Genetics of Autoimmune Diseases

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Immune system disorders congenital
Study type	Observational non invasive

Summary

ID

NL-OMON31645

Source
ToetsingOnline

Brief title
Genetics of Autoimmune Diseases

Condition

- Immune system disorders congenital
- Autoimmune disorders

Synonym
autoimmune disease

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: autoimmunity, genetics, linkage analysis

Outcome measures

Primary outcome

Genotypes of genetic markers

Secondary outcome

NA

Study description

Background summary

There is no organ in the body or there is an autoimmunity against it. These diseases have in common that in the blood autoantibodies are present. There are hundreds of different autoimmune disease, and some examples are: Graves-Basedow en Hashimoto, Addison, Rheumatoid Arthritis, Myasthenia, Lambert-Eaton , Systemic Lupus Erythematosus, Type 1 Diabetes, and Celiac disease. Every disease is specified by specific reaction to anitgens. For example, in Type 1Diabetes the defense system is directed against the insulin producing beta-cells of the Islets of Langerhans in the pancreas. This autoreactivity eventually leads to distruction of these cells and impaired functionality.
Despite lots of research it is unknown what the exact cause of AID is. In general it is assumed that it is an interplay between genetic and environmental factors.

From families and twin research it has become clear that the contribution of the hereditary component is between 15 and 70%, depending on the specific sickness, and that the inheritance is complex, i.e. the risk for AID is confered by an interplay between environmental and genetic factors. Indeed in the previous years some important genetic factors for AID have been identified. For nearly all AID, the major histocompatibility complex (MHC) on chromosome 6p21.3 has been shown the area in genome which consistently shows the highest association. The contribution of the MHC to the total genetic impact varies by AID, but explains for example for T1D and Celiac about 40% of heredity. It are mainly allelische variaties of DQB1 and DRB1 the haplotype, which are responsible for genetic risk. Sometimes the same DQB1-DRB1 haplotype has been associated in several AID, for example DQB1*02-DRB1*03 the haplotype have been associated with an increased risk for type of 1 diabetes, Celiac and Rheumatoid Arthritis. By large-scale association studies a number of other gene variants have been identified. A characteristic of these risk factors is that they give a relatively moderately raised risk for sickness. Because of the low risk

expected for these risk factors it is to detect them. This is illustrated by the large number of studies for which an association between AID is reported, but that cannot be confirmed consistent by other studies. Such low risk factors require a relatively large cohort of patients and controls to be able to successful detect the relative low marginal effect.

The genen which are so far found explain only one part of heredity/complex genetic context of AIZ. Since AIZ are a complex genetic sickness, can be adopted that genen still more will show an association with this sickness. Such as said detection of new genen is difficult by the lack of sufficient patients and controls association of certain candidate or genomische order show genen.

Study objective

The research strives for a large group of homogeneous AID patients, so that a powerful association study can be performed to detect genetic risk factors. These factors can be shared by several AIZ, or be specific is for a single AID. The aim of this study is the identification of those genetic variants that confer susceptibility of AID.

Study design

Despite years of research, a lot of candidate genes have not been sufficiently examined. Large genome-wide association studies are undertaken at this moment by other study groups in United Kingdom and America. These studies will report according to the expectations several associations which must be tested for their validity in the Dutch population. For this reason, we will collect a large group of minimally 500 Dutch AID patients, which can be used with controls already availllable for Case-Control study. The group size is determined by power-calculation; with these numbers it is possible with more than 80% probability that genetic factors are found which have a relative risk of 1.5 or more.

Study burden and risks

Single venapunture with neglactable risk.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adolescents (12-15 years)
Adolescents (16-17 years)
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

Patients older than 12 years, with an autoimmune disease with unknown etiology.

Exclusion criteria

symptomatic autoimmunity

Study design

Design

Study type:	Observational non invasive
Intervention model:	Other

Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Basic science

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	05-12-2008
Enrollment:	500
Type:	Actual

Ethics review

Approved WMO

Date:	26-02-2008
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL17792.041.07