INPLASY PROTOCOL

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Review Stage at time of this submission: Formal screening of search results against eligibility criteria.

Conflicts of interest:
No conflicts of interest.

The association of TGF beta 1 polymorphisms with different types of arthritis: a systematic review and meta-analysis

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Review question / Objective: To study the association between TGF beta 1 polymorphisms and different types of arthritis

Condition being studied: Arthritis is a general term for acute or chronic inflammatory diseases of joint. Common types of arthritis include rheumatoid arthritis, ankylosing spondylitis, psoriatic arthritis, osteoarthritis and others. Though the pathogenesis of different types of arthritis are different, genetic factors have been shown to play important roles in the development and progression of many types of arthritis. TGF beta 1 is a multifunctional cytokine that regulates the cell response and is involved in bone metabolism through joint soft tissue cells or synovial tissues. Eight polymorphisms have been identified in TGF beta 1 gene. Many studies have explored the association between TGF beta 1 gene polymorphisms and different types of arthritis such as rheumatoid arthritis, ankylosing spondylitis and osteoarthritis. However, the results were inconsistent. Thus, we perform this systematic review and meta-analysis to study the association between TGF beta 1 polymorphisms and the susceptibility to different types of arthritis.

INPLASY registration number: This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 18 July 2020 and was last updated on 18 July 2020 (registration number INPLASY202070082).

INTRODUCTION

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METHODS

Search strategy: A systematic literature search will be conducted in PubMed, Medline, Web of science, Cochrane Library, Biosis and four Chinese databases: China Biology Medicine (CBM), China National Knowledge Infrastructure (CNKI), Wanfang and CQVIP. The following search terms will be used and adjusted accordingly in Chinese: "arthritis" AND ("TGF-β1" OR "transforming growth factor beta1") AND ("polymorphism" OR "polymorphisms" OR "variant" OR "variants" OR "mutation" OR "mutations"). The references of related studies will also be screened to identified potentially relevant studies.

Participant or population: Patients with arthritis.

Intervention: TGF beta 1 gene mutant type.

Comparator: TGF beta 1 gene wild type.

Study designs to be included: Case control studies.

Eligibility criteria: Inclusion criteria: (1) Study that evaluated the association between TGF beta 1 polymorphisms and arthritis; (2) Case control study; (3) Study that provided detailed data of genotype or allele distributions; (4) English or Chinese language Exclusion criteria: (1) Meeting abstract, review or meta-analysis; (2) Animal or in vitro study (3) Family-based studies of pedigrees.

Information sources: Databases including PubMed, Medline, Web of science, Cochrane Library, Biosis and four Chinese databases: China Biology Medicine (CBM), China National Knowledge Infrastructure (CNKI), Wanfang and CQVIP. The references of related studies will also be screened to identified potentially relevant studies.

Main outcome(s): The association of TGF beta 1 polymorphisms with different types of arthritis.

Additional outcome(s): The association of TGF beta 1 polymorphisms with different types of arthritis in different ethnicity.

Quality assessment / Risk of bias analysis: The Newcastle-Ottawa Scale (NOS) will be used to assess the quality of included case control studies.

Strategy of data synthesis: The association of each type of TGF beta 1 polymorphism and each type of arthritis will be analyzed separately. Odds ratio (OR) and 95% percent CI will be calculated and P value less than 0.05 will be considered as statistically significant. The heterogeneity among included studies will be assessed by the I2 statistic. The random effects model will be used if the heterogeneity is high (I2>50% or p<0.1), otherwise fixed effect model will be used. The publication bias will be assessed by Egger's test. Statistical analyses will be performed using STATA software (version 15.1, StataCorp, College Station, US).

Subgroup analysis: Subgroup analysis will be conducted according to the ethnicity.

Sensibility analysis: Sensitivity analysis will be conducted by excluding a study one by one and repeating the meta-analysis when

the number of included studies is more than 3.

Country(ies) involved: China.

Keywords: Arthritis; TGF beta 1; polymorphism.

Contributions of each author:
Author 1 - Suling Liu - Suling Liu has the original idea for the article, performs the literature search, analyses the data and drafts the manuscript.
Author 2 - Jiaxiao Li - Jiaxiao Li performs the literature search, analyses the data and revises the manuscript.
Author 3 - Yang Cui - Yang Cui critically provides expertise in statistical analyse and critically revises the manuscript.