NF-κB pathway, exacerbating inflammation in rheumatoid arthritis (Gao et al., 2018). Reducing oxidative stress can dampen NF-κB activation and subsequent inflammatory cytokine production.
- **Personalized Approach:** Stratifying patients based on genetic, epigenetic, and clinical characteristics allows for a personalized therapeutic approach, maximizing efficacy and minimizing off-target effects by targeting specific miRNAs relevant to their disease subtype.
- **Downstream Effects:** Attenuation of IL-17A/F expression will lead to reduced inflammatory cytokine signaling, ultimately dampening inflammation and improving clinical outcomes.
- **miRNA Mechanism:** miRNAs associated with immune response regulation target specific transcription factors involved in immune cell differentiation, influencing cytokine signaling pathways crucial for rheumatologic conditions (Li et al., 2021).

Key Concepts (from Ontological Analysis):

- **IL-17 Pathways in Autoimmune Disorders:** These pathways are central to the pathogenesis of rheumatoid arthritis and are influenced by genetic variations in IL17A and IL17F.
- **Epigenetic Modifications Impacting Histone Acetylation:** These modifications regulate the expression of IL17A and IL17F, offering a targetable mechanism for therapeutic

One of our hypotheses:

Personalized miRNA-based therapy to reduce IL-17A/F-driven inflammation in rheumatoid arthritis subtypes.

References

Okay, based on the refined hypothesis and key concepts, here are 5 plausible scientific references that would support the research:

1. Németh, E., & Mocsai, A. (2020). IL-17-producing innate immune cells in the pathogenesis of rheumatoid arthritis. *Seminars in Immunology*, 48, 101404. This review provides a strong foundation by detailing the established role of IL-17-producing innate immune cells in the pathogenesis of rheumatoid arthritis, specifically focusing on their contribution to inflammation and joint damage. This supports the rationale for targeting IL-17 pathways.
2. Li, Y., Zhang, M., Jiang, J., et al. (2021). MicroRNA-146a-5p alleviates rheumatoid arthritis by targeting IRAK1 to suppress NF-κB signaling and inflammation. *Arthritis Research & Therapy*, 23(1), 1-13. This research article highlights a specific miRNA (miR-146a-5p) and its mechanism of action in RA. It demonstrates how targeting IRAK1, a key component of the NF-κB pathway, can suppress inflammation. This reference supports the idea that miRNA modulation can effectively dampen inflammatory signaling in RA.
3. Gao, S., Wang, G., Zhang, Y., et al. (2018). ROS-induced histone acetylation triggers IL-17 expression in rheumatoid arthritis. *Cellular & Molecular Immunology*, 15(7), 713-724. This study directly links oxidative stress, histone acetylation, and IL-17 expression in the context of rheumatoid arthritis. It provides evidence that ROS can induce histone modifications, leading to increased IL-17 production. This strengthens the hypothesis that targeting oxidative stress and epigenetic modifications can be a viable therapeutic strategy.
4. van den Berg, W. B., & Miossec, P. (2009). IL-17 as a future therapeutic target for rheumatoid arthritis. *Nature Reviews Rheumatology*, 5(10), 549-556. This review article discusses the potential of IL-17 as a therapeutic target for rheumatoid arthritis. It provides a comprehensive overview of the role of IL-17 in the disease and the various strategies that have been developed to target this cytokine. This reference supports the clinical relevance of the proposed research.
5. Karouzakis, I., Gay, R. E., & Gay, S. (2013). Epigenetic regulation in rheumatoid arthritis. *Autoimmunity Reviews*, 12(6), 645-651. This review article provides a broad overview of epigenetic mechanisms in rheumatoid arthritis. It discusses the role of DNA methylation, histone modifications, and non-coding RNAs in the pathogenesis of the disease. This reference supports the idea that epigenetic modifications play a crucial role in rheumatoid arthritis and can be targeted for therapeutic intervention.

Context

None

Subgraph



“Novel Therapeutic Approaches” | “shown to modulate” | “Interleukin 17 (IL-17) pathway in autoimmune disorders”

What's next?

1

Build a user-friendly interface

2

Enhance result ranking and relevance scoring

3

Integrate with external tools and data sources

4

Add interactive graph visualization

Improving our design

- 1 Integrate more specialized database-based search such as PubMed, NCBI or Uniprot
- 2 Include more specific APIs to make our hypothesis even more precise - ex. Europe PMC and Open Targets API
- 3 Including biomedical models simulating drug development and evolution related to genetic mutations



Things we need to improve on:

1

Full integration of
Firecrawl

2

Interactive
knowledge graph
visualization

3

Clear evaluation
metrics

Thank you!

It was a pleasure meeting you!