# PHIF: A Novel Diagnostic Marker and Therapeutic Target for Rheumatoid Arthritis

We are looking to out-license the technology for its commercialization.

# Identified a cytokine secreted by helper T cells derived from the inflamed synovium of RA patients that contributes to disease pathogenesis and progression

# ♦ Background

Rheumatoid arthritis (RA) develops in part due to the activation of B cells by helper T cells within the inflamed synovium, leading to the production of autoantibodies. Additionally, the activation of macrophages and fibroblasts, along with the increased production of inflammatory cytokines, contributes to joint destruction and disease progression. In RA diagnostics, anti-cyclic citrullinated peptide (anti-CCP) antibodies and rheumatoid factor (RF) are commonly used. However, approximately 30% of patients test negative for these markers, highlighting the need for more sensitive and accurate diagnostic methods. Furthermore, about 30% of treated patients exhibit insufficient therapeutic response, necessitating the development of new treatment strategies with novel mechanisms of action.

# ♦ Description

Kyoto University researchers analyzed helper T cells derived from the inflamed synovium of RA patients and identified a pathogenic helper inflammatory factor (PHIF) as a gene highly expressed in RA patients. PHIF not only promotes the differentiation of T peripheral helper (Tph) cells but also activates macrophages via the NF-κB signaling pathway (Fig.1). Furthermore, PHIF was found to be elevated in the serum of RA patients. These findings suggest that PHIF holds promise not only as a diagnostic marker for RA but also as a novel therapeutic target for drug development.

#### $\geq$ New method for diagnosing and continuous monitoring for RA patients

PHIF enables highly accurate diagnosis, with an AUC of 0.917 (Fig.2). Additionally, lower serum PHIF levels have been observed in patients in remission, indicating its potential use for continuous patient monitoring.

Drug discovery targeting the mechanism of action that lowers PHIF levels The researchers established a cell line suitable for screening PHIF inhibitors.

#### $\geq$ Promising novel therapeutic target for rheumatoid arthritis

PHIF not only promotes the differentiation of helper T cells in the inflamed synovium but also contributes to inflammation activation via macrophages. Therefore, suppressing the PHIF signaling pathway itself is expected to lead to the development of new therapeutic strategies.



### Fig.1. Mechanism of action of PHIF

PHIF is expressed in T peripheral helper (Tph) cells within the inflamed synovium. It not only promotes its own differentiation but also acts on monocytes and other cells to activate NF-kB in a TNF-independent manner, leading to tissue inflammation.



# Fig.2. ROC curve

The diagnostic model utilizing serum PHIF levels demonstrated high accuracy, with an AUC of 0.9167.

### Development Status

- The diagnostic accuracy analyzed using ELISA with an anti-PHIF antibody in patient serum.
- The pathophysiological mechanism of rheumatoid arthritis involving PHIF has been elucidated.

### Applications

- RA diagnosis
- Drug discovery marker for RA therapeutics
- Drug development targeting PHIF

## Offer

- Patent License
- **Options for Patent License**
- Collaborative Research

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