

CHAPTER 20

GENETICS

Doctoral Theses

01. KASHYAP (Sujit)
Functional Assessment of Novel Gene, ARL15, Implicated in Pathogenesis of Rheumatoid Arthritis.
Supervisor : Prof. B. K. Thelma
Th 24149

Abstract
(Not Verified)

Rheumatoid Arthritis (RA) is a chronic, inflammatory condition that affects more than 1% population globally, and is controlled by a combination of different genetic & environmental factors. ~ 100 susceptibility loci are known for RA but total heritability remains unexplained warranting continued studies. In the first ever genome wide association study on RA in the north Indian population performed previously in the laboratory, a novel gene *ARL15* (5p15.2) was identified in addition to the already established HLA loci. *ARL15* is a small G Protein belonging to ADP ribosyl family (*ARF*), and inhibition of this protein family in animal model of RA has been reported to have therapeutic potential. But importantly, expression of either *ARL15* or any other *ARF* genes and their probable role in RA patients has never been reported. Based on this background, this study aimed at functional characterization of *ARL15* to understand its implications, if any, for RA biology. Synovial fibroblasts cultured from synovial fluid and tissue samples collected from RA patients with informed consent were checked for homogeneity by FACS and presence of *ARL15* in RASF was confirmed by RT-PCR and western blots. Differential expression of *adiponectin*, *adiponectin receptor*, *GAPDH* and *IL6* was observed in RASF upon *ARL15* knockdown using siRNA along with lower mobility as assessed by invasion and migration assays. Global expression profiling by transcriptome sequencing in wildtype and knockdown *ARL15* in RASF showed significant differential expression of 25 mostly disease relevant genes. Attempts to assess therapeutic relevance of *ARL15* using collagen induced arthritis (CIA) mouse model showed considerable improvement in disease scores in mice treated with *ARL15* mAb. *ARL15* is likely involved in RA biology through inflammation and metabolic pathways, and preliminary evidence of its anti-inflammatory effect obtained in CIA mouse model warrants additional studies to demonstrate its potential as a drug gable target.

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2. Materials and methods
3. Functional characterization of adp ribosylaysion factor like protein 15 in rheumatoid arthritis synovial fibroblasts
4. *ARL15* regulates multiple genes of known functional relevance in rheumatoid arthritis biology
5. Evaluation of anti-arthritic potential of *ARL15* in CIA model of rheumatoid arthritis
6. Conclusion and perspective. Bibliography and appendices.

02. TANU PRIYA
Functional Characterization of bZIP Transcription Factor, "bzipG" in Dictyostelium Discoideum.
Supervisor : Dr. Aruna Naorem
Th 24150

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