Mutations in thyroid hormone receptor alpha 2

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Ethical review	Approved WMO
Status	Pending
Health condition type	Endocrine disorders congenital
Study type	Observational invasive

Summary

ID

NL-OMON39713

Source
ToetsingOnline

Brief title
TRα2 mutations

Condition

- Endocrine disorders congenital
- Thyroid gland disorders

Synonym
mutation in the binder of thyroid hormone, thyroid hormone receptor mutation

Research involving
Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W,EUR fellowship

Intervention

Keyword: 2, mutation, TR&alfa

Outcome measures

Primary outcome

The main parameters are (a) serum hormone and metabolite levels and (b) gene expression differences in skin fibroblasts and PBMCs from WT and mutant subjects.

Secondary outcome

na

Study description

Background summary

Thyroid hormone is crucial for normal development and metabolism and acts mainly via its nuclear receptors. The function of the T3 binding receptor isoforms is well understood. In contrast, TRa2 does not bind T3, despite representing a true isoform. The biological role of TRa2 is not understood. We identified a nonsense mutation in the THRA gene resulting in a premature stop of TRa2 in two related subjects. This family provides a unique possibility in investigating the biological function of TRa2 and pathophysiological consequences of this TRa2 premature stop. We hypothesize that TRα2 is an orphan receptor with an important role in specific signaling pathways and that mutations in TRα2 have pathophysiological consequences.

Study objective

The family with the TRα2 premature stop enables us to investigate the biological role of the orphan wild-type TRα2 and the consequences of its dysfunction. The primary objectives of this proposal are (i) to search for a biological function of TRα2 and (ii) to investigate if the function of TRα2 is abrogated in the patients with mutations in TRα2.

Study design

Observational study.

Study burden and risks

Venous blood samples will be take from fasted subjects. In total, approximately 15 cc blood will be drawn (5 ml for DNA extraction and 10 ml for serum measurements). Skin biopsies of the forearm will be taken using well-established techniques. Blood samples as well as skin biopsies are both regarded as minimal invasive procedures. Since the function of TRα2 is unknown, possible benefits are currently unclear. The discovery of a family with a mutant TRa2 provides the unique opportunity to investigate the pathophysiologic consequences of disrupted TRa2 signaling.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

All familiy members of patient with the TRα2 mutation will be tested.

Exclusion criteria

na

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	01-10-2012
Enrollment:	25
Type:	Anticipated

Ethics review

Approved WMO

Date:	05-02-2013
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

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	NL41698.078.12