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STUDY ON THE MECHANISM OF THE STIMULATION OF
ADENYLATE CYCLASE BY GRAVES' IgG IN SOLU-
BILIZED THYROID MEMBRANES. K.Inoue,Y.Fukue,
T.Mitsushashi,H.Uchimura,F.Takaku,Y.Manabe
and K.Ito.Third Department of Internal
Medicine,University of Tokyo and Ito Hos-
pital, Tokyo.

We examined whether the detergent solubi-
лизирован thyroid adenylate cyclase is stimu-
lated by TSH or Graves' IgG in vitro. Solubi-
zation of TSH receptor adenylate cyclase was performed by incubating crude
porcine thyroid membranes (10,000 g pellets)
in 25 mM Tris,50 mM NaCl,1% Lubrol PX PH 7.4
for 16 h at 4°C. Solubilized complex protein
was concentrated and used for experiments. 
Adenylate cyclase activity was measured by
Orgiazzì’s method. CAMP was assayed by RIA.
IgG was prepared by affinity column chroma-
tography with Protein A Sepharose.

Results 1) TSH Stimulated solubilized
adenylate cyclase in a dose dependent manner
(0.04 - 4 ml/ml). 2) Six of 14 TBI11 positive
G-IgG’s increased adenylate cyclase activity.
3) The binding of I-125-bTSH was found to the
solubilized protein complex. 4) Adenylate
cyclase responsiveness to TSH was observed.
Our results suggest that solubilized
porcine thyroid TSH receptor-adenylate cyclase
has TSH receptor, transducer and catalytic
unit. However, responsiveness of adenylate
acylase to some G-IgGs of patients with untreated Graves' disease may be lacking.

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CHANGES IN TSI AND TBI1 ACTIVITIES IN IgG OF
PATIENTS WITH GRAVES' DISEASE BY ADDING
BLOCKING IgG OF A PRIMARY MYXEDEMA PATIENT.
Y.Fukue,H.Uchimura,T.Mitsushashi,S.Okano*,
Y.Kanaji*, and F.Takaku. Third Department of
Internal Medicine, Faculty of Medicine, Uni-
versity of Tokyo, and Kanaji Hospital*, Tokyo.

Two methods are available, at present, to
assess abnormal IgGs in sera of Graves' pati-
teuts, thyroid stimulating IgG(TSI) and TSH-
bounding inhibiting IgG(TBI1). Both activi-
ties are not always paralleled with each
other in individual IgG. However, no evidence
has been reported that the IgG contains
both activities in its molecule or IgG is a
mixture of IgGs with varying TSI and TBI1.
The present study was performed to examine
changes in TSI and TBI1 activities in IgGs of
untreated Graves' patients (G-IgG) by add-
ing graded doses of a blocking IgG (B-IgG)
from a patient with nonoigrous myxedema.

Methods: Mixtures of IgG which were prepared by
adding varying doses (1,2,4 mgg-B-IgG to 10
mg G-IgG of each patient with a final volume
of 1ml and changes in TSI and TBI1 activi-
ties were assessed. TSI was measured by
porcine thyroid cell assay and TBI1 by
Smith's method.

Results: (1) Decrease in TSI activity and in-
crease in TBI1 value were observed in mixed
IgG (2) IgGs with varying TSI and TBI1 activi-
ties were obtained by mixing G-IgGs
with B-IgG.

Conclusion: Graves' IgGs might be mixture of
IgGs with varying TSI and TBI1 activities.

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PORCINE THYROID MEMBRANE-BINDING ANTIBODIES
IN PATIENTS WITH AUTONOMOUS THYROID DISEASE.
H.Uchimura,K.Inoue,K.Matsuda,Y.Fukue,T.
Mitsushashi,K.Kubota,N.Sasaki and F.Takaku.
The Third Department of Internal Medicine,
Faculty of Medicine,University of Tokyo.

Abnormal IgG(G-IgG) present in the sera of
patients with Graves' disease is postula-
ted to be antibodies to components of the
thyroid cell membrane, including TSH recep-
tor. Heterogeneity, such as thyroid stimula-
ting or inhibiting activity has been demons-
strated among G-IgG's. We conducted to test
the membrane binding IgG in patients with
thyroid disease by using 10,000 x g pellets
of porcine thyroid membranes. Membrane
proteins (500ug) was incubated with 1mg IgG
and I-Protein A in 1 ml 0.025M Tris,10 M
MMI and 10 M NaI at 4°C for 16 h. After
that tubes were centrifuged at 10,000 g for
15 min followed by two times washing. The
sediment was counted for 1291. Of 20
untreated patients with Graves' disease, 16
(80%) showed greater binding than upper
normal limits. Nine of 13 treated patients
with antithyroid drug became normal value.
Six of 10 patients with Hashimoto's thyroid
itis or subacute thyroiditis were observed in
normal range. The binding was not corre-
lated with TSI or TBI1 in individual patients.
No relationship was found between
TPOA or MCHA and the binding. These results
suggest that the porcine thyroid binding
IgG, although detected in patients with
Hashimoto's disease, might contain IgG which
plays a significant role in Graves' disease.

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EVALUATION OF TSH-RECEPTOR ANTIBODIES AS
PROGNOSTIC MARKERS AFTER CESSION
OF ANTITHYROID DRUG TREATMENT IN
PATIENTS WITH GRAVES' DISEASE.
K.Kasagi,J.K.Kim,Y.Iida,Y.Tokuda,K.Arai,
K.Endo,K.Torizuka.Kyoto University School
of Medicine, Kyoto

Clinical usefulness of TSAb(thyroid stimulating antibodies) and TBI1(TSH-
bounding inhibitor immunoglobulins) measurements for predicting prognosis of Graves' disease after cessation of antithyroid drug
treatment was evaluated, and compared with
that of T3 suppression test and the assess-
ment of goiter size. Incidence of TSAb,
TBI1, T3 suppressibility and large goiter
(transverse diameter >4.74 cm in male;
>4.74 cm in male), determined at the time
of discontinuation of treatment, was 87.5%
(n=14), 56.3% (9), 78.6% (11) and 81.3%
(13) in 16 relapsed patients, and 56.5%
(13), 24.1% (5), 35.7% (8) and 26.1%
(6) in 23 remitted patients. Both TSAb and TBI1
activities remarkably increased at the time
of relapse in the 16 patients. Among 34
patients remaining in remission, TSAb were
detected in 23 (67.6%), most of whom had
normal serum TSH levels determined by
an ultrasensitive immunoradiometric assay. It
is suggested that impaired response of the
thyroid to TSAb probably due to destructive
changes and/or shrinkage is involved in the
cause of clinical remission in most of the
patients. Remission was found to be predic-
table in all patients with any two of those
indices such as negative TSAb, positive T3
suppressibility and small goiter.

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