Kappa-deleting recombination excision circles (KRECs) and somatic hypermutation (SHM) in Down Syndrome B-lymphocytes.

Published: 12-05-2010
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To determine the replication history of DS-B-lymphocytes by KRECs in relation to somatic hypermutation.

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Congenital and hereditary disorders NEC
Study type	Observational non invasive

Summary

ID

NL-OMON34940

Source
ToetsingOnline

Brief title
BKS-Down; blood

Condition

- Congenital and hereditary disorders NEC
- Immunodeficiency syndromes

Synonym
Down syndrome

Research involving
Human

Sponsors and support

Primary sponsor: Jeroen Bosch Ziekenhuis

Source(s) of monetary or material Support: Stichting Peribosch

Intervention

Keyword: B-lymphocyte, Down syndrome, KRECS, SHM

Outcome measures

Primary outcome

Description of the replication history of DS-B-lymphocytes in relation to

reference groups. This replication history will be presented in divisions per

B-lymphocyte subpopulation.

Somatic hypermutation will be presented as the percentage of mutated V*3-20-J*

allels.

Secondary outcome

Not applicable.

Study description

Background summary

The increased frequency of haematological malignancies, autoimmune diseases and infections in Down Syndrome (DS), and the observed high frequency of hepatitis B surface antigen carriers, had already led in the 1970s to the hypothesis that DS is associated with abnormalities of the immune system. Indeed, many differences between the immune system of DS and non-DS individuals have been found throughout the years. Most research has been focused on the T-lymphocytopenia although the decreased numbers of B-lymphocytes are more profound. Moreover, lower numbers of CD21+, CD23+ and CD27+ B-lymphocyte are described and the responses to several vaccine antigens are low. These findings lead to the question whether DS-B-lymphocytes suffer from an intrinsic B-lymphocyte defect, decreased T-lymphocyte help or both.
The replication history of B-lymphocyte subpopulation can be determined by kappa-deleting recombination excision circles (KRECs). Per B-lymphocyte subpopulation (CD5+ B-lymphocytes, naive mature B-lymphocytes, natural effector B-lymphocytes and memory B-lymphocytes) the amount of divisions will be determined. These results provide information on the proliferation of

B-lymphocytes caused by either a T-lymphocyte dependent or T-lymphocyte independent antigen response.
Moreover, by assessing somatic hypermutation more knowledge will be obtained on the qualitative antibody response.

Study objective

To determine the replication history of DS-B-lymphocytes by KRECs in relation to somatic hypermutation.

Study design

An observational study will be performed. During a scheduled venipunction for medical purposes an extra 40 ml will be obtained. The medical history will be noted as well.

Study burden and risks

Patients will not experience any direct benifits from participation in this study. The blood will be obtained during a scheduled venipunction for medical purposes. Therefore the harm is limited as much as possible. The expected gain in knowledge on the DS immune system justifies this limited harm.

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)
Children (2-11 years)
Elderly (65 years and older)

Inclusion criteria

Down syndrome, age >7 years

Exclusion criteria

Infectious disease or treated for malignancy

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Other

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-09-2010
Enrollment:	12
Type:	Actual

Ethics review

Approved WMO Date:	12-05-2010
Application type:	First submission
Review commission:	METC Brabant (Tilburg)
Approved WMO Date:	08-06-2011
Application type:	Amendment
Review commission:	METC Brabant (Tilburg)

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	NL31797.028.10