

acta
endocrino
logica

Advances in Thyroidology

Cell- and Immunobiological Aspects

Proceedings of an International Merck-Symposium
organized by the Department of Internal Medicine,
Medical University Lübeck and
Deutsche Forschungsgemeinschaft, SFB 232,
held in Lübeck, 2nd to 4th October, 1986

EDITORS

B. E. WENZEL

G. F. BOTTAZZO

Supplementum 281

Copenhagen 1987

List of Contents

Autoantigen and antigen presentation in autoimmune thyroid disease

Thyroid cell MHC class II antigens: A perspective on the aetiology of autoimmune thyroid disease 13

T. F. Davies, S. H. Roman, W. A. Mackenzie, N. Goldsmith, S. M. Dower and L. A. Piccinini

Modulation of class-II antigen expression in human thyroid epithelial cell cultures 21

B. E. Wenzel, H. Arnholdt, S. Grammerstorf, R. Gutekunst and P. C. Scriba

Thyocyte HLA class II expression and regulation in relation to thyroid autoimmunity 27

Ian Todd, Ricardo Pujol-Borrell, Antonino Belfiore and Gian Franco Bottazzo

Aberrant expression of class II HLA antigens by the target cell: Cause or consequence of the autoimmune aggression? 35

Emilio L. Khoury

Dendritic cells in autoimmune thyroid disease 42

P. J. Kabel, H. A. M. Voorbij, R. D. van der Gaag, W. M. Wiersinga, M. de Haan and H. A. Drexhage

Thyroid peroxidase is the organ-specific 'microsomal' autoantigen involved in thyroid autoimmunity 49

Jean Ruf, Barbara Czarnocka, Catherine De Micco, Catherine Dutoit, Mireille Ferrand and Pierre Carayon

Cellular localization of the microsomal antigen and the thyroid peroxidase antigen 57

A. Pinchera, S. Mariotti, L. Chiovato, P. Vitti, G. Lopez, A. Lombardi, S. Anelli, R. Bechi and P. Carayon

Concept of a multigenic basis for the pathogenesis of spontaneous autoimmune thyroiditis 63

G. Wick

Effect of iodine intake and methimazole on lymphocytic thyroiditis in the BB/W rat 70

Lewis E. Braverman, Terri Paul, Walter Reinhardt, Michael C. Appel and Elsie M. Allen

Transplantation of human endocrine tissues to nude mice: A suitable in vivo model for the study of pathomechanisms involved in autoimmune thyroid diseases 77

K. H. Usadel, J. Teuber, R. Paschke, M. Junker and U. Schwedes

Thyocytes can synthesize HLA class II molecules 82

M. Londei, B. Grubeck-Loebenstein, M. Kissonerghis, P. Austin, J. Trowsdale, C. Greenall and M. Feldmann

Comparison of the cellular infiltrate of Hashimoto's thyroiditis in vivo and after in vitro cell growth 86

M. Londei, B. Grubeck-Loebenstein, C. Greenall, M. Turner and M. Feldmann

Stimulatory activities of antigen presenting cells in mixed leucocyte reactions (MLR) in thyroid diseases 89

B. Grubeck-Loebenstein, M. Londei, C. Greenall, K. Pirich, W. Waldhäusl and F. Feldmann

The influence of interleukin-1 on the function of in vitro cultured human thyroid cells in monolayers 93

Åse Krogh Rasmussen, Karine Bech, Ulla Feldt-Rasmussen, Svann Poulsen, Kaj Siersbæk-Nielsen, Thorkild Friis and K. Bendtzen

Reduced intrathyroidal K-cell activity in Graves' disease 96

U. Bogner and H. Schleusener

Is remission of Graves' disease regulated by anti-idiotypic antibodies?	99
<i>R. Paschke, J. Teuber, U. Schwedes and K. H. Usadel</i>	
Induction of experimental autoimmune thyroiditis by a 5–10 Kd peptidic fragment from porcine thyroglobulin	104
<i>J. Salamero, J. A. Boudier, J. J. Rémy and J. Charreire</i>	
Dysregulation of the immune system in obese strain chickens with Hashimoto-like thyroiditis: Intrinsic and extrinsic mechanisms	107
<i>K. Schauenstein, R. Fässler, G. Krömer and G. Wick</i>	
Characterization of thyroid infiltrating lymphocytes in Hashimoto's thyroiditis. Detection of B and T cells specific for thyroid antigens	111
<i>G. F. Del Prete, S. Mariotti, A. Tiri, M. Ricci, A. Pinchera and S. Romagnani</i>	
Graves' IgG stimulates thyroid epithelial cell proliferation in xenotransplanted human toxic diffuse goitre	115
<i>Erik Jörtsö, Lennart Tegler and Staffan Smeds</i>	
Thyrotoxic effect of high iodine doses on xenotransplanted autoimmune thyroid tissue in athymic nude mice	118
<i>Petra-Maria Schumm-Draeger, K. H. Usadel, B. O. Böhm, F. D. Maul, H. J. C. Wenisch, R. Senekowitsch, C. R. Pickardt and K. Schöffling</i>	
In vitro investigations in autoimmune thyroid disease	
The thyroid microenvironment in autoimmune thyroid disease: Effects of TSH and lymphokines on thyroid lymphocytes and thyroid cells	125
<i>S. M. McLachlan, C. A. S. Pegg, M. C. Atherton, S. L. Middleton, A. Dickinson, F. Clark and B. Rees Smith</i>	
Cellular and antibody mediated cytotoxicity in autoimmune thyroid disease	133
<i>Ulrich Bogner, Jack R. Wall and Horst Schleusener</i>	
Molecular cloning of antigens to thyroid autoantibodies using the expression vector lambda gt11	139
<i>Basil Rapoport, Hideshi Hirayu, Pui Seto and Ronald P. Magnusson</i>	
Restriction enzyme analysis of HLA class II DR β genes in patients with Graves' disease	146
<i>Bernhard O. Boehm, E. Schifferdecker, P. Kuehnl, C. Rosak and K. Schöffling</i>	
Polymorphism of the immunoglobulin heavy chain T cell receptor β -chain genes in Graves' disease	149
<i>A. Demaine, K. I. Welsh, B. S. Hawe and Nadir R. Farid</i>	
An anti-idiotypic antibody against Graves' IgG	152
<i>Beverley S. Hawe and N. R. Farid</i>	
The TSH-receptor: Structure and function	
The TSH receptor: Structure and interaction with autoantibodies in thyroid disease	157
<i>J. Furmaniak, Y. Nakajima, F. A. Hashim, F. M. Creagh, E. Davies Jones, R. D. Howells, S. M. McLachlan and B. Rees Smith</i>	
TSH receptor structure	166
<i>John Chan, Pilar Santisteban, Michele De Luca, Osamu Isozaki, Evelyn Grollman and Leonard Kohn</i>	
Characterization of monoclonal antibodies directed against the TSH receptor, as revealed with the cytochemical bioassay	173
<i>N. J. Marshall, L. D. Kohn and P. A. Ealey</i>	
About the porcine TSH receptor	181
<i>Nadir R. Farid and Goverdina Fahraeus-van Ree</i>	
Properties of thyrotropin receptor on cloned hybrid human thyroid cells	186
<i>Jean-Jacques Rémy, Jean Salamero and Jeannine Charreire</i>	
Inhomogenous TSH-binding in functional and proliferative thyroid disorders: Evidence for different membrane characteristics, TSH-receptor capping and TSH-receptor presentation on the inner surface of the follicular epithelium	193
<i>Hans-Wilhelm Müller-Gärtner, Claus Schneider, Volker Bay, Angela Tadt and Matthias Jessel</i>	

TSH and biogenic amine signals in the regulation of thyroid function: Independent regulation by protein kinase C and G proteins	199	Growth factor receptors in thyroid follicle cells	252
<i>Evelyn F. Grollman, Elisabeth Bone, John Chan, Daniella Corda, Osamu Isozaki, Claudio Marcocci, Pilar Santisteban and Leonard D. Kohn</i>		<i>K. Westermark, M. Lundqvist, G. Hacker, A. Karlsson and B. Westermark</i>	
Stimulation of Graves' thyroids in vitro	203	Evidence that thyroid growth promoting activity of immunoglobulin preparations is due to contamination with EGF	256
<i>R. Hörmann, J. Kirner, B. Saller and K. Mann</i>		<i>R. Gärtner, C. Tsavella, G. Bechtner and W. Greil</i>	
Immunoreactivity of PTH-binding in intact bovine kidney tissue and cultured cortical kidney cells indicative for specific receptors	207	The mechanism of TSH induced increase in binding of EGF to porcine thyroid cell monolayers; the role of thyroid hormones	260
<i>Axel Niendorf, Hartmut Arps, Manuela Sieck and Manfred Dietel</i>		<i>S. Atkinson and P. Kendall-Taylor</i>	
Thyroid cell growth		Control of the proliferation and differentiation of GEJ under platelet aggregating factor treatment	264
Control of thyroid cell proliferation: The example of the dog thyrocyte	215	<i>Y. Abramovici, N. Boucekkine, J. J. Rémy, J. Salamero and J. Charreire</i>	
<i>S. Reuse, P. Roger, F. Lamy, F. Foureau, C. Gerard and J. E. Dumont</i>		Inhibition of cAMP formation by EGF in thyroid follicles is mediated by intracellular Ca ⁺⁺ ...	267
Polarized properties of thyroid cells: A study with cultured porcine cells	220	<i>W. Greil, G. Niedernhuber, D. Stübner and R. Gärtner</i>	
<i>Jean Mauchamp, Odile Chabaud, Marianne Chambard, Corinne Gerard, Claude Penel and Bernard Verrier</i>		Stimulation of thyroid cell growth by thyrotropin and epidermal growth factor in isolated porcine thyroid follicles	270
Paracrine interaction between thyrocytes and fibroblasts	225	<i>H. Stracke, R. Bär, F. Müller and H. Schatz</i>	
<i>R. Gärtner, G. Bechtner, D. Stübner and W. Greil</i>		Thyrotropin (TSH) stimulates cell growth and DNA synthesis in monolayer cultures of human thyrocytes independent of the adenylate-cyclase system	273
Role of non-TSH factors in thyroid cell growth	231	<i>Peter E. Goretzki, Rainer Koob, Christine Koller and Hans-Dietrich Röher</i>	
<i>Margaret C. Eggo, Laura K. Bachrach and Gerard N. Burrow</i>		Adenylate cyclase stimulation and [³ H]thymidine incorporation in human thyroid tissues and thyrocyte cultures: The effect of IgG preparation from patients with different thyroid disorders	281
Expression of the c-myc proto-oncogene in growth stimulated porcine thyroid follicle cells	238	<i>Peter E. Goretzki, Michael West, Rainer Koob, Christine Koller, K. Joseph and Hans-Dietrich Röher</i>	
<i>N.-E. Heldin, F. A. Karlsson and B. Westermark</i>		Insulin and insulin-like growth factor-I (IGF-I) regulate differentiation as well as growth in FRTL-5 cells	288
The FRTL-5 thyroid cell strain as a model for studies on thyroid cell growth	242	<i>Osamu Isozaki, Pilar Santisteban, John Chan, Evelyn Grollman and Leonard Kohn</i>	
<i>Francesco Saverio Ambesi-Impiombato and Giovanni Villone</i>		Sodium/proton exchange in FRTL-5 thyroid cells: Role in the maintenance of intracellular pH and TSH-stimulated cell growth	293
Role of the adenylate cyclase-cAMP system on TSH-stimulated thyroid cell growth	246	<i>C. Marcocci, A. Pinchera and E. F. Grollman</i>	
<i>C. Marcocci, G. F. Fenzi and E. F. Grollman</i>			

Workshop on thyroid growth-stimulating immunoglobulins – A report	297	The specificity of autoantibodies in Graves' ophthalmopathy	330
<i>H. Schatz</i>		<i>P. Kendall-Taylor, D. Jones and S. Atkinson</i>	
Autoimmunity and thyroid growth: Methods, concepts and misconceptions	299	Pathophysiological and clinical implications of thyroid growth-stimulating immunoglobulins: Evidence for their intrathyroidal production	334
<i>J. E. Dumont, P. Roger and M. Ludgate</i>		<i>H. Schatz, I. Ludwig, F. Wiss and P. E. Goretzki</i>	
Clinical aspects of autoantibodies in thyroid diseases and related disorders		Ciamexon-treatment in endocrine ophthalmopathy	342
Thyrostatic drugs act through modulation of thyroid cell activity to induce remissions in Graves' disease	305	<i>Ch. Utech, K. G. Wulle, P. Pfannenstiel and W. Adam</i>	
<i>Robert Volpé, Anders Karlsson, Rolf Jansson and Per Anders Dahlberg</i>		Graves' autoantibodies to extrathyroidal TSH receptor: Their role in ophthalmopathy and pretibial myxedema	344
Effects of high and low doses of methimazole in patients with Graves' thyrotoxicosis	312	<i>C. M. Rotella, F. Alvarez, L. D. Kohn and R. Toccafondi</i>	
<i>G. Benker, D. Reinwein, H. Creutzig, H. Hirche, W. D. Alexander, D. McCruden, G. Galvan, G. Kahály, J. Beyer, J. H. Lazarus, H. Schatz, H. Schleusener, H.-G. Schneider, R. Ziegler, L. Tegler and O. R. Nilson</i>		Sera of patients with idiopathic myxedema contain IgG which block TSH-stimulated thyroid adenylate cyclase	348
Do HLA-DR-typing and measurement of TSH-receptor antibodies help in the prediction of the clinical course of Graves' thyrotoxicosis after anti-thyroid drug treatment?	318	<i>P. Vitti, L. Chiovato, A. Lombardi, G. Lopez, C. Mammoli, F. Santini, G. F. Fenzi and A. Pinchera</i>	
<i>H. Schleusener, J. Schwander, G. Holl, K. Badenhoop, J. Hensen, R. Finke, G. Schernthaner, W. R. Mayr and P. Kotulla</i>		Extrathyroidal synthesis and biologic action of thyroid receptor antibody (TRAb) in Graves' disease	352
On the clinical importance of thyroid microsomal and thyroglobulin antibody determination ..	325	<i>R. Paschke, H. G. Heinze, J. Teuber R. Schmeidl and K. H. Usadel</i>	
<i>W. A. Scherbaum</i>		Evidence of autoimmune pathogenesis in autonomous thyroid adenoma	355
		<i>Ch. Sellschopp, M. Derwahl, H. Schaube and H. Hamelmann</i>	
		Thyroid autoimmunity in 1987: A conclusive remark	358
		<i>G. F. Bottazzo</i>	

Modulation of class-II antigen expression in human thyroid epithelial cell cultures

B. E. Wenzel¹, H. Arnholdt², S. Grammerstorf¹,
R. Gutekunst¹ and P. C. Scriba¹

Department of Internal Medicine¹, Institute of Pathology², Medical University, Lübeck, FRG

Abstract. The modulation of HLA-D expression of thyroid epithelial cells (TEC) was studied *in vitro* by means of immunofluorescence. Under serum-free culture conditions, TSH and TSH-receptor antibodies induce HLA-D on TECs derived from GD-patients. Serum-free culture conditions provide a higher availability of TSH-receptors by a 'right side right' polarity of the cellular morphology. There was no evidence for IFN- γ producing cell contaminations on GD-TECs. TSH in contrast to IFN- γ does not induce HLA-DQ on TECs. HLA-DQ is not displayed by spontaneously class-II antigen expressing GD-TECs. Methimazole as well as perchlorate do not suppress HLA-D expression of TECs.

Classically, only immuno-competent cells, namely macrophages or dendritic cells are able to present antigen together with the immuno-regulatory class-II self-antigen (Balfour et al. 1981). These class-II antigens (in man HLA-D locii) can also be found *in vivo* (Hanafusa et al. 1983) and be induced on thyroid epithelial cells (TEC) by various agents *in vitro*. In this study we were interested in which potential *in vivo* regulators of thyroid cell functions could modulate HLA-D expression. We investigated the possibility that there might exist a mechanism to induce HLA-D expression different than the well documented pathway via IFN- γ (Todd et al. 1985; Davies et al. 1985; Weetman et al. 1985). Namely, the chronic stimulation of the TSH-receptor and/or the administration of iodine, methimazole, perchlorate, interferon- γ , TSH-receptor antibodies in TECs grown in culture medium with or without serum

supplementation was studied. This aimed at the role that polarity of three dimensional structures play in antigen-presentation *in vitro* as suggested *in vivo* (Londei et al. 1984; Wenzel et al. 1986).

Materials and Methods

Patients

Thyroid tissue was obtained from patients with Graves' disease (GD) or non-toxic goitre (NTG). GD-patients were iodine loaded for 10 days before surgery. They also had thyroid stimulating antibodies (TSA_b), and 6/7 had microsomal (M-antibodies). Patients with NTG were all void of thyroid antibodies.

Thyroid epithelial cells (TECs)

Thyroid tissue was minced, washed intensively with calcium- and magnesium-free phosphate buffer saline (PBS) and digested enzymatically two times for 1 h at 37°C with 4 mg/ml collagenase. Cells were then washed twice in PBS containing 10% foetal calf serum (FCS), separated from erythrocytes and auto-rosettes by density centrifugation, washed again and plated on 8 chamber glass slides (20 × 10⁴ cells/chamber) in Iscove medium. The medium was either supplemented with insulin, hydrocortisone, somastatin, human transferrin and gly-his-lys three peptide in 0.5% FCS (5H-medium) or with 10% FCS.

Cell cultures

TECs were allowed to adhere overnight to the glass slides. After washing with medium, slides were cultured for a further 4 to 5 days with, without, or combinations

of the following agents: interferon- γ (IFN- γ) 10 U/ml, bovine thyrotropin (bTSH) 1–100 mU/ml methimazole (MMI) 1–100 μ M; perchlorate (PC) 1–100 μ M; sodium iodide (NaI) 0.1 mM; IgG 0.1 mg/ml. In some experiments supernatants from TECs were collected after 2 days and tested on secondary TEC cultures.

Indirect immunofluorescence (IF)

After pre-incubation TECs were washed and incubated with monoclonal antibodies: Tü 22 – specific for HLA-DQ; Tü 35 – specific for HLA-DP/DR; Tü 39 – specific for HLA-DR/DP; DAKO-DRC1 – specific for T-cells (equivalent to OKT1); DAKO-DR reacting with the β -chain and DAKO-macrophage (\emptyset M). The M-antigen of thyroid cells was stained with inactivated, diluted patient's sera (α -M1: 320²; negative for α -Tg). Rabbit-anti-mouse-IgG (F(ab)₂)-FITC and TRITC conjugated rabbit-anti-human IgG were used as second antibodies. IF was assessed with an Olympus photo-fluorescence-microscope B-H2.

Further procedures

IgGs were prepared by ion-exchange chromatography. IgGs from GD-patients were TSab and α -M positive, while IgGs from NTG and normals had no autoantibodies as measured by specific ELISAs.

Materials

Collagenase (Dispase II) was from Boehringer, Mannheim, FRG. Foetal calf serum (FSC), Iscove medium

and all cell culture additives were from Biochrom, West-Berlin. Monoclonals, Tü-22/35/39 and interleukin-2 were from Biotest, Dreieich, FRG. FITC and TRITC conjugated second antibodies were from Dako-patt, Hamburg, FRG. Interferon- γ , Methimazole and all hormone additives were from Sigma Chemie, Munich, FRG. Sodium iodine and potassium perchlorate were from E. Merck, Darmstadt, FRG. Thyrotropin (Thyreostimulin) was from Organon, Munich FRG. Micro-Lab slides (Miles) and sheep erythrocytes were from Flow, Meckenheim, FRG. A BH-2 from Olympus Europe, Hamburg, FRG was used.

Results

TECs reassociate in cultures into dome-like structures sometime resembling micro-follicles as shown in Fig. 1. Under low serum conditions (5H-medium) the cellular polarity of these structures appears 'right side right'.

In Fig. 2 this particular morphology is demonstrated by nuclei surrounding a lumen with microvilli and filaments of TECs pointing inside. The ability of various agents to induce class-II depends on the source of the TECs, the agent used, and the polarity of cells in cultures. IFN- γ induced HLA-DR, but not M-antigen regardless

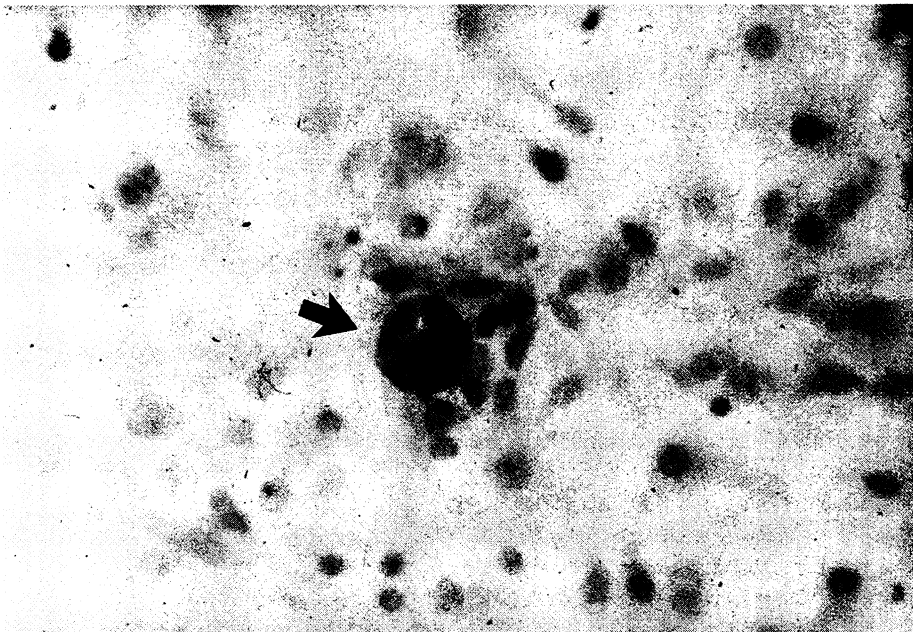


Fig. 1.

Re-association of thyroid epithelial cells under serum-free (5H-medium) culture conditions.

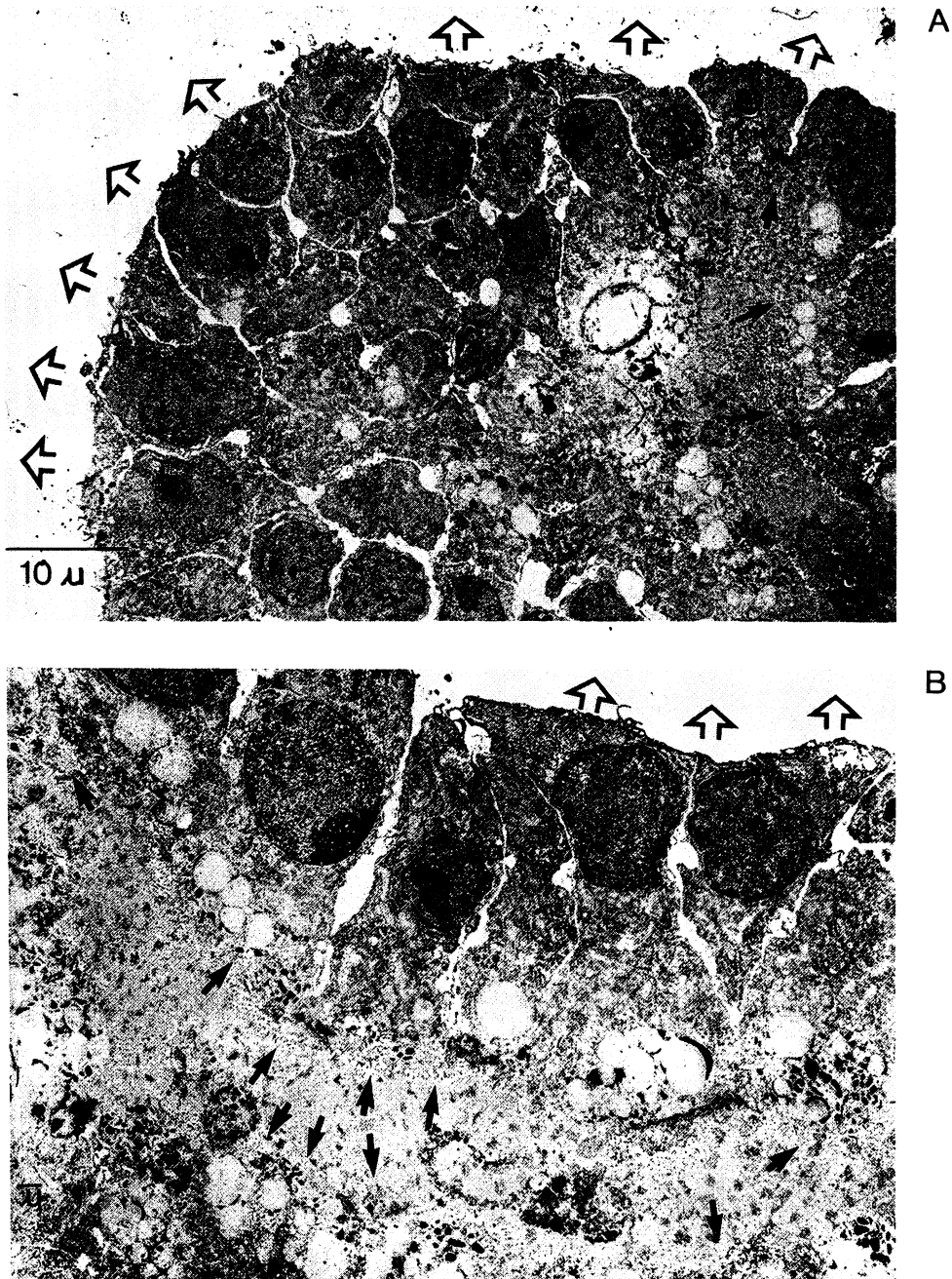


Fig. 2.

Electron-micrograph of follicle-like structures of thyroid epithelial cells grown in 5H-medium. A: Dome-structure; B: Close-up. \rightarrow site pointed to culture medium (outside). \rightarrow microvilli.

of the culture conditions or whether TECs derive from GD-patients or patients with NTG (Table 1).

All agents acting on the TSH-receptor, i.e. TSH and IgG from hyperthyroid GD-patients, induce

M-antigen (Table 1). HLA-DR together with M-antigen is only induced in 5H-medium (Fig. 3; Table 1).

A spontaneous expression of HLA-DR was ob-

Table 1.

Expression of HLA-DR and M-antigen by thyroid epithelial cells derived from patients with Graves' disease or with non-toxic goitre.

	Graves' disease				Non-toxic goitre	
	5H		FCS		5H	
	DR	M	DR	M	DR	M
IFN- γ	+++	-	+++	-	+++	-
TSH	++	+++	-	+++	-	+++
IgG*	++	+++	-	++	-	++
IgG ^{NTG}	-	-	-	-	-	-
IgG**	-	-	-	-	-	-

* Hyperthyroid GD-patients. ** Euthyroid GD-patients.

Table 2.

Spontaneous expression of HLA-DR by the thyroid epithelial cells derived from hyperthyroid patients with Graves' disease.

	5H (1 day)	5H (5 days)	5H (5 days + TSH)	SN*
HLA-DR	+	-	-	-
M-antigen	++	-	++	-

* Supernatant from spontaneously HLA-DR expressing thyroid epithelial cells applied on secondary NTG-cell cultures for 5 days.

A

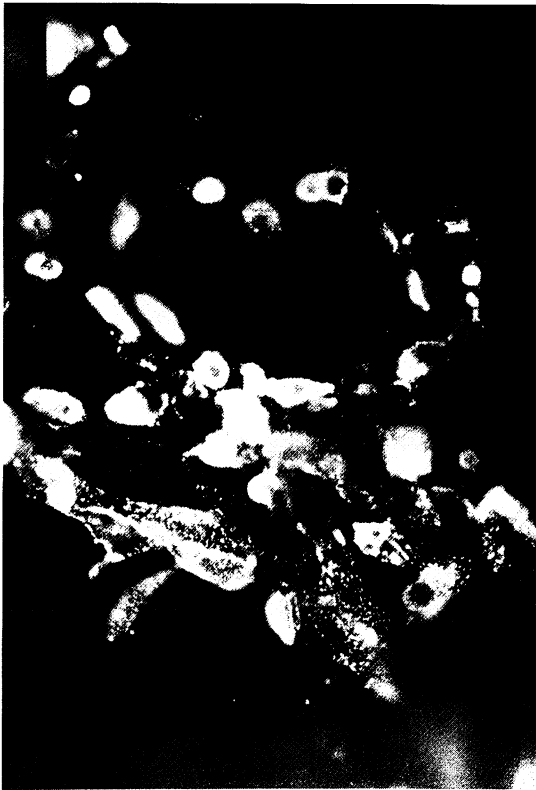


Fig. 3.

Expression of HLA-DR and M-antigen by thyroid epithelial cells from patients with Graves' disease. Cells were incubated with 1 mU/ml bTSH in 5H-medium for 4 days; magnification approx $\times 450$. A: α -M + a-hIgG-TRITC. B: α -HLA-DR + a-mIgG-FITC.

Table 3.

Expression of HLA-D polymorphism, lymphocyte-, macrophage-, and dendritic cell antigens by thyroid epithelial cells from Graves' patients.

	DR	DP/DR	DQ	T1/T2	øM	DRC1
IFN-γ	+++	++	+++	-	-	-
TSH	++	+	-	-	-	-
IgG*	++	+	-	-	-	-
5H (1 day)	+	(+)	-	-	-	-

* Cells grown in 5H-medium.

served in some TEC-cultures derived from GD-patients (Table 2). This disappeared after 5 days in culture. But HLA-DR expression could be re-induced with TSH. Supernatants (SN) of these particular TEC-cultures could not induce class-II expression, when applied on secondary TEC-cultures. When the HLA-D polymorphism of class-II expressing TECs was assessed, different staining patterns were observed with different inducing agents. While TSH, IgG-GD* induced, and spontaneously expressing TECs never displayed HLA-DQ, a bright stain of HLA-DQ was found after IFN-γ incubation (Table 3).

TEC-cultures were investigated by means of IF with specific monoclonal antibodies for contaminations with dendritic cells, macrophages or T-cells. Only in cultures with FCS could a weak staining of scattered macrophages sometimes be observed. When the effect of MMI or PC on IFN-γ or TSH induced HLA-D expression was investigated, only a slight decrease of HLA-D staining could be observed (Table 4).

Discussion

Admittedly, these in vitro studies can only give limited information about the induction of class-

II expression by TECs in vivo. Our studies suggest, however, that the chronic stimulation of TECs through the TSH-receptor as well as the cellular polarity of TECs play a role in the modulation of class-II expression. We postulate that the cellular polarity modulates the availability of TSH-receptors in TEC-cultures (Mauchamp et al. 1979). This appears to be the reason, why the induction and reexpression of class-II antigen by TSH could only be observed under serum free culture conditions. The class-II expression of TECs in vivo (Londei et al. 1984) resembles more generally the staining pattern we observed after induction with TSH than that with IFN-γ. In contrast to TEC-cultures expressing spontaneously HLA-DR and M-antigen, IFN-γ strongly induces HLA-DQ, and can induce in vitro TECs derived from autoimmune (GD) as well as non-immune (NTG) thyroid patients. Moreover, we could not detect by means of indirect IF contaminating dendritic cells, T-cells or macrophages which would account for IFN-γ production in our serum free culture system. In addition to that, the supernatants of spontaneously class-II expressing TEC-cultures could not induce class-II in secondary TECs, which one would expect if IFN-γ would be produced by contaminating activated lymphocytes in TECs. On the other hand, we could also

Table 4.

Effect of methimazole (MMI) and perchlorate (PC) on the HLA-DR of thyroid epithelial cells.

	IFN-γ	+MMI	+PC	+TSH	TSH	+MMI	+PC
DR	+++	+++	++	+++	++	++	+
DQ	+++	++	++	+++	-	-	-

not detect interleukin-1 in these supernatants (not shown).

The effect MMI has during suppression therapy of GD *in vivo* and on antibody synthesis *in vitro* (McGregor et al. 1980) has been attributed to immuno-suppressive effects. In our hands, MMI and PC have no effect on class-II expression of TECs. This reflects previous findings in recurrent hyperthyroidism of GD-patients (Carel et al. 1986) and findings in GD-therapy where MMI had the same effect as PC, which surely is not considered as an immuno-suppressive drug (Wenzel et al. 1984).

Acknowledgments

The expert technical assistance of Ms A. Bulasch is gratefully appreciated.

This project was supported by Deutsche Forschungsgemeinschaft SFB 232/C 4.

References

- Balfour B M, Drexhage H A, Kamperdijk E W A & Hoefsmit E C M (1981): Antigen-presenting cells, including Langerhans' cells, veiled cells and interdigitating cells; in microenvironments in haemopoietic and lymphoid differentiations. *Ciba Symp* 84: 281.
- Carel J C, Rémy J J, Zuchman D, Salamero J & Charreire J (1986): Role of methimazole on DR antigen expression on human thyroid epithelial cell cultures. In: Drexhage H A & Wiersinga W M (eds). *Thyroid and Autoimmunity*, pp 145–147. Excerpta Medica, Elsevier, Amsterdam.
- Davies T F (1985): Co-cultures of human thyroid monolayers and autologous T cells-impact of HLA class II antigen expression. *J Clin Endocrinol Metab* 61: 418–422.
- Hanafusa T, Pujol-Borrell R, Chiovato L, Russel R C G, Doniach D & Bottazzo G F (1983): Aberrant expression of HLA-DR antigen on thyrocytes in Graves' disease: relevance for auto-immunity. *Lancet* 2: 1111.
- Londei M, Lamb J R, Bottazzo G F & Feldmann M (1984): Epithelial cells expressing aberrant MHC class-II determinations can present antigen to cloned human T-cell. *Nature* 22: 639.
- Mauchamp J, Margotat A, Chambard M, Charrier B, Remy L & Michel-Bechet M (1979): Polarity of three-dimensional structures derived from isolated dog thyroid cells in primary culture. *Cell Tissue Res* 204: 417–430.
- McGregor A M, Petersen M M, McLachlan S M, Rocke P, Smith S R & Hall R (1980): Carbimazole and the autoimmune response in Graves' disease. *N Engl J Med* 303: 302.
- Todd I, Pujol-Borrell R, Hammond L J, Bottazzo G F & Feldmann M (1985): Interferon- γ induces HLA-DR expression by thyroid epithelium. *Clin Exp Immunol* 61: 265–273.
- Weetman A P, Volkman D J, Burman K D, Gerrald T L & Fauci A S (1985): The *in vitro* regulation of human thyrocyte HLA-DR antigen expression. *J Clin Endocrinol Metab* 61: 817–824.
- Wenzel B E, Gutekunst R, Mansky T, Schultek Th & Scriba P C (1986): Thyrotropin and IgG from patients with Graves' disease induce class-II antigen on human thyroid cells. In: Drexhage H A & Wiersinga W M (eds). *Thyroid and Autoimmunity*, pp 141–144. Excerpta Medica, Elsevier, Amsterdam.
- Wenzel K W & Lente J R (1984): Similar effects of thionamide drugs and perchlorate on thyroid-stimulating immunoglobulins in Graves' disease: evidence against an immunosuppressive action of thionamide drugs. *J Clin Endocrinol Metab* 58: 62.