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The thyrotropin receptor in thyroid carcinoma

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References



REFERENCES

- (1) Hundahl SA, Fleming ID, Fremgen AM, Menck HR. A National Cancer Data Base report on 53,856 cases of thyroid carcinoma treated in the U.S., 1985-1995. *Cancer*. 1998;83:2638-48.
- (2) Schlumberger MJ. Papillary and follicular thyroid carcinoma. *N Engl J Med*. 1998;338:297-306.
- (3) Haugen BR, Pacini F, Reiners C, Schlumberger M, Ladenson PW, Sherman SI et al. A comparison of recombinant human thyrotropin and thyroid hormone withdrawal for the detection of thyroid remnant or cancer. *J Clin Endocrinol Metab*. 1999;84:3877-85.
- (4) Kuijpers JL, Hansen B, Hamming JF, Ribot JG, Haak HR, Coebergh JW. Trends in treatment and long-term survival of thyroid cancer in southeastern Netherlands, 1960-1992. *Eur J Cancer*. 1998;34:1235-41.
- (5) Smit JW, Schroder-van der Elst JP, Karperien M, Que I, Stokkel M, van der HD et al. Iodide kinetics and experimental (131)I therapy in a xenotransplanted human sodium-iodide symporter-transfected human follicular thyroid carcinoma cell line. *J Clin Endocrinol Metab*. 2002;87:1247-53.
- (6) Sakoda LC, Horn-Ross PL. Reproductive and menstrual history and papillary thyroid cancer risk: the San Francisco Bay Area thyroid cancer study. *Cancer Epidemiol Biomarkers Prev*. 2002;11:51-57.
- (7) Burrow GN, Burke WR, Himmelhoch JM, Spencer RP, Hershman JM. Effect of lithium on thyroid function. *J Clin Endocrinol Metab*. 1971;32:647-52.
- (8) Hand, S and Wittekind, Ch. *Thyroid Gland, Oral Cavity and Oropharynx ICD-O C73. UICC TNM Classification of Malignant Tumors* . 2002. New York, Wiley Liss.
- (9) Sobin LH, Wittekind C. *TNM Classification of Malignant Tumors*. 6 ed. Wiley, Hoboken, New Jersey; 2002.
- (10) Kukkonen ST, Haapiainen RK, Franssila KO, Sivula AH. Papillary thyroid carcinoma: the new, age-related TNM classification system in a retrospective analysis of 199 patients. *World J Surg*. 1990;14:837-41.
- (11) Wittekind C, Wagner G. *TNM Classification of malignant tumors*. 5 ed. Springer Berlin; 1997.
- (12) Sobrinho-Simoes M, Preto A, Rocha AS, Castro P, Maximo V, Fonseca E et al. Molecular pathology of well-differentiated thyroid carcinomas. *Virchows Arch*. 2005;447:787-93.
- (13) Fagin JA. How thyroid tumors start and why it matters: kinase mutants as targets for solid cancer pharmacotherapy. *J Endocrinol*. 2004;183:249-56.
- (14) Soares P, Sobrinho-Simoes M. Recent advances in cytometry, cytogenetics and molecular genetics of thyroid tumors and tumor-like lesions. *Pathol Res Pract*. 1995;191:304-17.
- (15) Tallini G. Molecular pathobiology of thyroid neoplasms. *Endocr Pathol*. 2002;13:271-88.
- (16) Cinti R, Yin L, Ilc K, Berger N, Basolo F, Cuccato S et al. RET rearrangements in papillary thyroid carcinomas and adenomas detected by interphase FISH. *Cytogenet Cell Genet*. 2000;88:56-61.

- (17) Corvi R, Berger N, Balczon R, Romeo G. RET/PCM-1: a novel fusion gene in papillary thyroid carcinoma. *Oncogene*. 2000;19:4236-42.
- (18) Klugbauer S, Jauch A, Lengfelder E, Demidchik E, Rabes HM. A novel type of RET rearrangement (PTC8) in childhood papillary thyroid carcinomas and characterization of the involved gene (RFG8). *Cancer Res*. 2000;60:7028-32.
- (19) Nikiforov YE, Rowland JM, Bove KE, Monforte-Munoz H, Fagin JA. Distinct pattern of ret oncogene rearrangements in morphological variants of radiation-induced and sporadic thyroid papillary carcinomas in children. *Cancer Res*. 1997;57:1690-1694.
- (20) Grieco M, Santoro M, Berlingieri MT, Melillo RM, Donghi R, Bongarzone I et al. PTC is a novel rearranged form of the ret proto-oncogene and is frequently detected in vivo in human thyroid papillary carcinomas. *Cell*. 1990;60:557-63.
- (21) Santoro M, Chiappetta G, Cerrato A, Salvatore D, Zhang L, Manzo G et al. Development of thyroid papillary carcinomas secondary to tissue- specific expression of the RET/PTC1 oncogene in transgenic mice. *Oncogene*. 1996;12:1821-26.
- (22) Santoro M, Dathan NA, Berlingieri MT, Bongarzone I, Paulin C, Grieco M et al. Molecular characterization of RET/PTC3; a novel rearranged version of the RETproto-oncogene in a human thyroid papillary carcinoma. *Oncogene*. 1994;9:509-16.
- (23) Santoro M, Grieco M, Melillo RM, Fusco A, Vecchio G. Molecular defects in thyroid carcinomas: role of the RET oncogene in thyroid neoplastic transformation. *Eur J Endocrinol*. 1995;133:513-22.
- (24) Santoro M, Carlomagno F, Hay ID, Herrmann MA, Grieco M, Melillo R et al. Ret oncogene activation in human thyroid neoplasms is restricted to the papillary cancer subtype. *J Clin Invest*. 1992;89:1517-22.
- (25) Viglietto G, Chiappetta G, Martinez-Tello FJ, Fukunaga FH, Tallini G, Rigopoulou D et al. RET/PTC oncogene activation is an early event in thyroid carcinogenesis. *Oncogene*. 1995;11:1207-10.
- (26) Greco A, Pierotti MA, Bongarzone I, Pagliardini S, Lanzi C, Della PG. TRK-T1 is a novel oncogene formed by the fusion of TPR and TRK genes in human papillary thyroid carcinomas. *Oncogene*. 1992;7:237-42.
- (27) Xing M. BRAF mutation in thyroid cancer. *Endocr Relat Cancer*. 2005;12:245-62.
- (28) Soares P, Trovisco V, Rocha AS, Lima J, Castro P, Preto A et al. BRAF mutations and RET/PTC rearrangements are alternative events in the etiopathogenesis of PTC. *Oncogene*. 2003;22:4578-80.
- (29) Puxeddu E, Moretti S, Elisei R, Romei C, Pascucci R, Martinelli M et al. BRAF(V599E) mutation is the leading genetic event in adult sporadic papillary thyroid carcinomas. *J Clin Endocrinol Metab*. 2004;89:2414-20.
- (30) Fukushima T, Suzuki S, Mashiko M, Ohtake T, Endo Y, Takebayashi Y et al. BRAF mutations in papillary carcinomas of the thyroid. *Oncogene*. 2003;22:6455-57.
- (31) Ivan M, Bond JA, Prat M, Comoglio PM, Wynford-Thomas D. Activated ras and ret oncogenes induce over-expression of c-met (hepatocyte growth factor receptor) in human thyroid epithelial cells. *Oncogene*. 1997;14:2417-23.

- (32) Tung WS, Shevlin DW, Kaleem Z, Tribune DJ, Wells SAJ, Goodfellow PJ. Allelotype of follicular thyroid carcinomas reveals genetic instability consistent with frequent nondisjunctional chromosomal loss. *Genes Chromosomes Cancer*. 1997;19:43-51.
- (33) Kroll TG, Sarraf P, Pecciarini L, Chen CJ, Mueller E, Spiegelman BM et al. PAX8-PPARGgamma1 fusion oncogene in human thyroid carcinoma [corrected] [published erratum appears in *Science* 2000 Sep 1;289(5484):1474]. *science*. 2000;289:1357-60.
- (34) Ying H, Suzuki H, Furumoto H, Walker R, Meltzer P, Willingham MC et al. Alterations in genomic profiles during tumor progression in a mouse model of follicular thyroid carcinoma. *Carcinogenesis*. 2003;24:1467-79.
- (35) Vecchio G, Santoro M. Oncogenes and thyroid cancer. *Clin Chem Lab Med*. 2000;38:113-16.
- (36) Caillou B, Troalen F, Baudin E, Talbot M, Filetti S, Schlumberger M et al. Na⁺/I⁻ symporter distribution in human thyroid tissues: an immunohistochemical study. *J Clin Endocrinol Metab*. 1998;83:4102-6.
- (37) Lazar V, Bidart JM, Caillou B, Mahe C, Lacroix L, Filetti S et al. Expression of the Na⁺/I⁻ symporter gene in human thyroid tumors: a comparison study with other thyroid-specific genes. *J Clin Endocrinol Metab*. 1999;84:3228-34.
- (38) McHenry CR, Rosen IB, Walfish PG. Prospective management of nodal metastases in differentiated thyroid cancer. *Am J Surg*. 1991;162:353-56.
- (39) Dohan O, Baloch Z, Banrevi Z, LiVolsi V, Carrasco N. Rapid communication: predominant intracellular overexpression of the Na⁺/I⁻ symporter (NIS) in a large sampling of thyroid cancer cases. *J Clin Endocrinol Metab*. 2001;86:2697-700.
- (40) Ravetto C, Colombo L, Dottorini ME. Usefulness of fine-needle aspiration in the diagnosis of thyroid carcinoma: a retrospective study in 37,895 patients. *Cancer*. 2000;90:357-63.
- (41) Haugen BR, Woodmansee WW, McDermott MT. Towards improving the utility of fine-needle aspiration biopsy for the diagnosis of thyroid tumors. *Clin Endocrinol (Oxf)*. 2002;56:281-90.
- (42) Demeure MJ, Clark OH. Surgery in the treatment of thyroid cancer. *Endocrinol Metab Clin North Am*. 1990;19:663-83.
- (43) Mazzaferri EL, Kloos RT. Clinical review 128: Current approaches to primary therapy for papillary and follicular thyroid cancer. *J Clin Endocrinol Metab*. 2001;86:1447-63.
- (44) Baudin E, Travagli JP, Ropers J, Mancusi F, Bruno-Bossio G, Caillou B et al. Microcarcinoma of the thyroid gland: the Gustave-Roussy Institute experience [see comments]. *Cancer*. 1998;83:553-59.
- (45) DeGroot LJ, Kaplan EL, McCormick M, Straus FH. Natural history, treatment, and course of papillary thyroid carcinoma. *J Clin Endocrinol Metab*. 1990;71:414-24.
- (46) Katoh R, Sasaki J, Kurihara H, Suzuki K, Iida Y, Kawaoi A. Multiple thyroid involvement (intraglandular metastasis) in papillary thyroid carcinoma. A clinicopathologic study of 105 consecutive patients. *Cancer*. 1992;70:1585-90.
- (47) ROSE RG, KELSEY MP, RUSSELL WO, IBANEZ ML, WHITE EC, CLARK RL. Follow-up study of thyroid cancer

treated by unilateral lobectomy. *Am J Surg.* 1963;106:494-500.:494-500.

- (48) Utiger RD. Follow-up of patients with thyroid carcinoma [editorial; comment]. *N Engl J Med.* 1997;337:928-30.
- (49) Mazzaferri EL, Jhiang SM. Long-term impact of initial surgical and medical therapy on papillary and follicular thyroid cancer. *Am J Med.* 1994;97:418-28.
- (50) Tubiana M, Schlumberger M, Rougier P, Laplanche A, Benhamou E, Gardet P et al. Long-term results and prognostic factors in patients with differentiated thyroid carcinoma. *Cancer.* 1985;55:794-804.
- (51) Simpson WJ, Panzarella T, Carruthers JS, Gospodarowicz MK, Sutcliffe SB. Papillary and follicular thyroid cancer: impact of treatment in 1578 patients. *Int J Radiat Oncol Biol Phys.* 1988;14:1063-75.
- (52) Sherman SI, Tielens ET, Sostre S, Wharam MD, Jr., Ladenson PW. Clinical utility of posttreatment radioiodine scans in the management of patients with thyroid carcinoma. *J Clin Endocrinol Metab.* 1994;78:629-34.
- (53) Tenenbaum F, Corone C, Schlumberger M, Parmentier C. Thyroglobulin measurement and postablative iodine-131 total body scan after total thyroidectomy for differentiated thyroid carcinoma in patients with no evidence of disease. *Eur J Cancer.* 1996;32A:1262.
- (54) Sawka AM, Thepamongkhon K, Brouwers M, Thabane L, Browman G, Gerstein HC. Clinical review 170: A systematic review and metaanalysis of the effectiveness of radioactive iodine remnant ablation for well-differentiated thyroid cancer. *J Clin Endocrinol Metab.* 2004;89:3668-76.
- (55) Samaan NA, Schultz PN, Hickey RC, Goepfert H, Haynie TP, Johnston DA et al. The results of various modalities of treatment of well differentiated thyroid carcinomas: a retrospective review of 1599 patients. *J Clin Endocrinol Metab.* 1992;75:714-20.
- (56) Mazzaferri EL. Thyroid remnant 131I ablation for papillary and follicular thyroid carcinoma. *Thyroid.* 1997;7:265-71.
- (57) Rubino C, De Vathaire F, Dottorini ME, Hall P, Schwartz C, Couette JE et al. Second primary malignancies in thyroid cancer patients. *Br J Cancer.* 2003;89:1638-44.
- (58) Pacini F, Ladenson PW, Schlumberger M, Driedger A, Luster M, Kloos RT et al. Radioiodine ablation of thyroid remnants after preparation with recombinant human thyrotropin in differentiated thyroid carcinoma: results of an international, randomized, controlled study. *J Clin Endocrinol Metab.* 2006;91:926-32.
- (59) Pacini F, Schlumberger M, Harmer C, Berg GG, Cohen O, Duntas L et al. Post-surgical use of radioiodine (131I) in patients with papillary and follicular thyroid cancer and the issue of remnant ablation: a consensus report. *Eur J Endocrinol.* 2005;153:651-59.
- (60) Schlumberger M, Challeton C, De Vathaire F, Parmentier C. Treatment of distant metastases of differentiated thyroid carcinoma. *J Endocrinol Invest.* 1995;18:170-172.
- (61) Schlumberger M, Challeton C, De Vathaire F, Travagli JP, Gardet P, Lumbroso JD et al. Radioactive iodine treatment and external radiotherapy for lung and bone metastases from thyroid carcinoma. *J Nucl Med.* 1996;37:598-605.

- (62) Eustatia-Rutten CF, Smit JW, Romijn JA, van der Kleij-Corssmit EP, Pereira AM, Stokkel MP et al. Diagnostic value of serum thyroglobulin measurements in the follow-up of differentiated thyroid carcinoma, a structured meta-analysis. *Clin Endocrinol (Oxf)*. 2004;61:61-74.
- (63) Spencer CA, Wang CC. Thyroglobulin measurement. Techniques, clinical benefits, and pitfalls. *Endocrinol Metab Clin North Am*. 1995;24:841-63.
- (64) Spencer CA, Takeuchi M, Kazarosyan M. Current status and performance goals for serum thyroglobulin assays. *Clin Chem*. 1996;42:164-73.
- (65) Van Herle AJ, Uller RP, Matthews NI, Brown J. Radioimmunoassay for measurement of thyroglobulin in human serum. *J Clin Invest*. 1973;52:1320-1327.
- (66) Mariotti S, Barbesino G, Caturegli P, Marino M, Manetti L, Pacini F et al. Assay of thyroglobulin in serum with thyroglobulin autoantibodies: an unobtainable goal? *J Clin Endocrinol Metab*. 1995;80:468-72.
- (67) Ericsson UB, Christensen SB, Thorell JI. A high prevalence of thyroglobulin autoantibodies in adults with and without thyroid disease as measured with a sensitive solid-phase immunosorbent radioassay. *Clin Immunol Immunopathol*. 1985;37:154-62.
- (68) Ligabue A, Poggioli MC, Zacchini A. Interference of specific autoantibodies in the assessment of serum thyroglobulin. *J Nucl Biol Med*. 1993;37:273-79.
- (69) Schlumberger M, Pacini F, Wiersinga WM, Toft A, Smit JW, Sanchez FF et al. Follow-up and management of differentiated thyroid carcinoma: a European perspective in clinical practice. *Eur J Endocrinol*. 2004;151:539-48.
- (70) Span PN, Slegers MJ, Van Den Broek WJ, Ross HA, Nieuwlaet WA, Hermus AR et al. Quantitative detection of peripheral thyroglobulin mRNA has limited clinical value in the follow-up of thyroid cancer patients. *Ann Clin Biochem*. 2003;40:94-99.
- (71) Bugalho MJ, Domingues RS, Pinto AC, Garrao A, Catarino AL, Ferreira T et al. Detection of thyroglobulin mRNA transcripts in peripheral blood of individuals with and without thyroid glands: evidence for thyroglobulin expression by blood cells. *Eur J Endocrinol*. 2001;145:409-13.
- (72) Roddiger SJ, Bojunga J, Klee V, Stanisch M, Renneberg H, Lindhorst E et al. Detection of thyroid peroxidase mRNA in peripheral blood of patients with malignant and benign thyroid diseases. *J Mol Endocrinol*. 2002;29:287-95.
- (73) Cooper DS, Doherty GM, Haugen BR, Kloos RT, Lee SL, Mandel SJ et al. Management guidelines for patients with thyroid nodules and differentiated thyroid cancer. *Thyroid*. 2006;16:109-42.
- (74) Torlontano M, Crocetti U, D'Aloiso L, Bonfitto N, Di Giorgio A, Modoni S et al. Serum thyroglobulin and ¹³¹I whole body scan after recombinant human TSH stimulation in the follow-up of low-risk patients with differentiated thyroid cancer. *Eur J Endocrinol*. 2003;148:19-24.
- (75) Frasoldati A, Pesenti M, Gallo M, Caroggio A, Salvo D, Valcavi R. Diagnosis of neck recurrences in patients with differentiated thyroid carcinoma. *Cancer*. 2003;97:90-96.
- (76) Pacini F, Molinaro E, Castagna MG, Agate L, Elisei R, Ceccarelli C et al. Recombinant human thyrotropin-stimulated serum thyroglobulin combined with neck ultrasonography has the highest sensitivity in

- monitoring differentiated thyroid carcinoma. *J Clin Endocrinol Metab.* 2003;88:3668-73.
- (77) Hooft L, Hoekstra OS, Deville W, Lips P, Teule GJ, Boers M et al. Diagnostic accuracy of 18F-fluorodeoxyglucose positron emission tomography in the follow-up of papillary or follicular thyroid cancer. *J Clin Endocrinol Metab.* 2001;86:3779-86.
- (78) Schluter B, Bohuslavizki KH, Beyer W, Plotkin M, Buchert R, Clausen M. Impact of FDG PET on patients with differentiated thyroid cancer who present with elevated thyroglobulin and negative 131I scan. *J Nucl Med.* 2001;42:71-76.
- (79) Van Tol KM, Jager PL, Piers DA, Pruim J, de Vries EG, Dullaart RP et al. Better yield of (18)fluorodeoxyglucose-positron emission tomography in patients with metastatic differentiated thyroid carcinoma during thyrotropin stimulation. *Thyroid.* 2002;12:381-87.
- (80) Stokkel MP, Reigman HI, Verkooijen RB, Smit JW. Indium-111-Octreotide scintigraphy in differentiated thyroid carcinoma metastases that do not respond to treatment with high-dose I-131. *J Cancer Res Clin Oncol.* 2003;129:287-94.
- (81) Stokkel MP, Verkooijen RB, Smit JW. Indium-111 octreotide scintigraphy for the detection of non-functioning metastases from differentiated thyroid cancer: diagnostic and prognostic value. *Eur J Nucl Med Mol Imaging.* 2004;31:950-957.
- (82) Biondi B, Filetti S, Schlumberger M. Thyroid-hormone therapy and thyroid cancer: a reassessment. *Nat Clin Pract Endocrinol Metab.* 2005;1:32-40.
- (83) Pujol P, Daures JP, Nsakala N, Baldet L, Bringer J, Jaffiol C. Degree of thyrotropin suppression as a prognostic determinant in differentiated thyroid cancer. *J Clin Endocrinol Metab.* 1996;81:4318-23.
- (84) Cooper DS, Specker B, Ho M, Sperling M, Ladenson PW, Ross DS et al. Thyrotropin suppression and disease progression in patients with differentiated thyroid cancer: results from the National Thyroid Cancer Treatment Cooperative Registry. *Thyroid.* 1998;8:737-44.
- (85) Jonklaas J, Sarlis NJ, Litofsky D, Ain KB, Bigos ST, Brierley JD et al. Outcomes of patients with differentiated thyroid carcinoma following initial therapy. *Thyroid.* 2006;16:1229-42.
- (86) Heemstra KA, Hamdy NA, Romijn JA, Smit JW. The effects of thyrotropin-suppressive therapy on bone metabolism in patients with well-differentiated thyroid carcinoma. *Thyroid.* 2006;16:583-91.
- (87) Biondi B, Palmieri EA, Klain M, Schlumberger M, Filetti S, Lombardi G. Subclinical hyperthyroidism: clinical features and treatment options. *Eur J Endocrinol.* 2005;152:1-9.
- (88) Pacini F, Agate L, Elisei R, Capezzone M, Ceccarelli C, Lippi F et al. Outcome of differentiated thyroid cancer with detectable serum Tg and negative diagnostic (131)I whole body scan: comparison of patients treated with high (131)I activities versus untreated patients. *J Clin Endocrinol Metab.* 2001;86:4092-97.
- (89) Ruegemer JJ, Hay ID, Bergstralh EJ, Ryan JJ, Offord KP, Gorman CA. Distant metastases in differentiated thyroid carcinoma: a multivariate analysis of prognostic variables. *J Clin Endocrinol Metab.* 1988;67:501-8.
- (90) Haugen BR. Management of the patient with progressive radioiodine non-responsive disease. *Semin*

Surg Oncol. 1999;16:34-41.

- (91) De Besi P, Busnardo B, Toso S, Girelli ME, Nacamulli D, Simioni N et al. Combined chemotherapy with bleomycin, adriamycin, and platinum in advanced thyroid cancer. *J Endocrinol Invest.* 1991;14:475-80.
- (92) Ain KB, Egorin MJ, DeSimone PA. Treatment of anaplastic thyroid carcinoma with paclitaxel: phase 2 trial using ninety-six-hour infusion. Collaborative Anaplastic Thyroid Cancer Health Intervention Trials (CATCHIT) Group. *Thyroid.* 2000;10:587-94.
- (93) Venkataraman GM, Yatin M, Marcinek R, Ain KB. Restoration of iodide uptake in dedifferentiated thyroid carcinoma: relationship to human Na⁺/I⁻-symporter gene methylation status. *J Clin Endocrinol Metab.* 1999;84:2449-57.
- (94) Kitazono M, Robey R, Zhan Z, Sarlis NJ, Skarulis MC, Aikou T et al. Low concentrations of the histone deacetylase inhibitor, depsipeptide (FR901228), increase expression of the Na⁺/I⁻ symporter and iodine accumulation in poorly differentiated thyroid carcinoma cells. *J Clin Endocrinol Metab.* 2001;86:3430-3435.
- (95) Furuya F, Shimura H, Suzuki H, Taki K, Ohta K, Haraguchi K et al. Histone deacetylase inhibitors restore radioiodide uptake and retention in poorly differentiated and anaplastic thyroid cancer cells by expression of the sodium/iodide symporter thyroperoxidase and thyroglobulin. *Endocrinology.* 2004;145:2865-75.
- (96) Faivre S, Chieze S, Delbaldo C, Ady-Vago N, Guzman C, Lopez-Lazaro L et al. Phase I and pharmacokinetic study of aplidine, a new marine cyclodepsipeptide in patients with advanced malignancies. *J Clin Oncol.* 2005;23:7871-80.
- (97) Castaigne S, Chomienne C, Daniel MT, Ballerini P, Berger R, Fenaux P et al. All-trans retinoic acid as a differentiation therapy for acute promyelocytic leukemia. I. Clinical results [see comments]. *Blood.* 1990;76:1704-9.
- (98) McBurney MW, Costa S, Pratt MA. Retinoids and cancer: a basis for differentiation therapy. [Review] [107 refs]. *Cancer Invest.* 1993;11:590-598.
- (99) Lotan R. Retinoids as modulators of tumor cells invasion and metastasis. [Review] [87 refs]. *Semin Cancer Biol.* 1991;2:197-208.
- (100) Schmutzler C, Brtko J, Bienert K, Kohrle J. Effects of retinoids and role of retinoic acid receptors in human thyroid carcinomas and cell lines derived therefrom. *Exp Clin Endocrinol Diabetes.* 1996;104 Suppl 4:16-19.
- (101) Schmutzler C, Kohrle J. Retinoic acid redifferentiation therapy for thyroid cancer. *Thyroid.* 2000;10:393-406.
- (102) Van Herle AJ, Agatep ML, Padua DN, III, Totanes TL, Canlapan DV, Van Herle HM et al. Effects of 13 cis-retinoic acid on growth and differentiation of human follicular carcinoma cells (UCLA R0 82 W-1) in vitro. *J Clin Endocrinol Metab.* 1990;71:755-63.
- (103) Havekes B, Schroder Van Der Elst JP, van der PG, Goslings BM, Romijn JA, Smit JW. Beneficial effects of retinoic acid on extracellular matrix degradation and attachment behaviour in follicular thyroid carcinoma cell lines. *J Endocrinol.* 2000;167:229-38.

- (104) Schmutzler C, Schmitt TL, Glaser F, Loos U, Kohrle J. The promoter of the human sodium/iodide-symporter gene responds to retinoic acid. *Mol Cell Endocrinol.* 2002;189:145-55.
- (105) Simon D, Kohrle J, Schmutzler C, Mainz K, Reiners C, Roher HD. Redifferentiation therapy of differentiated thyroid carcinoma with retinoic acid: basics and first clinical results. *Exp Clin Endocrinol Diabetes.* 1996;104 Suppl 4:13-15.
- (106) Simon D, Koehrle J, Reiners C, Boerner AR, Schmutzler C, Mainz K et al. Redifferentiation therapy with retinoids: therapeutic option for advanced follicular and papillary thyroid carcinoma. *World J Surg.* 1998;22:569-74.
- (107) Simon D, Korber C, Krausch M, Segering J, Groth P, Gorges R et al. Clinical impact of retinoids in redifferentiation therapy of advanced thyroid cancer: final results of a pilot study. *Eur J Nucl Med Mol Imaging.* 2002;29:775-82.
- (108) Coelho SM, Corbo R, Buescu A, Carvalho DP, Vaisman M. Retinoic acid in patients with radioiodine non-responsive thyroid carcinoma. *J Endocrinol Invest.* 2004;27:334-39.
- (109) Short SC, Suovuori A, Cook G, Vivian G, Harmer C. A phase II study using retinoids as redifferentiation agents to increase iodine uptake in metastatic thyroid cancer. *Clin Oncol (R Coll Radiol).* 2004;16:569-74.
- (110) Elisei R, Vivaldi A, Agate L, Ciampi R, Molinaro E, Piampiani P et al. All-trans-retinoic acid treatment inhibits the growth of retinoic acid receptor beta messenger ribonucleic acid expressing thyroid cancer cell lines but does not reinduce the expression of thyroid-specific genes. *J Clin Endocrinol Metab.* 2005;90:2403-11.
- (111) Haugen BR, Larson LL, Pugazhenth U, Hays WR, Klopper JP, Kramer CA et al. Retinoic acid and retinoid X receptors are differentially expressed in thyroid cancer and thyroid carcinoma cell lines and predict response to treatment with retinoids. *J Clin Endocrinol Metab.* 2004;89:272-80.
- (112) Farol LT, Hymes KB. Bexarotene: a clinical review. *Expert review of anticancer therapy.* 2004;4:180-188.
- (113) Liu YY, Stokkel MP, Pereira AM, Corssmit EP, Morreau HA, Romijn JA et al. Bexarotene increases uptake of radioiodide in metastases of differentiated thyroid carcinoma. *Eur J Endocrinol.* 2006;154:525-31.
- (114) Philips JC, Petite C, Willi JP, Buchegger F, Meier CA. Effect of peroxisome proliferator-activated receptor gamma agonist, rosiglitazone, on dedifferentiated thyroid cancers. *Nucl Med Commun.* 2004;25:1183-86.
- (115) Ohta K, Endo T, Haraguchi K, Hershman JM, Onaya T. Ligands for peroxisome proliferator-activated receptor gamma inhibit growth and induce apoptosis of human papillary thyroid carcinoma cells. *J Clin Endocrinol Metab.* 2001;86:2170-2177.
- (116) Wong WW, Dimitroulakos J, Minden MD, Penn LZ. HMG-CoA reductase inhibitors and the malignant cell: the statin family of drugs as triggers of tumor-specific apoptosis. *Leukemia.* 2002;16:508-19.
- (117) Demierre MF, Higgins PD, Gruber SB, Hawk E, Lippman SM. Statins and cancer prevention. *Nat Rev Cancer.* 2005;5:930-942.
- (118) Wang CY, Zhong WB, Chang TC, Lai SM, Tsai YF. Lovastatin, a 3-hydroxy-3-methylglutaryl coenzyme A

reductase inhibitor, induces apoptosis and differentiation in human anaplastic thyroid carcinoma cells. *J Clin Endocrinol Metab.* 2003;88:3021-26.

- (119) Zhong WB, Liang YC, Wang CY, Chang TC, Lee WS. Lovastatin suppresses invasiveness of anaplastic thyroid cancer cells by inhibiting Rho geranylgeranylation and RhoA/ROCK signaling. *Endocr Relat Cancer.* 2005;12:615-29.
- (120) Yao CJ, Lai GM, Chan CF, Cheng AL, Yang YY, Chuang SE. Dramatic synergistic anticancer effect of clinically achievable doses of lovastatin and troglitazone. *Int J Cancer.* 2006;118:773-79.
- (121) Frohlich E, Machicao F, Wahl R. Action of thiazolidinediones on differentiation, proliferation and apoptosis of normal and transformed thyrocytes in culture. *Endocr Relat Cancer.* 2005;12:291-303.
- (122) Bunone G, Vigneri P, Mariani L, Buto S, Collini P, Pilotti S et al. Expression of angiogenesis stimulators and inhibitors in human thyroid tumors and correlation with clinical pathological features. *Am J Pathol.* 1999;155:1967-76.
- (123) Bauer AJ, Terrell R, Doniparthi NK, Patel A, Tuttle RM, Saji M et al. Vascular endothelial growth factor monoclonal antibody inhibits growth of anaplastic thyroid cancer xenografts in nude mice. *Thyroid.* 2002;12:953-61.
- (124) Ye C, Feng C, Wang S, Liu X, Lin Y, Li M. Antiangiogenic and antitumor effects of endostatin on follicular thyroid carcinoma. *Endocrinology.* 2002;143:3522-28.
- (125) Levine AM, Tulpule A, Quinn DI, Gorospe G, III, Smith DL, Hornor L et al. Phase I study of antisense oligonucleotide against vascular endothelial growth factor: decrease in plasma vascular endothelial growth factor with potential clinical efficacy. *J Clin Oncol.* 2006;24:1712-19.
- (126) Schiff BA, McMurphy AB, Jasser SA, Younes MN, Doan D, Yigitbasi OG et al. Epidermal growth factor receptor (EGFR) is overexpressed in anaplastic thyroid cancer, and the EGFR inhibitor gefitinib inhibits the growth of anaplastic thyroid cancer. *Clin Cancer Res.* 2004;10:8594-602.
- (127) Carlomagno F, Vitagliano D, Guida T, Napolitano M, Vecchio G, Fusco A et al. The kinase inhibitor PP1 blocks tumorigenesis induced by RET oncogenes. *Cancer Res.* 2002;62:1077-82.
- (128) Carlomagno F, Anaganti S, Guida T, Salvatore G, Troncone G, Wilhelm SM et al. BAY 43-9006 inhibition of oncogenic RET mutants. *J Natl Cancer Inst.* 2006;98:326-34.
- (129) Younes MN, Yigitbasi OG, Park YW, Kim SJ, Jasser SA, Hawthorne VS et al. Antivascular therapy of human follicular thyroid cancer experimental bone metastasis by blockade of epidermal growth factor receptor and vascular growth factor receptor phosphorylation. *Cancer Res.* 2005;65:4716-27.
- (130) Stokkel MP, Verkooijen RB, Bouwsma H, Smit JW. Six month follow-up after ¹¹¹In-DTPA-octreotide therapy in patients with progressive radioiodine non-responsive thyroid cancer: a pilot study. *Nucl Med Commun.* 2004;25:683-90.
- (131) Teunissen JJ, Kwekkeboom DJ, Krenning EP. Staging and treatment of differentiated thyroid carcinoma with radiolabeled somatostatin analogs. *Trends Endocrinol Metab.* 2006;17:19-25.
- (132) Szkudlinski MW, Fremont V, Ronin C, Weintraub BD. Thyroid-stimulating hormone and thyroid-stimulating hormone receptor structure-function relationships. *Physiol Rev.* 2002;82:473-502.

- (133) Prummel MF, Brokken LJ, Wiersinga WM. Ultra short-loop feedback control of thyrotropin secretion. *Thyroid*. 2004;14:825-29.
- (134) Kopp P. The TSH receptor and its role in thyroid disease. *Cell Mol Life Sci*. 2001;58:1301-22.
- (135) Shupnik MA, Chin WW, Habener JF, Ridgway EC. Transcriptional regulation of the thyrotropin subunit genes by thyroid hormone. *J Biol Chem*. 1985;260:2900-2903.
- (136) Taylor T, Gyves P, Burgunder JM. Thyroid hormone regulation of TRH mRNA levels in rat paraventricular nucleus of the hypothalamus changes during ontogeny. *Neuroendocrinology*. 1990;52:262-67.
- (137) Vassart G, Pardo L, Costagliola S. A molecular dissection of the glycoprotein hormone receptors. *Trends Biochem Sci*. 2004;29:119-26.
- (138) Szkudlinski MW, Teh NG, Grossmann M, Tropea JE, Weintraub BD. Engineering human glycoprotein hormone superactive analogues. *Nat Biotechnol*. 1996;14:1257-63.
- (139) Farid NR, Szkudlinski MW. Minireview: structural and functional evolution of the thyrotropin receptor. *Endocrinology*. 2004;145:4048-57.
- (140) Van Sande J, Dequanter D, Lothaire P, Massart C, Dumont JE, Erneux C. Thyrotropin stimulates the generation of inositol 1,4,5-trisphosphate in human thyroid cells. *J Clin Endocrinol Metab*. 2006;91:1099-107.
- (141) Saiardi A, Falasca P, Civitareale D. Synergistic transcriptional activation of the thyrotropin receptor promoter by cyclic AMP-responsive-element-binding protein and thyroid transcription factor 1. *Biochem J*. 1995;310:491-96.
- (142) Yokomori N, Tawata M, Saito T, Shimura H, Onaya T. Regulation of the rat thyrotropin receptor gene by the methylation-sensitive transcription factor GA-binding protein. *Mol Endocrinol*. 1998;12:1241-49.
- (143) Saji M, Akamizu T, Sanchez M, Obici S, Avvedimento E, Gottesman ME et al. Regulation of thyrotropin receptor gene expression in rat FRTL-5 thyroid cells. *Endocrinology*. 1992;130:520-533.
- (144) Davies T, Mariani R, Latif R. The TSH receptor reveals itself. *J Clin Invest*. 2002;110:161-64.
- (145) Wadsworth HL, Russo D, Nagayama Y, Chazenbalk GD, Rapoport B. Studies on the role of amino acids 38-45 in the expression of a functional thyrotropin receptor. *Mol Endocrinol*. 1992;6:394-98.
- (146) Kursawe R, Paschke R. Modulation of TSHR signaling by posttranslational modifications. *Trends Endocrinol Metab*. 2007;18:199-207.
- (147) Loosfelt H, Pichon C, Jolivet A, Misrahi M, Caillou B, Jamous M et al. Two-subunit structure of the human thyrotropin receptor. *Proc Natl Acad Sci U S A*. 1992;89:3765-69.
- (148) Cetani F, Tonacchera M, Vassart G. Differential effects of NaCl concentration on the constitutive activity of the thyrotropin and the luteinizing hormone/chorionic gonadotropin receptors. *FEBS Lett*. 1996;378:27-31.
- (149) Baratti-Elbaz C, Ghinea N, Lahuna O, Loosfelt H, Pichon C, Milgrom E. Internalization and recycling pathways of the thyrotropin receptor. *Mol Endocrinol*. 1999;13:1751-65.

- (150) Postiglione MP, Parlato R, Rodriguez-Mallon A, Rosica A, Mithbaakar P, Maresca M et al. Role of the thyroid-stimulating hormone receptor signaling in development and differentiation of the thyroid gland. *Proc Natl Acad Sci U S A*. 2002;99:15462-67.
- (151) Paschke R, Ludgate M. The thyrotropin receptor in thyroid diseases. *N Engl J Med*. 1997;337:1675-81.
- (152) Hollowell JG, Staehling NW, Flanders WD, Hannon WH, Gunter EW, Spencer CA et al. Serum TSH, T(4), and thyroid antibodies in the United States population (1988 to 1994): National Health and Nutrition Examination Survey (NHANES III). *J Clin Endocrinol Metab*. 2002;87:489-99.
- (153) Rapoport B, Chazenbalk GD, Jaume JC, McLachlan SM. The thyrotropin (TSH) receptor: interaction with TSH and autoantibodies. *Endocr Rev*. 1998;19:673-716.
- (154) Kosugi S, Ban T, Akamizu T, Valente W, Kohn LD. Use of thyrotropin receptor (TSHR) mutants to detect stimulating TSHR antibodies in hypothyroid patients with idiopathic myxedema, who have blocking TSHR antibodies. *J Clin Endocrinol Metab*. 1993;77:19-24.
- (155) Tanaka K, Sonoo H, Yamamoto Y, Udagawa K, Kunisue H, Arime I et al. Changes of expression level of the differentiation markers in papillary thyroid carcinoma under thyrotropin suppression therapy in vivo immunohistochemical detection of thyroglobulin, thyroid peroxidase, and thyrotropin receptor [In Process Citation]. *J Surg Oncol* 2000 Oct ;75 (2):108 -16.75:108-16.
- (156) Brabant G, Maenhaut C, Kohrle J, Scheumann G, Dralle H, Hoang-Vu C et al. Human thyrotropin receptor gene: expression in thyroid tumors and correlation to markers of thyroid differentiation and dedifferentiation. *Mol Cell Endocrinol*. 1991;82:R7-12.
- (157) Agretti P, Chiovato L, De Marco G, Marcocci C, Mazzi B, Sellari-Franceschini S et al. Real-time PCR provides evidence for thyrotropin receptor mRNA expression in orbital as well as in extraorbital tissues. *Eur J Endocrinol*. 2002;147:733-39.
- (158) Spitzweg C, Heufelder AE. Update on the thyroid sodium iodide symporter: a novel thyroid antigen emerging on the horizon. *Eur J Endocrinol*. 1997;137:22-23.
- (159) Prabhakar BS, Bahn RS, Smith TJ. Current perspective on the pathogenesis of Graves' disease and ophthalmopathy. *Endocr Rev*. 2003;24:802-35.
- (160) Inoue M, Tawata M, Yokomori N, Endo T, Onaya T. Expression of thyrotropin receptor on clonal osteoblast-like rat osteosarcoma cells. *Thyroid*. 1998;8:1059-64.
- (161) Abe E, Marians RC, Yu W, Wu XB, Ando T, Li Y et al. TSH is a negative regulator of skeletal remodeling. *Cell*. 2003;115:151-62.
- (162) Morimura T, Tsunekawa K, Kasahara T, Seki K, Ogiwara T, Mori M et al. Expression of type 2 iodothyronine deiodinase in human osteoblast is stimulated by thyrotropin. *Endocrinology*. 2005;146:2077-84.
- (163) Tsai JA, Janson A, Bucht E, Kindmark H, Marcus C, Stark A et al. Weak evidence of thyrotropin receptors in primary cultures of human osteoblast-like cells. *Calcif Tissue Int*. 2004;74:486-91.
- (164) Sun L, Davies TF, Blair HC, Abe E, Zaidi M. TSH and bone loss. *Ann N Y Acad Sci*. 2006;1068:309-18.
- (165) Galliford TM, Murphy E, Williams AJ, Bassett JH, Williams GR. Effects of thyroid status on bone

- metabolism: a primary role for thyroid stimulating hormone or thyroid hormone? *Minerva Endocrinol.* 2005;30:237-46.
- (166) Sampath TK, Simic P, Sendak R, Draca N, Bowe AE, O'Brien S et al. Thyroid-stimulating hormone restores bone volume, microarchitecture, and strength in aged ovariectomized rats. *J Bone Miner Res.* 2007;22:849-59.
- (167) Bassett JH, O'Shea PJ, Sriskantharajah S, Rabier B, Boyde A, Howell PG et al. Thyroid hormone excess rather than thyrotropin deficiency induces osteoporosis in hyperthyroidism. *Mol Endocrinol.* 2007;21:1095-107.
- (168) Leitolf H, Tong KP, Grossmann M, Weintraub BD, Szkudlinski MW. Bioengineering of human thyrotropin superactive analogs by site-directed "lysine-scanning" mutagenesis. Cooperative effects between peripheral loops. *J Biol Chem.* 2000;275:27457-65.
- (169) Grossmann M, Leitolf H, Weintraub BD, Szkudlinski MW. A rational design strategy for protein hormone superagonists. *Nat Biotechnol.* 1998;16:871-75.
- (170) Matzuk MM, Kornmeier CM, Whitfield GK, Kourides IA, Boime I. The Glycoprotein Alpha-Subunit Is Critical for Secretion and Stability of the Human Thyrotropin Beta-Subunit. *Molecular Endocrinology.* 1988;2:95-100.
- (171) Boime I, Ben Menahem D. Glycoprotein hormone structure-function and analog design. *Recent Prog Horm Res.* 1999;54:271-88.
- (172) Grossmann M, Wong R, Szkudlinski MW, Weintraub BD. Human thyroid-stimulating hormone (hTSH) subunit gene fusion produces hTSH with increased stability and serum half-life and compensates for mutagenesis-induced defects in subunit association. *J Biol Chem.* 1997;272:21312-16.
- (173) Grossmann M, Szkudlinski MW, Zeng H, Kraiem Z, Ji I, Tropea JE et al. Role of the carboxy-terminal residues of the alpha-subunit in the expression and bioactivity of human thyroid-stimulating hormone. *Mol Endocrinol.* 1995;9:948-58.
- (174) Pastan I, Hassan R, FitzGerald DJ, Kreitman RJ. Immunotoxin treatment of cancer. *Annu Rev Med.* 2007;58:221-37.:221-37.
- (175) Brinkmann U, Pai LH, FitzGerald DJ, Willingham M, Pastan I. B3(Fv)-PE38KDEL, a single-chain immunotoxin that causes complete regression of a human carcinoma in mice. *Proc Natl Acad Sci U S A.* 1991;88:8616-20.
- (176) Gilbert JA, Gianoukakis AG, Salehi S, Moorhead J, Rao PV, Khan MZ et al. Monoclonal pathogenic antibodies to the thyroid-stimulating hormone receptor in Graves' disease with potent thyroid-stimulating activity but differential blocking activity activate multiple signaling pathways. *J Immunol.* 2006;176:5084-92.
- (177) Olsnes S, Kozlov JV. *Ricin.* 2001;39:1723-28.
- (178) Smallshaw JE, Ghetie V, Rizo J, Fulmer JR, Trahan LL, Ghetie MA et al. Genetic engineering of an immunotoxin to eliminate pulmonary vascular leak in mice. *Nat Biotechnol.* 2003;21:387-91.
- (179) Pastan I, Kreitman RJ. Immunotoxins for targeted cancer therapy. *Adv Drug Deliv Rev.* 1998;31:53-88.

- (180) Leland P, Taguchi J, Husain SR, Kreitman RJ, Pastan I, Puri RK. Human breast carcinoma cells express type II IL-4 receptors and are sensitive to antitumor activity of a chimeric IL-4-Pseudomonas exotoxin fusion protein in vitro and in vivo. *Mol Med*. 2000;6:165-78.
- (181) Kreitman RJ, Wilson WH, Bergeron K, Raggio M, Stetler-Stevenson M, FitzGerald DJ et al. Efficacy of the anti-CD22 recombinant immunotoxin BL22 in chemotherapy-resistant hairy-cell leukemia. *N Engl J Med*. 2001;345:241-47.
- (182) FitzGerald DJ, Kreitman R, Wilson W, Squires D, Pastan I. Recombinant immunotoxins for treating cancer. *Int J Med Microbiol*. 2004;293:577-82.
- (183) Kreitman RJ, Pastan I. Immunotoxins in the treatment of hematologic malignancies. *Curr Drug Targets*. 2006;7:1301-11.
- (184) Pelham HR, Roberts LM, Lord JM. Toxin entry: how reversible is the secretory pathway? *Trends Cell Biol*. 1992;2:183-85.
- (185) Chaudhary VK, Jinno Y, Gallo MG, FitzGerald D, Pastan I. Mutagenesis of Pseudomonas exotoxin in identification of sequences responsible for the animal toxicity. *J Biol Chem*. 1990;265:16306-10.
- (186) Jackson ME, Simpson JC, Girod A, Pepperkok R, Roberts LM, Lord JM. The KDEL retrieval system is exploited by Pseudomonas exotoxin A, but not by Shiga-like toxin-1, during retrograde transport from the Golgi complex to the endoplasmic reticulum. *J Cell Sci*. 1999;112:467-75.
- (187) Hessler JL, Kreitman RJ. An early step in Pseudomonas exotoxin action is removal of the terminal lysine residue, which allows binding to the KDEL receptor. *Biochemistry*. 1997;36:14577-82.
- (188) Collier RJ. Understanding the mode of action of diphtheria toxin: a perspective on progress during the 20th century. *Toxicon*. 2001;39:1793-803.
- (189) Naglich JG, Metherall JE, Russell DW, Eidels L. Expression Cloning of A Diphtheria-Toxin Receptor - Identity with A Heparin-Binding Egf-Like Growth-Factor Precursor. *Cell*. 1992;69:1051-61.
- (190) O'Keefe D, Collier RJ. Cloned diphtheria toxin within the periplasm of Escherichia coli causes lethal membrane damage at low pH. *Proc Natl Acad Sci U S A*. 1989;86:343-46.
- (191) Seetharam S, Chaudhary VK, FitzGerald D, Pastan I. Increased cytotoxic activity of Pseudomonas exotoxin and two chimeric toxins ending in KDEL. *J Biol Chem*. 1991;266:17376-81.
- (192) Costagliola S, Morgenthaler NG, Hoermann R, Badenhop K, Struck J, Freitag D et al. Second generation assay for thyrotropin receptor antibodies has superior diagnostic sensitivity for Graves' disease. *J Clin Endocrinol Metab*. 1999;84:90-97.
- (193) Vitti P, Elisei R, Tonacchera M, Chiovato L, Mancusi F, Rago T et al. Detection of thyroid-stimulating antibody using Chinese hamster ovary cells transfected with cloned human thyrotropin receptor. *J Clin Endocrinol Metab*. 1993;76:499-503.
- (194) Wallaschowski H, Paschke R. Detection of thyroid stimulating (TSAB)- and thyrotropin stimulation blocking (TSBAB) antibodies with CHO cell lines expressing different TSH-receptor numbers. *Clin Endocrinol (Oxf)*. 1999;50:365-72.

- (195) Massart C, Gibassier J, Verite F, Fergelot P, Maugendre D. Use of Chinese hamster ovary cell lines transfected with cloned human thyrotropin receptor for the measurement of thyroid-stimulating antibodies: advantages and difficulties. *Clin Chim Acta*. 2000;291:67-81.
- (196) Ochi Y, Kajita Y, Wu L, Iidaka M, Nagayama Y. Augmentative effect of polyethylene glycol, polyvinyl alcohol and dextran on thyroid-stimulating antibody stimulated cAMP production in FRTL-5 cells and CHO cells expressing human TSH receptor. *Horm Res*. 2000;53:20-25.
- (197) Takasu N, Yamashiro K, Ochi Y, Sato Y, Nagata A, Komiya I et al. TSBAb (TSH-stimulation blocking antibody) and TSAb (thyroid stimulating antibody) in TSBAb-positive patients with hypothyroidism and Graves' patients with hyperthyroidism. *Horm Metab Res*. 2001;33:232-37.
- (198) Watson PF, Ajjan RA, Phipps J, Metcalfe R, Weetman AP. A new chemiluminescent assay for the rapid detection of thyroid stimulating antibodies in Graves' disease. *Clin Endocrinol (Oxf)*. 1998;49:577-81.
- (199) Evans C, Morgenthaler NG, Lee S, Llewellyn DH, Clifton-Bligh R, John R et al. Development of a luminescent bioassay for thyroid stimulating antibodies. *J Clin Endocrinol Metab*. 1999;84:374-77.
- (200) Jordan NJ, Rinderle C, Ashfield J, Morgenthaler NG, Lazarus J, Ludgate M et al. A luminescent bioassay for thyroid blocking antibodies. *Clin Endocrinol (Oxf)*. 2001;54:355-64.
- (201) Minich WB, Lenzner C, Bergmann A, Morgenthaler NG. A coated tube assay for the detection of blocking thyrotropin receptor autoantibodies. *J Clin Endocrinol Metab*. 2004;89:352-56.
- (202) Crile G, Jr. Endocrine dependency of papillary carcinomas of the thyroid. *JAMA*. 1966;195:721-24.
- (203) Goldberg LD, Ditchek NT. Thyroid carcinoma with spinal cord compression. *JAMA*. 1981;245:953-54.
- (204) BALME HW. Metastatic carcinoma of the thyroid successfully treated with thyroxine. *Lancet*. 1954;266:812-13.
- (205) Ichikawa Y, Saito E, Abe Y, Homma M, Muraki T. Presence of TSH receptor in thyroid neoplasms. *J Clin Endocrinol Metab*. 1976;42:395-98.
- (206) Carayon P, Thomas-Morvan C, Castanas E, Tubiana M. Human thyroid cancer: membrane thyrotropin binding and adenylate cyclase activity. *J Clin Endocrinol Metab*. 1980;51:915-20.
- (207) Clark OH, Gerend PL, Goretzki P, Nissenson RA. Characterization of the thyrotropin receptor-adenylate cyclase system in neoplastic human thyroid tissue. *J Clin Endocrinol Metab*. 1983;57:140-147.
- (208) Roger P, Taton M, Van Sande J, Dumont JE. Mitogenic effects of thyrotropin and adenosine 3',5'-monophosphate in differentiated normal human thyroid cells in vitro. *J Clin Endocrinol Metab*. 1988;66:1158-65.
- (209) Goretzki PE, Frilling A, Simon D, Roeher HD. Growth regulation of normal thyroids and thyroid tumors in man. *Recent Results Cancer Res*. 1990;118:48-63.
- (210) Schlumberger M, Baudin E. Serum thyroglobulin determination in the follow-up of patients with differentiated thyroid carcinoma. *Eur J Endocrinol*. 1998;138:249-52.
- (211) Pacini F, Schlumberger M, Dralle H, Elisei R, Smit JW, Wiersinga W. European consensus for the

management of patients with differentiated thyroid carcinoma of the follicular epithelium. *Eur J Endocrinol.* 2006;154:787-803.

- (212) Cooper DS, Doherty GM, Haugen BR, Kloos RT, Lee SL, Mandel SJ et al. Management Guidelines for Patients with Thyroid Nodules and Differentiated Thyroid Cancer. *Thyroid.* 2006;..
- (213) Heemstra KA, Liu YY, Stokkel M, Kievit J, Corssmit E, Pereira AM et al. Serum thyroglobulin concentrations predict disease-free remission and death in differentiated thyroid carcinoma. *Clin Endocrinol (Oxf).* 2007;66:58-64.
- (214) Morgenthaler NG, Froehlich J, Rendl J, Willnich M, Alonso C, Bergmann A et al. Technical evaluation of a new immunoradiometric and a new immunoluminometric assay for thyroglobulin. *Clin Chem.* 2002;48:1077-83.
- (215) Pacini F, Schlumberger M, Dralle H, Elisei R, Smit JW, Wiersinga W. European consensus for the management of patients with differentiated thyroid carcinoma of the follicular epithelium. *Eur J Endocrinol.* 2006;154:787-803.
- (216) Cooper DS, Doherty GM, Haugen BR, Kloos RT, Lee SL, Mandel SJ et al. Management Guidelines for Patients with Thyroid Nodules and Differentiated Thyroid Cancer. *Thyroid.* 2006;..
- (217) Smit JW, Eustatia-Rutten CF, Corssmit EP, Pereira AM, Frolich M, Bleeker GB et al. Reversible diastolic dysfunction after long-term exogenous subclinical hyperthyroidism: a randomized, placebo-controlled study. *J Clin Endocrinol Metab.* 2005;90:6041-47.
- (218) Shellman YG, Ribble D, Miller L, Gendall J, Vanbuskirk K, Kelly D et al. Lovastatin-induced apoptosis in human melanoma cell lines. *Melanoma Res.* 2005;15:83-89.
- (219) Park C, Lee I, Kang WK. Lovastatin-induced E2F-1 modulation and its effect on prostate cancer cell death. *Carcinogenesis.* 2001;22:1727-31.
- (220) Muller C, Bockhorn AG, Klusmeier S, Kiehl M, Roeder C, Kalthoff H et al. Lovastatin inhibits proliferation of pancreatic cancer cell lines with mutant as well as with wild-type K-ras oncogene but has different effects on protein phosphorylation and induction of apoptosis. *Int J Oncol.* 1998;12:717-23.
- (221) Motomura W, Nagamine M, Tanno S, Sawamukai M, Takahashi N, Kohgo Y et al. Inhibition of cell invasion and morphological change by troglitazone in human pancreatic cancer cells. *J Gastroenterol.* 2004;39:461-68.
- (222) Yu J, Qiao L, Zimmermann L, Ebert MP, Zhang H, Lin W et al. Troglitazone inhibits tumor growth in hepatocellular carcinoma in vitro and in vivo. *Hepatology.* 2006;43:134-43.
- (223) Yang YC, Tsao YP, Ho TC, Choung IP. Peroxisome proliferator-activated receptor-gamma agonists cause growth arrest and apoptosis in human ovarian carcinoma cell lines. *Int J Gynecol Cancer.* 2007;17:418-25.
- (224) Ray DM, Akbiyik F, Phipps RP. The peroxisome proliferator-activated receptor gamma (PPARGgamma) ligands 15-deoxy-Delta12,14-prostaglandin J2 and ciglitazone induce human B lymphocyte and B cell lymphoma apoptosis by PPARGgamma-independent mechanisms. *J Immunol.* 2006;177:5068-76.
- (225) Freudlsperger C, Moll I, Schumacher U, Thies A. Anti-proliferative effect of peroxisome proliferator-

- activated receptor gamma agonists on human malignant melanoma cells in vitro. *Anticancer Drugs*. 2006;17:325-32.
- (226) Li M, Lee TW, Mok TS, Warner TD, Yim AP, Chen GG. Activation of peroxisome proliferator-activated receptor-gamma by troglitazone (TGZ) inhibits human lung cell growth. *J Cell Biochem*. 2005;96:760-774.
- (227) Patel L, Pass I, Coxon P, Downes CP, Smith SA, Macphee CH. Tumor suppressor and anti-inflammatory actions of PPARgamma agonists are mediated via upregulation of PTEN. *Curr Biol*. 2001;11:764-68.
- (228) Teresi RE, Shaiu CW, Chen CS, Chatterjee VK, Waite KA, Eng C. Increased PTEN expression due to transcriptional activation of PPARgamma by Lovastatin and Rosiglitazone. *Int J Cancer*. 2006;118:2390-2398.
- (229) Frohlich E, Machicao F, Wahl R. Action of thiazolidinediones on differentiation, proliferation and apoptosis of normal and transformed thyrocytes in culture. *Endocr Relat Cancer*. 2005;12:291-303.
- (230) Andela VB, Pirri M, Schwarz EM, Puzas EJ, O'Keefe RJ, Rosenblatt JD et al. The mevalonate synthesis pathway as a therapeutic target in cancer. *Clin Orthop Relat Res*. 2003;S59-S66.
- (231) Hirai A, Nakamura S, Noguchi Y, Yasuda T, Kitagawa M, Tatsuno I et al. Geranylgeranylated rho small GTPase(s) are essential for the degradation of p27Kip1 and facilitate the progression from G1 to S phase in growth-stimulated rat FRTL-5 cells. *J Biol Chem*. 1997;272:13-16.
- (232) Noguchi Y, Nakamura S, Yasuda T, Kitagawa M, Kohn LD, Saito Y et al. Newly synthesized Rho A, not Ras, is isoprenylated and translocated to membranes coincident with progression of the G1 to S phase of growth-stimulated rat FRTL-5 cells. *J Biol Chem*. 1998;273:3649-53.
- (233) Pruitt K, Der CJ. Ras and Rho regulation of the cell cycle and oncogenesis. *Cancer Lett*. 2001;171:1-10.
- (234) Denicourt C, Dowdy SF. Cip/Kip proteins: more than just CDKs inhibitors. *Genes Dev*. 2004;18:851-55.
- (235) Gil J, Peters G. Regulation of the INK4b-ARF-INK4a tumor suppressor locus: all for one or one for all. *Nat Rev Mol Cell Biol*. 2006;7:667-77.
- (236) Maddika S, Ande SR, Panigrahi S, Paranjothy T, Weglarczyk K, Zuse A et al. Cell survival, cell death and cell cycle pathways are interconnected: implications for cancer therapy. *Drug Resist Updat*. 2007;10:13-29.
- (237) Yano M, Matsumura T, Senokuchi T, Ishii N, Murata Y, Taketa K et al. Statins Activate Peroxisome Proliferator-Activated Receptor {gamma} Through Extracellular Signal-Regulated Kinase 1/2 and p38 Mitogen-Activated Protein Kinase-Dependent Cyclooxygenase-2 Expression in Macrophages. *Circ Res*. 2007.
- (238) Weng LP, Gimm O, Kum JB, Smith WM, Zhou XP, Wynford-Thomas D et al. Transient ectopic expression of PTEN in thyroid cancer cell lines induces cell cycle arrest and cell type-dependent cell death. *Hum Mol Genet*. 2001;10:251-58.
- (239) Burstein HJ, Demetri GD, Mueller E, Sarraf P, Spiegelman BM, Winer EP. Use of the peroxisome proliferator-activated receptor (PPAR) gamma ligand troglitazone as treatment for refractory breast cancer: a phase II study. *Breast Cancer Res Treat*. 2003;79:391-97.

- (240) Thibault A, Samid D, Tompkins AC, Figg WD, Cooper MR, Hohl RJ et al. Phase I study of lovastatin, an inhibitor of the mevalonate pathway, in patients with cancer. *Clin Cancer Res*. 1996;2:483-91.
- (241) Szkudlinski MW, Grossmann M, Weintraub BD. Structure-function studies of human TSH - New advances in design of glycoprotein hormone analogs. *Trends in Endocrinology and Metabolism*. 1996;7:277-86.
- (242) Prummel MF, Brokken LJ, Wiersinga WM. Ultra short-loop feedback control of thyrotropin secretion. *Thyroid*. 2004;14:825-29.
- (243) Grossmann M, Leitolf H, Weintraub BD, Szkudlinski MW. A rational design strategy for protein hormone superagonists. *Nature Biotechnology*. 1998;16:871-75.
- (244) Hovens GC, Buiting AM, Karperien M, Ballieux BE, van der PG, Pereira AM et al. A bioluminescence assay for thyrotropin receptor antibodies predicts serum thyroid hormone levels in patients with de novo Graves' disease. *Clin Endocrinol (Oxf)*. 2006;64:429-35.
- (245) Dai G, Levy O, Carrasco N. Cloning and characterization of the thyroid iodide transporter. *Nature*. 1996;379:458-60.
- (246) Sugino K, Kure Y, Iwasaki H, Matsumoto A. Does total thyroidectomy induce metabolic bone disturbance? *Int Surg*. 1992;77:178-80.
- (247) Sandvig K, van Deurs B. Delivery into cells: lessons learned from plant and bacterial toxins. *Gene Ther*. 2005;12:865-72.
- (248) Grossmann M, Szkudlinski MW, Tropea JE, Bishop LA, Thotakura NR, Schofield PR et al. Expression of human thyrotropin in cell lines with different glycosylation patterns combined with mutagenesis of specific glycosylation sites. Characterization of a novel role for the oligosaccharides in the in vitro and in vivo bioactivity. *J Biol Chem*. 1995;270:29378-85.
- (249) Azzam N, Bar-Shalom R, Kraiem Z, Fares F. Human thyrotropin (TSH) variants designed by site-directed mutagenesis block TSH activity in vitro and in vivo. *Endocrinology*. 2005;146:2845-50.
- (250) Hollowell JG, Staehling NW, Flanders WD, Hannon WH, Gunter EW, Spencer CA et al. Serum TSH, T(4), and thyroid antibodies in the United States population (1988 to 1994): National Health and Nutrition Examination Survey (NHANES III). *J Clin Endocrinol Metab*. 2002;87:489-99.
- (251) Rapoport B, Chazenbalk GD, Jaume JC, McLachlan SM. The thyrotropin (TSH) receptor: interaction with TSH and autoantibodies. *Endocr Rev*. 1998;19:673-716.
- (252) Paschke R, Ludgate M. The thyrotropin receptor in thyroid diseases. *N Engl J Med*. 1997;337:1675-81.
- (253) Kosugi S, Ban T, Akamizu T, Valente W, Kohn LD. Use of thyrotropin receptor (TSHR) mutants to detect stimulating TSHR antibodies in hypothyroid patients with idiopathic myxedema, who have blocking TSHR antibodies. *J Clin Endocrinol Metab*. 1993;77:19-24.
- (254) Costagliola S, Morgenthaler NG, Hoermann R, Badenhoop K, Struck J, Freitag D et al. Second generation assay for thyrotropin receptor antibodies has superior diagnostic sensitivity for Graves' disease. *J Clin Endocrinol Metab*. 1999;84:90-97.
- (255) McKenzie JM, Zakarija M. Fetal and neonatal hyperthyroidism and hypothyroidism due to maternal TSH

- receptor antibodies. *Thyroid*. 1992;2:155-59.
- (256) Vitti P, Elisei R, Tonacchera M, Chiovato L, Mancusi F, Rago T et al. Detection of thyroid-stimulating antibody using Chinese hamster ovary cells transfected with cloned human thyrotropin receptor. *J Clin Endocrinol Metab*. 1993;76:499-503.
- (257) Wallaschofski H, Paschke R. Detection of thyroid stimulating (TSAB)- and thyrotropin stimulation blocking (TSBAB) antibodies with CHO cell lines expressing different TSH-receptor numbers. *Clin Endocrinol (Oxf)*. 1999;50:365-72.
- (258) Massart C, Gibassier J, Verite F, Fergelot P, Maugendre D. Use of Chinese hamster ovary cell lines transfected with cloned human thyrotropin receptor for the measurement of thyroid-stimulating antibodies: advantages and difficulties. *Clin Chim Acta*. 2000;291:67-81.
- (259) Ochi Y, Kajita Y, Wu L, Iidaka M, Nagayama Y. Augmentative effect of polyethylene glycol, polyvinyl alcohol and dextran on thyroid-stimulating antibody stimulated cAMP production in FRTL-5 cells and CHO cells expressing human TSH receptor. *Horm Res*. 2000;53:20-25.
- (260) Takasu N, Yamashiro K, Ochi Y, Sato Y, Nagata A, Komiya I et al. TSBAb (TSH-stimulation blocking antibody) and TSAb (thyroid stimulating antibody) in TSBAb-positive patients with hypothyroidism and Graves' patients with hyperthyroidism. *Horm Metab Res*. 2001;33:232-37.
- (261) Watson PF, Ajjan RA, Phipps J, Metcalfe R, Weetman AP. A new chemiluminescent assay for the rapid detection of thyroid stimulating antibodies in Graves' disease. *Clin Endocrinol (Oxf)*. 1998;49:577-81.
- (262) Evans C, Morgenthaler NG, Lee S, Llewellyn DH, Clifton-Bligh R, John R et al. Development of a luminescent bioassay for thyroid stimulating antibodies. *J Clin Endocrinol Metab*. 1999;84:374-77.
- (263) Jordan NJ, Rinderle C, Ashfield J, Morgenthaler NG, Lazarus J, Ludgate M et al. A luminescent bioassay for thyroid blocking antibodies. *Clin Endocrinol (Oxf)*. 2001;54:355-64.
- (264) Minich WB, Lenzner C, Bergmann A, Morgenthaler NG. A coated tube assay for the detection of blocking thyrotropin receptor autoantibodies. *J Clin Endocrinol Metab*. 2004;89:352-56.
- (265) Watson PF, Ajjan RA, Phipps J, Metcalfe R, Weetman AP. A new chemiluminescent assay for the rapid detection of thyroid stimulating antibodies in Graves' disease. *Clin Endocrinol (Oxf)*. 1998;49:577-81.
- (266) Evans C, Morgenthaler NG, Lee S, Llewellyn DH, Clifton-Bligh R, John R et al. Development of a luminescent bioassay for thyroid stimulating antibodies. *J Clin Endocrinol Metab*. 1999;84:374-77.
- (267) Evans C, Morgenthaler NG, Lee S, Llewellyn DH, Clifton-Bligh R, John R et al. Development of a luminescent bioassay for thyroid stimulating antibodies. *J Clin Endocrinol Metab*. 1999;84:374-77.
- (268) Watson PF, Ajjan RA, Phipps J, Metcalfe R, Weetman AP. A new chemiluminescent assay for the rapid detection of thyroid stimulating antibodies in Graves' disease. *Clin Endocrinol (Oxf)*. 1998;49:577-81.
- (269) Takasu N, Yamashiro K, Ochi Y, Sato Y, Nagata A, Komiya I et al. TSBAb (TSH-stimulation blocking antibody) and TSAb (thyroid stimulating antibody) in TSBAb-positive patients with hypothyroidism and Graves' patients with hyperthyroidism. *Horm Metab Res*. 2001;33:232-37.
- (270) Watanabe Y, Tahara K, Hirai A, Tada H, Kohn LD, Amino N. Subtypes of anti-TSH receptor antibodies

classified by various assays using CHO cells expressing wild-type or chimeric human TSH receptor. *Thyroid*. 1997;7:13-19.

- (271) Ochi Y, Hamazu M, Kajita Y, Nagata A. Demonstration of anti-TSH antibody in TSH binding inhibitory immunoglobulin-positive sera of patients with Graves' disease. *Clin Endocrinol (Oxf)*. 2002;56:405-12.
- (272) Werner SC. Modification of the classification of the eye changes of Graves' disease. *Am J Ophthalmol*. 1977;83:725-27.
- (273) Perret J, Ludgate M, Libert F, Gerard C, Dumont JE, Vassart G et al. Stable expression of the human TSH receptor in CHO cells and characterization of differentially expressing clones. *Biochem Biophys Res Commun*. 1990;171:1044-50.
- (274) Evans C, Morgenthaler NG, Lee S, Llewellyn DH, Clifton-Bligh R, John R et al. Development of a luminescent bioassay for thyroid stimulating antibodies. *J Clin Endocrinol Metab*. 1999;84:374-77.
- (275) Watson PF, Ajjan RA, Phipps J, Metcalfe R, Weetman AP. A new chemiluminescent assay for the rapid detection of thyroid stimulating antibodies in Graves' disease. *Clin Endocrinol (Oxf)*. 1998;49:577-81.
- (276) Jordan NJ, Rinderle C, Ashfield J, Morgenthaler NG, Lazarus J, Ludgate M et al. A luminescent bioassay for thyroid blocking antibodies. *Clin Endocrinol (Oxf)*. 2001;54:355-64.
- (277) Minich WB, Lenzner C, Bergmann A, Morgenthaler NG. A coated tube assay for the detection of blocking thyrotropin receptor autoantibodies. *J Clin Endocrinol Metab*. 2004;89:352-56.
- (278) Evans C, Morgenthaler NG, Lee S, Llewellyn DH, Clifton-Bligh R, John R et al. Development of a luminescent bioassay for thyroid stimulating antibodies. *J Clin Endocrinol Metab*. 1999;84:374-77.
- (279) Watson PF, Ajjan RA, Phipps J, Metcalfe R, Weetman AP. A new chemiluminescent assay for the rapid detection of thyroid stimulating antibodies in Graves' disease. *Clin Endocrinol (Oxf)*. 1998;49:577-81.
- (280) Morgenthaler NG, Hodak K, Seissler J, Steinbrenner H, Pampel I, Gupta M et al. Direct binding of thyrotropin receptor autoantibody to in vitro translated thyrotropin receptor: a comparison to radioreceptor assay and thyroid stimulating bioassay. *Thyroid*. 1999;9:466-75.
- (281) Wallaschofski H, Paschke R. Detection of thyroid stimulating (TSAB)- and thyrotropin stimulation blocking (TSBAB) antibodies with CHO cell lines expressing different TSH-receptor numbers. *Clin Endocrinol (Oxf)*. 1999;50:365-72.
- (282) Massart C, Gibassier J, Verite F, Fergelot P, Maugeudre D. Use of Chinese hamster ovary cell lines transfected with cloned human thyrotropin receptor for the measurement of thyroid-stimulating antibodies: advantages and difficulties. *Clin Chim Acta*. 2000;291:67-81.
- (283) Evans C, Morgenthaler NG, Lee S, Llewellyn DH, Clifton-Bligh R, John R et al. Development of a luminescent bioassay for thyroid stimulating antibodies. *J Clin Endocrinol Metab*. 1999;84:374-77.
- (284) Jordan NJ, Rinderle C, Ashfield J, Morgenthaler NG, Lazarus J, Ludgate M et al. A luminescent bioassay for thyroid blocking antibodies. *Clin Endocrinol (Oxf)*. 2001;54:355-64.
- (285) Massart C, Gibassier J, Verite F, Fergelot P, Maugeudre D. Use of Chinese hamster ovary cell lines transfected with cloned human thyrotropin receptor for the measurement of thyroid-stimulating

- antibodies: advantages and difficulties. *Clin Chim Acta*. 2000;291:67-81.
- (286) Hirayu H, Magnusson RP, Rapoport B. Studies on the mechanism of desensitization of the cyclic AMP response to TSH stimulation in a cloned rat thyroid cell line. *Mol Cell Endocrinol*. 1985;42:21-27.
- (287) Damante G, Foti D, Catalfamo R, Filetti S. Desensitization of the thyroid cyclic AMP response to thyroid stimulating immunoglobulin: comparison with TSH. *Metabolism*. 1987;36:768-73.
- (288) Lalli E, Sassone-Corsi P. Thyroid-stimulating hormone (TSH)-directed induction of the CREM gene in the thyroid gland participates in the long-term desensitization of the TSH receptor. *Proc Natl Acad Sci U S A*. 1995;92:9633-37.
- (289) Bidey SP, Ryder K, Gaines-Das R, Marshall NJ, Ekins RP. A comparison of the bioactivity of human and bovine thyrotrophin preparations, as determined by intracellular cyclic AMP responses of cultured FRTL-5 cells and human thyroid cell monolayers. *Acta Endocrinol (Copenh)*. 1984;106:482-89.
- (290) Reader SC, Davison B, Robertson WR, Lambert A. Assessment of the bioactivity of human and bovine thyrotrophin preparations using a porcine thyroid cell bioassay. *Ann Clin Biochem*. 1989;26:341-45.
- (291) Nissim M, Lee KO, Petrick PA, Dahlberg PA, Weintraub BD. A sensitive thyrotropin (TSH) bioassay based on iodide uptake in rat FRTL-5 thyroid cells: comparison with the adenosine 3',5'-monophosphate response to human serum TSH and enzymatically deglycosylated bovine and human TSH. *Endocrinology*. 1987;121:1278-87.
- (292) Ando T, Latif R, Davies TF. Concentration-dependent regulation of thyrotropin receptor function by thyroid-stimulating antibody. *J Clin Invest*. 2004;113:1589-95.
- (293) Tada H, Mizuta I, Takano T, Tatsumi KI, Izumi Y, Hidaka Y et al. Blocking-type anti-TSH receptor antibodies and relation to responsiveness to antithyroid drug therapy and remission in Graves' disease. *Clin Endocrinol (Oxf)*. 2003;58:403-8.
- (294) Lenzner C, Morgenthaler NG. The effect of thyrotropin-receptor blocking antibodies on stimulating autoantibodies from patients with Graves' disease. *Thyroid*. 2003;13:1153-61.
- (295) Gerding MN, van der Meer JW, Broenink M, Bakker O, Wiersinga WM, Prummel MF. Association of thyrotrophin receptor antibodies with the clinical features of Graves' ophthalmopathy. *Clin Endocrinol (Oxf)*. 2000;52:267-71.
- (296) De Bellis A, Bizzarro A, Conte M, Coronella C, Solimeno S, Perrino S et al. Relationship between longitudinal behaviour of some markers of eye autoimmunity and changes in ocular findings in patients with Graves' ophthalmopathy receiving corticosteroid therapy. *Clin Endocrinol (Oxf)*. 2003;59:388-95.
- (297) Gerding MN, van der Meer JW, Broenink M, Bakker O, Wiersinga WM, Prummel MF. Association of thyrotrophin receptor antibodies with the clinical features of Graves' ophthalmopathy. *Clin Endocrinol (Oxf)*. 2000;52:267-71.
- (298) Gerding MN, van der Meer JW, Broenink M, Bakker O, Wiersinga WM, Prummel MF. Association of thyrotrophin receptor antibodies with the clinical features of Graves' ophthalmopathy. *Clin Endocrinol (Oxf)*. 2000;52:267-71.
- (299) Jordan NJ, Rinderle C, Ashfield J, Morgenthaler NG, Lazarus J, Ludgate M et al. A luminescent bioassay

for thyroid blocking antibodies. *Clin Endocrinol (Oxf)*. 2001;54:355-64.

- (300) Minich WB, Lenzner C, Bergmann A, Morgenthaler NG. A coated tube assay for the detection of blocking thyrotropin receptor autoantibodies. *J Clin Endocrinol Metab*. 2004;89:352-56.
- (301) Chiovato L, Santini F, Vitti P, Bendinelli G, Pinchera A. Appearance of thyroid stimulating antibody and Graves' disease after radioiodine therapy for toxic nodular goitre. *Clin Endocrinol (Oxf)*. 1994;40:803-6.
- (302) Nygaard B, Faber J, Veje A, Hegedus L, Hansen JM. Appearance of Graves'-like disease after radioiodine therapy for toxic as well as non-toxic multinodular goitre. *Clin Endocrinol (Oxf)*. 1995;43:129-30.
- (303) Nygaard B, Metcalfe RA, Phipps J, Weetman AP, Hegedus L. Graves' disease and thyroid associated ophthalmopathy triggered by ¹³¹I treatment of non-toxic goiter. *J Endocrinol Invest*. 1999;22:481-85.
- (304) Nygaard B, Faber J, Veje A, Hegedus L, Hansen JM. Transition of nodular toxic goiter to autoimmune hyperthyroidism triggered by ¹³¹I therapy. *Thyroid*. 1999;9:477-81.
- (305) Nygaard B, Knudsen JH, Hegedus L, Scient AV, Hansen JE. Thyrotropin receptor antibodies and Graves' disease, a side-effect of ¹³¹I treatment in patients with nontoxic goiter. *J Clin Endocrinol Metab*. 1997;82:2926-30.
- (306) Wallaschowski H, Muller D, Georgi P, Paschke R. Induction of TSH-receptor antibodies in patients with toxic multinodular goitre by radioiodine treatment. *Horm Metab Res*. 2002;34:36-39.
- (307) Dunkelmann S, Wolf R, Koch A, Kittner C, Groth P, Schuemichen C. Incidence of radiation-induced Graves' disease in patients treated with radioiodine for thyroid autonomy before and after introduction of a high-sensitivity TSH receptor antibody assay. *Eur J Nucl Med Mol Imaging*. 2004;31:1428-34.
- (308) Rapoport B, Chazenbalk GD, Jaume JC, McLachlan SM. The thyrotropin (TSH) receptor: interaction with TSH and autoantibodies. *Endocr Rev*. 1998;19:673-716.
- (309) Paschke R, Ludgate M. The thyrotropin receptor in thyroid diseases. *N Engl J Med*. 1997;337:1675-81.
- (310) Kosugi S, Ban T, Akamizu T, Valente W, Kohn LD. Use of thyrotropin receptor (TSHR) mutants to detect stimulating TSHR antibodies in hypothyroid patients with idiopathic myxedema, who have blocking TSHR antibodies. *J Clin Endocrinol Metab*. 1993;77:19-24.
- (311) Nygaard B, Faber J, Veje A, Hegedus L, Hansen JM. Transition of nodular toxic goiter to autoimmune hyperthyroidism triggered by ¹³¹I therapy. *Thyroid*. 1999;9:477-81.
- (312) Nygaard B, Knudsen JH, Hegedus L, Scient AV, Hansen JE. Thyrotropin receptor antibodies and Graves' disease, a side-effect of ¹³¹I treatment in patients with nontoxic goiter. *J Clin Endocrinol Metab*. 1997;82:2926-30.
- (313) Dunkelmann S, Wolf R, Koch A, Kittner C, Groth P, Schuemichen C. Incidence of radiation-induced Graves' disease in patients treated with radioiodine for thyroid autonomy before and after introduction of a high-sensitivity TSH receptor antibody assay. *Eur J Nucl Med Mol Imaging*. 2004;31:1428-34.
- (314) Chiovato L, Fiore E, Vitti P, Rocchi R, Rago T, Dokic D et al. Outcome of thyroid function in Graves' patients treated with radioiodine: role of thyroid-stimulating and thyrotropin-blocking antibodies and of radioiodine-induced thyroid damage. *J Clin Endocrinol Metab*. 1998;83:40-46.

- (315) Michelangeli VP, Poon C, Topliss DJ, Colman PG. Specific effects of radioiodine treatment on TSAb and TBAb levels in patients with Graves' disease. *Thyroid*. 1995;5:171-76.
- (316) Vitti P, Elisei R, Tonacchera M, Chiovato L, Mancusi F, Rago T et al. Detection of thyroid-stimulating antibody using Chinese hamster ovary cells transfected with cloned human thyrotropin receptor. *J Clin Endocrinol Metab*. 1993;76:499-503.
- (317) Wallaschofski H, Paschke R. Detection of thyroid stimulating (TSAB)- and thyrotropin stimulation blocking (TSBAB) antibodies with CHO cell lines expressing different TSH-receptor numbers. *Clin Endocrinol (Oxf)*. 1999;50:365-72.
- (318) Massart C, Gibassier J, Verite F, Fergelot P, Maugendre D. Use of Chinese hamster ovary cell lines transfected with cloned human thyrotropin receptor for the measurement of thyroid-stimulating antibodies: advantages and difficulties. *Clin Chim Acta*. 2000;291:67-81.
- (319) Takasu N, Yamashiro K, Ochi Y, Sato Y, Nagata A, Komiya I et al. TSBAbs (TSH-stimulation blocking antibody) and TSAB (thyroid stimulating antibody) in TSBAbs-positive patients with hypothyroidism and Graves' patients with hyperthyroidism. *Horm Metab Res*. 2001;33:232-37.
- (320) Watson PF, Ajjan RA, Phipps J, Metcalfe R, Weetman AP. A new chemiluminescent assay for the rapid detection of thyroid stimulating antibodies in Graves' disease. *Clin Endocrinol (Oxf)*. 1998;49:577-81.
- (321) Evans C, Morgenthaler NG, Lee S, Llewellyn DH, Clifton-Bligh R, John R et al. Development of a luminescent bioassay for thyroid stimulating antibodies. *J Clin Endocrinol Metab*. 1999;84:374-77.
- (322) Jordan NJ, Rinderle C, Ashfield J, Morgenthaler NG, Lazarus J, Ludgate M et al. A luminescent bioassay for thyroid blocking antibodies. *Clin Endocrinol (Oxf)*. 2001;54:355-64.
- (323) Minich WB, Lenzner C, Bergmann A, Morgenthaler NG. A coated tube assay for the detection of blocking thyrotropin receptor autoantibodies. *J Clin Endocrinol Metab*. 2004;89:352-56.
- (324) Watson PF, Ajjan RA, Phipps J, Metcalfe R, Weetman AP. A new chemiluminescent assay for the rapid detection of thyroid stimulating antibodies in Graves' disease. *Clin Endocrinol (Oxf)*. 1998;49:577-81.
- (325) Evans C, Morgenthaler NG, Lee S, Llewellyn DH, Clifton-Bligh R, John R et al. Development of a luminescent bioassay for thyroid stimulating antibodies. *J Clin Endocrinol Metab*. 1999;84:374-77.
- (326) Hovens, G. C., Buiting, A. M., Karperien, M., Balieux, B. E., van der Pluijm, G., Pereira, A. M., Romijn, J. A., and Smit, J. W. A Bio-Luminescence Assay for Thyrotropin Receptor Antibodies Predicts Serum Thyroid Hormone Levels in Patients with de novo Graves' Disease. *Clin Endocrinol (Oxf)*. 64, 429-435. 2006.
- (327) Wallaschofski H, Muller D, Georgi P, Paschke R. Induction of TSH-receptor antibodies in patients with toxic multinodular goitre by radioiodine treatment. *Horm Metab Res*. 2002;34:36-39.
- (328) Syed AA, Evans C, Ludgate M, Lazarus JH. Early changes in thyroid-stimulating antibody activity following radioiodine therapy. *Med Princ Pract*. 2003;12:266-68.
- (329) Kok SW, Smit JW, de Craen AJ, Goslings BM, Eck-Smit BL, Romijn JA. Clinical outcome after standardized versus dosimetric radioiodine treatment of hyperthyroidism: an equivalence study. *Nucl Med Commun*. 2000;21:1071-78.

- (330) Michelangeli VP, Poon C, Topliss DJ, Colman PG. Specific effects of radioiodine treatment on TSAb and TBAb levels in patients with Graves' disease. *Thyroid*. 1995;5:171-76.
- (331) Yoshida K, Aizawa Y, Kaise N, Fukazawa H, Kiso Y, Sayama N et al. Role of thyroid-stimulating blocking antibody in patients who developed hypothyroidism within one year after ¹³¹I treatment for Graves' disease. *Clin Endocrinol (Oxf)*. 1998;48:17-22.
- (332) Perret J, Ludgate M, Libert F, Gerard C, Dumont JE, Vassart G et al. Stable expression of the human TSH receptor in CHO cells and characterization of differentially expressing clones. *Biochem Biophys Res Commun*. 1990;171:1044-50.
- (333) Soule J, Mayfield R. Graves' disease after ¹³¹I therapy for toxic nodule. *Thyroid*. 2001;11:91-92.
- (334) Dunkelman S, Wolf R, Koch A, Kittner C, Groth P, Schuemichen C. Incidence of radiation-induced Graves' disease in patients treated with radioiodine for thyroid autonomy before and after introduction of a high-sensitivity TSH receptor antibody assay. *Eur J Nucl Med Mol Imaging*. 2004;31:1428-34.
- (335) Nygaard B, Knudsen JH, Hegedus L, Scient AV, Hansen JE. Thyrotropin receptor antibodies and Graves' disease, a side-effect of ¹³¹I treatment in patients with nontoxic goiter. *J Clin Endocrinol Metab*. 1997;82:2926-30.
- (336) Nygaard B, Faber J, Veje A, Hegedus L, Hansen JM. Transition of nodular toxic goiter to autoimmune hyperthyroidism triggered by ¹³¹I therapy. *Thyroid*. 1999;9:477-81.
- (337) Chiovato L, Santini F, Vitti P, Bendinelli G, Pinchera A. Appearance of thyroid stimulating antibody and Graves' disease after radioiodine therapy for toxic nodular goitre. *Clin Endocrinol (Oxf)*. 1994;40:803-6.
- (338) Wallaschofski H, Muller D, Georgi P, Paschke R. Induction of TSH-receptor antibodies in patients with toxic multinodular goitre by radioiodine treatment. *Horm Metab Res*. 2002;34:36-39.
- (339) Syed AA, Evans C, Ludgate M, Lazarus JH. Early changes in thyroid-stimulating antibody activity following radioiodine therapy. *Med Princ Pract*. 2003;12:266-68.
- (340) Wallaschofski H, Muller D, Georgi P, Paschke R. Induction of TSH-receptor antibodies in patients with toxic multinodular goitre by radioiodine treatment. *Horm Metab Res*. 2002;34:36-39.
- (341) Syed AA, Evans C, Ludgate M, Lazarus JH. Early changes in thyroid-stimulating antibody activity following radioiodine therapy. *Med Princ Pract*. 2003;12:266-68.
- (342) Dunkelman S, Wolf R, Koch A, Kittner C, Groth P, Schuemichen C. Incidence of radiation-induced Graves' disease in patients treated with radioiodine for thyroid autonomy before and after introduction of a high-sensitivity TSH receptor antibody assay. *Eur J Nucl Med Mol Imaging*. 2004;31:1428-34.
- (343) Nygaard B, Knudsen JH, Hegedus L, Scient AV, Hansen JE. Thyrotropin receptor antibodies and Graves' disease, a side-effect of ¹³¹I treatment in patients with nontoxic goiter. *J Clin Endocrinol Metab*. 1997;82:2926-30.
- (344) Nygaard B, Faber J, Veje A, Hegedus L, Hansen JM. Transition of nodular toxic goiter to autoimmune hyperthyroidism triggered by ¹³¹I therapy. *Thyroid*. 1999;9:477-81.
- (345) Nygaard B, Metcalfe RA, Phipps J, Weetman AP, Hegedus L. Graves' disease and thyroid associated

- ophthalmopathy triggered by ¹³¹I treatment of non-toxic goiter. *J Endocrinol Invest.* 1999;22:481-85.
- (346) Wilson R, McKillop JH, Chopra M, Thomson JA. The effect of antithyroid drugs on B and T cell activity in vitro. *Clin Endocrinol (Oxf).* 1988;28:389-97.
- (347) Cohen SB, Weetman AP. Antithyroid drugs ameliorate thymectomy-induced experimental autoimmune thyroiditis. *Autoimmunity.* 1988;1:51-58.
- (348) Allen EM, Rajatanavin R, Nogimori T, Cushing G, Ingbar SH, Braverman LE. The effect of methimazole on the development of spontaneous lymphocytic thyroiditis in the diabetes-prone BB/W rat. *Am J Med Sci.* 1986;292:267-71.
- (349) Balazs C, Kiss E, Leovey A, Farid NR. The immunosuppressive effect of methimazole on cell-mediated immunity is mediated by its capacity to inhibit peroxidase and to scavenge free oxygen radicals. *Clin Endocrinol (Oxf).* 1986;25:7-16.
- (350) Akuzawa M, Murakami M, Yamada M, Satoh T, Shimizu H, Mori M. Preserved activation of thyrotropin receptor antibody to stimulate thyroid function despite long-term treatment in euthyroid patients with Graves' disease. *Eur J Endocrinol.* 1998;138:281-85.
- (351) Paschke R, Vogg M, Kristoferitsch R, Aktuna D, Wawschinek O, Eber O et al. Methimazole has no dose-related effect on the intensity of the intrathyroidal autoimmune process in relapsing Graves' disease. *J Clin Endocrinol Metab.* 1995;80:2470-2474.
- (352) Rittmaster RS, Zwicker H, Abbott EC, Douglas R, Givner ML, Gupta MK et al. Effect of methimazole with or without exogenous L-thyroxine on serum concentrations of thyrotropin (TSH) receptor antibodies in patients with Graves' disease. *J Clin Endocrinol Metab.* 1996;81:3283-88.
- (353) Escobar-Morreale HF, Serrano-Gotarredona J, Villar LM, Garcia-Robles R, Gonzalez-Porque P, Sancho JM et al. Methimazole has no dose-related effect on the serum concentrations of soluble class I major histocompatibility complex antigens, soluble interleukin-2 receptor, and beta 2-microglobulin in patients with Graves' disease. *Thyroid.* 1996;6:29-36.
- (354) Chiovato L, Fiore E, Vitti P, Rocchi R, Rago T, Dokic D et al. Outcome of thyroid function in Graves' patients treated with radioiodine: role of thyroid-stimulating and thyrotropin-blocking antibodies and of radioiodine-induced thyroid damage. *J Clin Endocrinol Metab.* 1998;83:40-46.
- (355) Michelangeli VP, Poon C, Topliss DJ, Colman PG. Specific effects of radioiodine treatment on TSAb and TBAb levels in patients with Graves' disease. *Thyroid.* 1995;5:171-76.

